

Dairy consumption and risk of falls in 2 European cohorts of older adults

Short running head: **Dairy consumption and risk of falls in older adults**

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1 **ABSTRACT**

2 **Background & aims:** Some previous evidence have linked dairy products with greater
3 muscle mass, bone mineral density and lower risk of osteoporosis. However, other
4 authors have found a detrimental effect of milk on the risk of hip fracture. The aim of
5 this study was to assess the prospective association between dairy consumption and risk
6 of falls in older adults.

7 **Methods:** We used data from 2 cohorts of community-dwellers aged ≥ 60 y: the Seniors-
8 ENRICA cohort with 2,981 individuals, and the UK Biobank cohort with 8,927
9 participants. In the Seniors-ENRICA, dairy consumption was assessed with a validated
10 diet history in 2008-10, and falls were ascertained up to 2015. In the UK Biobank study,
11 dairy consumption was obtained with 3-5 multiple-pass 24-h food records in 2006-10,
12 and falls were assessed up to 2016.

13 **Results:** A total of 801 individuals in the Seniors-ENRICA and 201 in the UK Biobank
14 experienced ≥ 1 fall. After adjustment for potential confounders, dairy products were not
15 associated with risk of falls in the Seniors-ENRICA [hazard ratio (95% confidence
16 interval) per 1-serving increment in total dairy consumption: 1.02 (0.93-1.11), milk:
17 0.93 (0.85-1.01), yogurt: 1.05 (0.96-1.15), and cheese: 0.96 (0.88-1.05)]. Corresponding
18 figures in the UK Biobank were: total dairy: 1.19 (1.00-1.41), milk: 1.53 (1.13-2.08),
19 yogurt: 1.10 (0.90-1.31), and cheese: 1.02 (0.87-1.22).

20 **Conclusions:** These results suggest a null association between habitual dairy
21 consumption and the risk of falling in older adults. Whether milk consumption may
22 increase the risk of falls, as observed in the UK Biobank cohort, merits further study.

23 **Keywords:** older adults, epidemiology, milk, yogurt, cheese.

24 **INTRODUCTION**

25 Falls in older persons are a major public health problem, as they increase the risk of
26 many adverse health outcomes and death (1). However, studies that evaluate the
27 association between diet and risk of falling are scarce, so only a few of them have
28 examined the role of nutrients, such as calcium (2), vitamin D (2, 3) and proteins (4),
29 diet patterns (5) and individual foods (6, 7).

30 Dairy products are an important source of energy, proteins, vitamins and minerals,
31 including calcium, potassium and vitamin D, which are important nutrients for bone and
32 muscle health (8). Previous studies have linked dairy products with a lower risk of
33 frailty (9), cardiovascular disease (10, 11) and type 2 diabetes (12, 13), which are also
34 predictors of falls in older people. Furthermore, in a cross-sectional study, a higher
35 dairy consumption was associated with lower prevalence of falls, greater lean body
36 mass and better physical performance in women (14). Likewise, dairy products have
37 been associated with greater muscle mass (14, 15) and greater bone mineral density
38 (16), as well as with lower risk of osteoporosis and functional disability (17-20). These
39 results might suggest that dairy intake could prevent falls through the improvement of
40 the musculoskeletal system. On the other hand, some authors have hypothesized a
41 detrimental effect of milk on the risk of hip fracture (19,21) because of its content of D-
42 galactose; however, this hypothesis has not been confirmed in a recent study (22).
43 Lastly, since each type of dairy product provides different amounts of nutrients and
44 bioactive compounds, they might also have different effects on health (10).

45 The aim of this study was to evaluate the prospective association between dairy
46 products consumption, specifically, total dairy, milk, yogurt and cheese, and risk of
47 falling. We assessed this association in 2 cohorts of community-dwelling older adults

48 from Spain and the United Kingdom (UK), to better understand the underlying role of
49 population characteristics and to improve the external validity of the results.

50 MATERIAL AND METHODS

51 Study design and participants

52 *The Seniors-ENRICA study*

53 The ENRICA study (Study on Nutrition and Cardiovascular Risk in Spain) was
54 established in 2008-2010 with 12,948 individuals representative of the non-
55 institutionalized population of Spain aged ≥ 18 y (23). Of them, 3,289 participants aged
56 ≥ 60 y comprised the Seniors-ENRICA cohort. Information about socio-demographic
57 characteristics, lifestyle, health status and morbidity were collected at baseline through a
58 telephone interview. Moreover, two home visits were performed to assess food
59 consumption, conduct a physical examination and obtain blood and urine samples. Two
60 waves of data collection were subsequently performed in 2012 and 2015 to update the
61 information of the cohort. The Clinical Research Ethics Committee of ‘La Paz’
62 University Hospital in Madrid approved the study protocol, and the study participants
63 gave their informed written consent.

64 *The UK Biobank study*

65 The UK Biobank cohort has recruited more than half a million individuals between 40-
66 69 years (81,725 were ≥ 60 y) in the UK during the period 2006-2010 (24). At baseline,
67 participants completed a touchscreen questionnaire, conducted a face-to-face interview,
68 underwent a physical exam, and provided biological samples. Two waves of data
69 collection (in 2012-2013 and 2014-2016) have been performed in a subsample of
70 participants to update the information of the cohort. The UK Biobank study was
71 conducted under generic ethical approval from the NHS National Research Ethics
72 Service (ref 11/NW/0382, 17 June 2011).

73 Study variables

74 *Dairy products and other dietary variables*

75 In the Seniors-ENRICA, dietary information was collected through a validated
76 electronic diet history developed from the one used in the European Prospective
77 Investigation into Cancer and Nutrition cohort study in Spain (25). This method of diet
78 assessment included 880 different foods and allows for taking different portion sizes
79 and cooking methods into account, as well as weekly and seasonal variations in food
80 consumption. The dairy products recorded were: whole milk, part-skim and skim milk,
81 whole- and low-fat yogurt, and cheese. We transformed the quantity consumed (ml or g
82 per day) into serving/day, by dividing the total amount of each food by the standard
83 serving size (200 ml of milk, 125 g of yogurt and 40 g of cheese) (9, 22). In the
84 validation study we found a moderate to good correlation between consumption of dairy
85 products estimated from the diet history and the mean of seven 24-hour recalls during
86 one year ($r=0.68$). Total energy intake and calcium, protein, and saturated fat were
87 estimated using standard food composition tables (25) and were adjusted for energy
88 intake using the residual method (26). Adherence to the Mediterranean diet was
89 assessed with the Mediterranean Diet Adherence Screener (MEDAS) (27). This score
90 includes 14 items on food consumption and food intake habits characteristic of the
91 traditional Mediterranean diet in Spain. The MEDAS score ranges from 0 to 14, with a
92 higher score indicating greater adherence (**Supplemental table 1**).

93 In the UK Biobank, food consumption was assessed through five web-based 24-h
94 recalls (Oxford WebQ) (28), which included more than 200 foods frequently consumed
95 in the UK and allowed for considering seasonal variations. For the present analyses, we
96 selected the participants who completed at least three 24-h recalls. Dairy products
97 recorded were: whole milk, part-skim and skim milk, powdered milk, full- and low-fat
98 yogurt, and cheese. The reported consumptions for each type of dairy were: none, 0.5, 1,

99 2, 3, 4, 5 and ≥ 6 servings/day. The mean of consumption in servings/day was calculated
100 among the available 24-h recalls for each participant. Nutrient intakes were estimated
101 with standard foods composition tables in the UK (29) and adjusted for energy by the
102 residual method. Finally, adherence to the Mediterranean diet as per the MEDAS score
103 was also assessed in this population as an indicator of diet quality. Two items in the
104 score were excluded for not having this information in the cohort: the item on the
105 amount of olive oil consumed, and the item related to “sofrito” (a type of cooking that
106 uses a sauce made with fried tomato and vegetables). Thus, in the UK Biobank the
107 MEDAS score ranged from 0 to 12 (**Supplemental table 1**).

108 *Falls*

109 In the Seniors-ENRICA study, self-reported incident falls were assessed by asking the
110 participants at the follow-up waves (2012 and 2015): “How many times have you fallen
111 down since the last interview?” We categorized the answers into: having no falls, and
112 ≥ 1 fall. In addition, participants reported if because of the fall, they had suffered a
113 fracture. In the UK Biobank study, information about self-reported falls was obtained
114 from the touchscreen questionnaire at baseline and the subsequent two follow-up waves
115 by asking the participants: “In the last year have you had any falls?” The possible
116 answers were “no falls”, “only one fall”, and “more than one fall”. This variable was
117 also categorized into: having no falls, and ≥ 1 fall.

118 *Mortality*

119 In the Seniors-ENRICA study, we performed a computerized search of the National
120 Death Index to evaluate all-cause mortality (30). This information was available for
121 99.9% of the cohort. In the UK Biobank study, death certificates from the National

122 Health Service (NHS) Information Centre (England and Wales) and the NHS Central
123 Register Scotland (Scotland) provided information about vital status (31).

124 *Other variables*

125 In the Seniors-ENRICA, data on age, sex, educational level (\leq primary, secondary,
126 university), smoking status (never, former, current smoker) and alcohol intake
127 (abstainer: <0.1 g/d, moderate drinker: 0.1-39 g/d in men and 0.1-23 g/d in women, and
128 heavy drinker: ≥ 40 g/d in men and ≥ 24 g/d in women) (32) were collected at baseline.
129 Weight and height were measured in each participant under standardized conditions.
130 Body mass index (BMI) was calculated as weight (kg) divided by the squared height
131 (m). Physical activity during leisure time (metabolic equivalent tasks-h/week) was
132 evaluated with the EPIC-cohort questionnaire, validated in Spain (33). Self-reported
133 sleep duration (h/d) was also recorded. Blood pressure (BP) was measured with a
134 validated sphygmomanometer using standardized procedures, and hypertension was
135 defined as systolic BP ≥ 140 mm Hg, diastolic BP ≥ 90 mm Hg, or being under
136 hypertensive drug treatment. Twelve-hour-fasting serum glucose was measured, and
137 type 2 diabetes was defined as glucose ≥ 126 mg/dl or being on oral antidiabetic drugs
138 or insulin. Participants were considered frail when they met three or more of the
139 following five self-reported criteria proposed by Morley et al. (34): fatigue, reduced
140 resistance, reduced aerobic capacity, having several illnesses and a significant weight
141 loss during the previous. Participants also reported if they had been diagnosed with
142 osteo-muscular disease (osteo-arthritis or arthritis) by a physician. Finally, use of
143 sleeping pills was assessed.

144 In 2013, several other measurements were performed to assess sarcopenia in this
145 population. Percentage of body fat (%BF) was measured by bioelectrical
146 impedanciometry and skeletal muscle mass (SMM) with the equation developed by

147 Janssen (35). Skeletal muscle mass index (SMI) was obtained by dividing SMM by
148 height squared. Muscle strength was approached through grip strength, considering the
149 highest value of two consecutive measures on the dominant hand using a Jamar
150 dynamometer. Physical performance was measured using the Short Physical
151 Performance Battery (SPPB), following the protocols of the National Institute on Aging
152 (36).

153 In the UK Biobank study, most of the variables were collected and categorized as in
154 Seniors-ENRICA study. However, physical activity was ascertained with questions
155 from the short International Physical Activity Questionnaire (IPAQ) (37) and the
156 presence of diabetes, hypertension or osteo-muscular disease was self-reported by the
157 participants.

158 **Statistical analyses**

159 In the Seniors-ENRICA, we excluded 308 participants: 4 with missing data on dairy
160 consumption, 13 with implausible values of energy intake (outside the range of 800-
161 5,000 kcal/d for men and 500-4,000 kcal/d for women), and 291 who were frail or
162 lacked data on this variable at baseline (because frailty is a strong predictor of falls) (38)

163 In the UK Biobank, among those ≥ 60 y, we excluded 72,798 participants: 69,476 with
164 < 3 web-based 24-h diet recalls, 137 with missing data on dairy, 939 with implausible
165 high or low energy intake, and 2,246 who reported falls or lacked data on falls at
166 baseline. This resulted in an analytical sample of 2,981 individuals in the Seniors-
167 ENRICA and 8,927 in the UK Biobank study (**Supplemental figure 1**).

168 We categorized dairy products consumption into tertiles of servings/day, except for
169 milk in the UK Biobank study, which was categorized in two groups (yes vs no
170 consumption), due to the very low consumption reported. We used the lowest tertile as

171 reference for the analyses. Person-years of follow-up were calculated from the date of
172 the baseline questionnaire until the date of the outcome (falling), death, loss to follow-
173 up, or the end of the study, whichever came first. To assess the association between
174 categories of dairy consumption and the incidence of falls, we used Cox regression
175 models to estimate hazard ratios (HR) with 95% confidence intervals (CI) for each
176 category of dairy consumption. We built several models: the first one adjusted for age
177 and sex; the second one additionally adjusted for other potential confounders, including
178 education, smoking, alcohol intake, BMI, physical activity, sleep duration, energy
179 intake, MEDAS score, hypertension, diabetes and use of sleeping pills; and a third
180 model further adjusted for osteo-muscular disease, to explore its role in the studied
181 relationship. Moreover, when we assessed the specific association for milk, yogurt, and
182 cheese, we built a fourth model additionally adjusted for the other types of dairy
183 products. To investigate the linear dose-response relation, we modeled the categories of
184 dairy products consumption as continuous variables. Likewise, we calculated the risk of
185 falls associated with a 1-serving/d increment for the different types of dairy. We also
186 performed some sensitivity analyses by excluding participants with cardiovascular
187 disease, hip fracture and those who were heavy alcohol drinkers at baseline since they
188 had higher risk of falling than other population subgroups. This analysis was not
189 possible to be done for milk consumption and risk of falling in UK Biobank due to the
190 low number of cases among milk consumers. We also adjusted our main analyses by
191 markers of sarcopenia status (percentage of lean mass, handgrip strength and gait speed)
192 to explore the implication of sarcopenia in the studied association in the Seniors-
193 ENRICA cohort, which had these measurements done. Moreover, we analyzed the
194 relationship between the different dairy products and the risk of falls with fracture in the
195 Seniors-ENRICA study. We did not use data on falls with fractures in the UK Biobank

196 cohort due to the very small number found (n= 19). Finally, in order to account for
197 changes in dairy consumption during follow-up, we estimated the cumulative
198 consumption by using dietary information available in Seniors-ENRICA at baseline and
199 in the first follow-up wave, 2 years later (in the UK Biobank study, repeated diet
200 measurement was not available).

201 The main analyses were stratified by sex, hypertension, type 2 diabetes, osteo-muscular
202 disease, sleep duration, protein intake and physical activity; also, likelihood-ratio tests
203 comparing models with and without interactions terms were used to assess if results
204 varied across strata. These analyses were performed only in the Seniors-ENRICA since
205 in the UK Biobank the number of falls was too low.

206 Finally, to test the non-linear trends of risk of falls according to total dairy products
207 consumption, we used restricted cubic-splines with three knots. We conducted the
208 analyses separately in each cohort using Stata (version 15.0; Stata Corp., College
209 Station).

210 **RESULTS**

211 Characteristics of the participants in each cohort according to tertiles of total dairy
212 consumption are presented in **Table 1**. In the Seniors-ENRICA, participants in the
213 highest vs. lowest tertile were less frequently men and less often current smokers or
214 heavy drinkers. Also, they had a higher BMI, a higher intake of energy, calcium,
215 protein, and saturated fat, and a lower adherence to the Mediterranean diet. The
216 distribution of dairy consumption was similar in the UK Biobank, with the exception
217 that those with higher consumption also had higher education and adherence to the
218 Mediterranean diet.

219 The intake of both total dairy and each type of dairy products was higher in Spain than
220 in the UK, except for low fat yogurt (**Table 2**). Average total dairy intake was 2.28
221 (standard deviation: 1.36) servings/d among participants in the Seniors-ENRICA, and
222 0.92 (0.64) servings/d in those in the UK Biobank. Milk accounted for a large part of
223 this consumption in Spain (45%) but not in UK (19%). In addition, part-skim milk was
224 the most consumed type of milk in both cohorts (40% and 67%, respectively).

225 In the Seniors-ENRICA study, over 7.2 years of follow-up (median follow-up, 5.4 y),
226 801 individuals reported ≥ 1 falls (**Table 3**). No association was found between the
227 consumption of total dairy or any type of dairy products and the risk of falls, neither in
228 the crude- nor in the fully-adjusted analyses [fully-adjusted hazard ratio (95%
229 confidence interval) per 1-serving/d increment in total dairy consumption: 1.02 (0.93-
230 1.11), milk: 0.93 (0.85-1.01), yogurt: 1.05 (0.96-1.15), and cheese: 0.96 (0.88- 1.05)].
231 Neither we found any difference in this association by categories of sex, morbidity,
232 sleep duration, protein intake and physical activity level (p for interaction >0.05 in all
233 cases) (**Supplemental table 2**). Moreover, we did not find any association between

234 dairy products and the risk of falls with fracture (**Supplemental table 3**). Also, when
235 cumulative dairy consumption was used as exposure, we still observed a null
236 association with falls risk (**Supplemental table 4**). Similar results were also obtained
237 when we excluded participants with cardiovascular disease, hip fracture and those who
238 were heavy alcohol drinkers at baseline, or when we adjusted our analyses by markers
239 of sarcopenia status (**Supplemental tables 5 y 6**).

240 Over 10.2 years of follow-up in the UK Biobank study (median follow-up, 3.2 y), 201
241 people reported ≥ 1 falls (**Table 4**). Participants in the highest tertile of total dairy
242 consumption showed a higher risk of falls in the crude model [HR: 1.51 (95% CI: 1.07,
243 2.13), p-trend 0.02], compared to those of the lowest tertile. However, in the fully-
244 adjusted model, this association became non-significant [1.41, (0.99, 2.01) p-trend
245 0.06]. As regards milk consumption, participants who consumed any amount had a
246 higher risk of falls [fully-adjusted HR 1.53 (1.13, 2.08)] compared to non-consumers.
247 We did not find any statistically significant association between the consumption of
248 yogurt or cheese and the risk of falls by comparing the highest vs. the lowest tertile.
249 Also, when we excluded participants with cardiovascular disease, hip fracture and those
250 who were heavy alcohol drinkers at baseline, we found a null association between the
251 consumption of total dairy and the risk of falls; of note, the positive association between
252 milk consumption and the risk of falls found in the total population disappeared in this
253 subsample (**Supplemental table 7**).

254 Finally, when analyzing the relation between total dairy and the risk of falls using non-
255 parametric techniques, some differences between the two cohorts were observed.
256 Whereas in the Seniors-ENRICA cohort there was no suggestion of a trend, in the UK
257 Biobank, a statistically significant increased risk of falls in those participants who
258 consumed >1.5 servings/day was observed (**Supplemental figure 2**).

259 **DISCUSSION**

260 In this study using data from two European cohorts, we generally did not find an
261 association between the different types of dairy products and the risk of falls,
262 independently of population characteristics or among subgroups of participants. There
263 was a suggestion of an increased risk of falls among those who consumed milk in the
264 UK Biobank; however, this result has to be confirmed in future studies.

265 In the scientific literature, we have only identified one study that examined the
266 association between the consumption of dairy products and the risk of falling (14). In
267 this cross-sectional study, no effect of dairy on falls was observed (14). However,
268 authors found a protective association when results were adjusted for non-dairy
269 proteins. Moreover, in a recent systematic review and meta-analysis including 18
270 observational studies, Bian et al. (21) found that individuals with higher consumption of
271 yogurt and cheese had a lower risk of hip fracture, a serious consequence of falls.
272 Nevertheless, as in our results from the UK Biobank cohort, the authors found a
273 nonlinear positive dose-response association between milk intake and the risk of hip
274 fracture across a range of milk consumption from 0 to 600 g/day (21). Therefore, our
275 results in the UK Biobank cohort might be driven by those with very high milk intake,
276 although we could not test this hypothesis due to the low number of study participants
277 with such a high consumption.

278 On the other hand, in the largest study examining the association between milk intake
279 and the risk of mortality and fractures, Michaëlsson et al. (19) found an increased risk of
280 fractures among women who consumed ≥ 3 glasses/d of milk. Among the possible
281 explanations for this finding was the D-galactose present in milk, but not in fermented
282 dairy products. In animal studies, D-galactose has been associated with chronic
283 inflammation, increased oxidative stress and accelerated aging (39-41), which are also

284 factors that might influence falls risk (42,43). Moreover, milk consumption has been
285 positively associated with biomarkers of inflammation and oxidative stress in men and
286 women (19). However, an alternative explanation for this positive association could be
287 the nutritional quality of the background diet. For example, older adults with dentition
288 problems often have diets with poorer nutritional status and inadequate protein intake
289 (44), so for these people dairy could be an important source of protein. In this case, the
290 results found in the UK Biobank cohort might be explained by reverse causation. This
291 explanation is reinforced by the fact that the sensitivity analyses done after eliminating
292 those participants who had a high baseline risk of falls (participants with CVD, previous
293 hip fracture and heavy alcohol drinkers), showed no association. In addition, Ding et al.
294 (45) suggest that the health effect of replacing dairy products depends on the nature of
295 the food for which it is replaced. In our study, we adjusted the analyses for the overall
296 quality of the diet, but we did not have information about changes in the consumption of
297 dairy products among these participants to examine its impact on health.

298 The divergences in the results found in both cohorts may also be driven for the
299 characteristics of the participants. In the Seniors-ENRICA, mean age was higher and the
300 prevalence of chronic conditions was more elevated than in the UK Biobank study,
301 which may explain the larger number of incident falls. In addition, the UK Biobank
302 study is not a representative sample of the UK population, so the participants in this
303 study could be considered healthier across several health parameters. In the same way,
304 we can also speculate that social and environmental conditions may play a role in the
305 studied association by modulating both, the likelihood of falling because of inadequate
306 urban conditions for the older people and the social support available to avoid situations
307 of high risk in this population.

308 One of the strengths of this study was the use of two prospective cohorts from countries
309 with different amount and proportion of consumption of dairy products, as well as
310 different socioeconomic characteristics and lifestyle. Additional strengths were the long
311 follow-up period and the large number of potential confounders that were accounted for
312 in the analyses. Specifically, the adjustment for a diet quality score allowed examining
313 the effect of dairy independently from the diet pattern where this food group was
314 consumed, since it has been suggested that dairy products are nutrient-dense foods that
315 may simply reflect a better diet, as in the UK Biobank (46).

316 This study also has some limitations. Measurement of dairy consumption relied only on
317 the baseline measurements since dietary information in the UK Biobank study has not
318 been updated during follow-up; therefore, possible changes that may have occurred in
319 participants' diets were not taken into account. However, sensitivity analyses performed
320 in the Seniors-ENRICA cohort showed that results using cumulative consumption of
321 dairy products were quite similar than those performed with the baseline measure of
322 diet. Also the relatively low consumption of skim-fat milk and yogurt did not allow for
323 additional analyses for these categories of dairy products; however, current evidence on
324 high-fat vs. low-fat dairy does not conclusively suggest that any of these groups has a
325 beneficial effect on health compared to the other group (10). The measurement of falls
326 was self-reported and some events could have been missed because of the recall bias.
327 Since dietary information was collected when participants already had 60 years old, this
328 null association may not reflect the effect of dairy consumption throughout the life on
329 the development of long-term diseases with an impact on the risk of falls, such as
330 osteoporosis. Finally, as in any observational study, some residual confounding may
331 persist despite relatively exhaustive adjustment.

332 **CONCLUSIONS**

333 In conclusion, our results suggest that habitual dairy consumption in the advanced age is
334 not associated with the risk of falling in older adults and therefore, its consumption does
335 not pose a risk for falls in this population. Whether milk consumption might increase
336 the risk of falls, as observed in the UK Biobank cohort, merits further study.

337 **ACKNOWLEDGEMENTS**

338 This research has been conducted with the use of the UK Biobank Resource under
339 application number 29009. UK Biobank is an open access resource. Bona fide
340 researchers can apply to use the UK Biobank data by registering and applying
341 (<http://www.ukbiobank.ac.uk/register-apply/>).

342 **STATEMENT OF AUTOSHIP**

343 The authors' contributions were as follows: MMF, EAS and ELG: designed the
344 research; MMF: performed the statistical analyses; all authors: contributed to
345 interpretation of the results; MMF, EAS and ELG: drafted the manuscript; ELG:
346 supervised the conduct of research and had primary responsibility for final content; and
347 all authors reviewed the manuscript for important intellectual content, and read and
348 approved the final manuscript.

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355 **CONFLICT OF INTEREST STATEMENT**

356 The authors declare that they have no competing interests.

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REFERENCES

1. Masud T, Morris RO. Epidemiology of falls. *Age Ageing* 2001;30(4):3-7.
2. López-Torres Hidalgo J, Grupo ANVITAD. Effect of calcium and vitamin D in the reduction of falls in the elderly: a randomized trial versus placebo. *Med Clin (Barc)* 2014;142(3):95-102.
3. Ringe JD. The effect of Vitamin D on falls and fractures. *Scand J Clin Lab Invest Suppl* 2012;243:73-8.
4. Zoltick ES, Sahni S, McLean RR, Quach L, Casey VA, Hannan MT. Dietary protein intake and subsequent falls in older men and women: the Framingham Study. *J Nutr Health Aging* 2011;15(2):147-52.
5. Ballesteros JM, Struijk EA, Rodriguez-Artalejo F, Lopez-Garcia E. Mediterranean diet and risk of falling in community-dwelling older adults. *Clin Nutr* 2019; doi:10.1016/j.clnu.2019.02.004.
6. Machado-Fragua MD, Struijk EA, Ballesteros JM, Ortolá R, Rodriguez-Artalejo F, Lopez-Garcia E. Habitual coffee consumption and risk of falls in 2 European cohorts of older adults. *Am J Clin Nutr* 2019;109(5):1431-38.
7. Ortolá R, Garcia-Esquinas E, Galan I, Guallar-Castillon P, Lopez-Garcia E, Banegas JR, Rodriguez-Artalejo F. Patterns of alcohol consumption and risk of falls in older adults: a prospective cohort study. *Osteoporos Int* 2017;28(11):3143-52.
8. Wijesinha-Bettoni R, Burlingame B. Milk and dairy product composition. In: Muehlhoff E, Bennett A, McMahon D, editors. *Milk and dairy products in human nutrition*. Roma: Food and Agriculture Organization of the United Nations (FAO); 2013. p.41-90.

9. Lana A, Rodriguez-Artalejo F, Lopez-Garcia E. Dairy consumption and risk of frailty in older adults: a prospective cohort study. *J Am Geriatr Soc* 2015;63(9):1852-60.
10. Yu E, Hu FB. Dairy products, dairy fatty acids, and the prevention of cardiometabolic disease: a review of recent evidence. *Curr Atheroscler Rep* 2018;20(5):24.
11. Dehghan M, Mente A, Rangarajan S, Sheridan P, Mohan V, Iqbal R, Gupta R, Lear S, Wentzel-Viljoen E, Avezum A, et al. Association of dairy intake with cardiovascular disease and mortality in 21 countries from five continents (PURE): a prospective cohort study. *Lancet* 2018;392(10161):2288-97.
12. Gijssbers L, Ding EL, Malik VS, de Goede J, Geleijnse JM, Soedamah-Muthu SS. Consumption of dairy foods and diabetes incidence: a dose-response meta-analysis of observational studies. *Am J Clin Nutr* 2016;103(4):1111-24.
13. Vissers LET, Sluijs I, van der Schouw YT, Forouhi NG, Imamura F, Burgess S, Barricarte A, Boeing H, Bonet C, Chirilaque MD, Fagherazzi G, Franks PW, Freisling H, Gunter MJ, Quirós JR, Ibsen DB, Kaaks R, Key T, Khaw KT, Kühn T, Mokoroa O, Nilsson PM, Overvad K, Pala V, Palli D, Panico S, Sacerdote C, Spijkerman AMW, Tjønneland A, Tumino R, Rodriguez-Barranco M, Rolandsson O, Riboli E, Sharp SJ, Langenberg C, Wareham NJ. Dairy product intake and risk of type 2 diabetes in EPIC-interact: a mendelian randomization study. *Diabetes Care* 2019;42(4):568-75.
14. Radavelli-Bagatini S, Zhu K, Lewis JR, Dhaliwal SS, Prince RL. Association of dairy intake with body composition and physical function in older community-dwelling women. *J Acad Nutr Diet* 2013;113(12):1669-74.

15. Radavelli-Bagatini S, Zhu K, Lewis JR, Prince RL. Dairy food intake, peripheral bone structure, and muscle mass in elderly ambulatory women. *J Bone Miner Res* 2014;29(7):1691-700.
16. Mangano KM, Noel SE, Sahni S, Tucker KL. Higher dairy intakes are associated with higher bone mineral density among adults with sufficient vitamin D status: results from the Boston Puerto Rican Osteoporosis Study. *J Nutr* 2019;149(1):139-48.
17. Hong H, Kim EK, Lee JS. Effects of calcium intake, milk and dairy product intake, and blood vitamin D level on osteoporosis risk in Korean adults: analysis of the 2008 and 2009 Korea National Health and Nutrition Examination Survey. *Nutr Res Pract* 2013;7(5):409-17.
18. Park SJ, Jung JH, Kim MS, Lee HJ. High dairy products intake reduces osteoporosis risk in Korean postmenopausal women: A 4 year follow-up study. *Nutr Res Pract* 2018;12(5):436-42.
19. Michaëlsson K, Wolk A, Langenskiöld D, Basu S, Warensjö Lemming E, Melhus H, Byberg L. Milk intake and risk of mortality and fractures in women and men: cohort studies. *BMJ* 2014;349:g6015.
20. Yoshida D, Ohara T, Hata J, Shibata M, Hirakawa Y, Honda T, Uchida K, Takasugi S, Kitazono T, Kiyohara Y, Ninomiya T. Dairy consumption and risk of functional disability in an elderly Japanese population: the Hisayama Study. *Am J Clin Nutr* 2019;109(6):1664-71.
21. Bian S, Hu J, Zhang K, Wang Y, Yu M, Ma J. Dairy product consumption and risk of hip fracture: a systematic review and meta-analysis. *BMC Public Health* 2018;18(1):165.

22. Feskanich D, Meyer HE, Fung TT, Bischoff-Ferrari HA, Willett WC. Milk and other dairy foods and risk of hip fracture in men and women. *Osteoporos Int* 2018;29(2):385-96.
23. Rodriguez-Artalejo F, Graciani A, Guallar-Castillón P, León-Muñoz LM, Zuluaga MC, López-García E, Gutiérrez-Fisac JL, Taboada JM, Aguilera MT, Regidor E, et al. Rationale and methods of the study on nutrition and cardiovascular risk in Spain (ENRICA). *Rev Esp Cardiol* 2011;64:876-82.
24. Sudlow C, Gallacher J, Allen N, Beral V, Burton P, Danesh J, Downey P, Elliott P, Green J, Landray M, et al. UK Biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. *PLoS Med* 2015;12 (3):e1001779.
25. Guallar-Castillón P, Sagardui-Villamor J, Balboa-Castillo T, Sala-Vila A, Ariza Astolfi MJ, Sarrión Pelous MD, León-Muñoz LM, Graciani A, Laclaustra M, Benito C, et al. Validity and reproducibility of a Spanish dietary history. *PLoS One* 2014;9:e86074.
26. Willett WC. *Nutritional Epidemiology*. Third Edition. New York, NY: Oxford University Press, 2012.
27. Schröder H, Fitó M, Estruch R, Martínez-González MA, Corella D, Salas-Salvadó J, Lamuela-Raventós R, Ros E, Salaverria I, Fiol M, Lapetra J, Vinyoles E, Gomez-Gracia E, Lahoz C, Serra-Majem L, Pintó X, Ruiz-Gutierrez V, Covas MI. A short screener is valid for assessing Mediterranean diet adherence among older Spanish men and women. *J Nutr* 2011;141(6):1140-5.
28. Galante J, Adamska L, Young A, Young H, Littlejohns TJ, Gallacher J, Allen N. The acceptability of repeat Internet-based hybrid diet assessment of previous 24-

- h dietary intake: administration of the Oxford WebQ in UK Biobank. *Br J Nutr* 2016;115(4):681-6.
29. Holland B, Welch A, Unwin I, Buss DH, Paul AA, Southgate DAT (1991). McCance and Widdowson's. *The Composition of Foods*. 5th edition. Cambridge: Royal Society of Chemistry.
30. Martínez-Gómez D, Guallar-Castillón P, León-Muñoz LM, López-García E, Rodríguez-Artalejo F. Combined impact of traditional and non-traditional health behaviors on mortality: a national prospective cohort study in Spanish older adults. *BMC Med* 2013;11:47.
31. Wade KH, Carlsake D, Sattar N, Davey Smith G, Timpson NJ. BMI and Mortality in UK Biobank: Revised Estimates Using Mendelian Randomization. *Obesity (Silver Spring)* 2018;26(11):1796-1806.
32. Ortolá R, García-Esquinas E, Galán I, Guallar-Castillón P, López-García E, Banegas JR, Rodríguez-Artalejo F. Patterns of alcohol consumption and risk of falls in older adults: a prospective cohort study. *Osteoporos Int* 2017;28(11):3143-52.
33. Pols MA, Peeters PH, Ocke MC, Slimani N, Bueno-de-Mesquita HB, Collette HJ. Estimation of reproducibility and relative validity of the questions included in the EPIC Physical Activity Questionnaire. *Int J Epidemiol* 1997;26:S181-9.
34. Morley JE, Malmstrom TK, Miller DK. A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. *J Nutr Health Aging* 2012;16:601-608.
35. Janssen I, Heymsfield SB, Baumgartner RN, Ross R. Estimation of skeletal muscle mass by bioelectrical impedance analysis. *J Appl Physiol* (1985). 2000;89(2):465-71.

36. Guralnik JM, Ferrucci L, Pieper CF, Leveille SG, Markides KS, Ostir GV, et al. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. *J Gerontol A Biol Sci Med Sci.* 2000;55:M221-231.
37. Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, Pratt M, Ekelund U, Yngve A, Sallis JF, et al. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc* 2003;35(8):1381-95.
38. Kojima G. Frailty as a predictor of future falls among community-dwelling older people: a systematic review and meta-analysis. *J Am Med Dir Assoc* 2015;16(12):1027-33.
39. Song X, Bao M, Li D, Li YM. Advanced glycation in D-galactose induced mouse aging model. *Mech Ageing Dev* 1999;108:239-51.
40. Cui X, Zuo P, Zhang Q, Li X, Hu Y, Long J. Chronic systemic D-galactose exposure induces memory loss, neurodegeneration, and oxidative damage in mice: protective effects of R-alpha-lipoic acid. *J Neurosci Res* 2006;83:1584-90.
41. Hao L, Huang H, Gao J, Marshall C, Chen Y, Xiao M. the influence of gender, age and treatment time on brain oxidative stress and memory impairment induced by d-galactose in mice. *Neurosci Lett* 2014;571C:45-9.
42. Britton GB, O'Bryant SE, Johnson LA, Hall JR, Villareal AE, Oviedo DC, Lao ARP, Carreira MB, For The Panama Aging Research Initiative SG. Inflammatory biomarkers, depressive symptoms and falls among the elderly in Panama. *Curr Aging Sci* 2019;11(4):236-41.

43. Verghese J, Ayers E. Biology of falls: preliminary cohort study suggesting a possible role for oxidative stress. *J Am Geriatr Soc* 2017;65(6):1306-9.
44. Saarela RK, Lindroos E, Soini H, Hiltunen K, Muurinen S, Suominen MH, Pitkälä KH. Dentition, nutritional status and adequacy of dietary intake among older residents in assisted living facilities. *Gerontology* 2016;33(2):225-32.
45. Ding M, Li J, Qi L, Ellervik C, Zhang X, Manson JE, Stampfer M, Chavarro JE, Rexrode KM, Kraft P, et al. Associations of dairy intake with risk of mortality in women and men: three prospective cohort studies. *BMJ* 2019;367:I6204.
46. van Staveren WA, Steijns JM, de Groot LC. Dairy products as essential contributors of (micro-) nutrients in reference food patterns: an outline for elderly people. *J Am Coll Nutr* 2008;27(6):747S-54S.

Table 1. Baseline characteristics of participants across tertiles of dairy consumption in the Seniors-ENRICA and in the UK Biobank study.

	Seniors-ENRICA study (N=2,981)			UK Biobank study (N=8,927)		
	Total dairy consumption, servings/d ^b			Total dairy consumption, servings/d ^c		
	Tertile 1 (0-1.62)	Tertile 2 (1.63-2.62)	Tertile 3 (2.63-12.0)	Tertile 1 (0-0.60)	Tertile 2 (0.61-1.12)	Tertile 3 (1.13-6.50)
Participants, n	994	994	993	3224	2728	2975
Age, y	68.7 (6.5)	69.1 (6.5)	69.4 (6.7)	63.7 (2.7)	63.7 (2.7)	63.7 (2.5)
Men, %	49.7	45.5	43.7*	58.6	50.0	49.9**
Educational level, %						
≤ Primary	55.9	58.5	57.2	11.7	9.5	7.1
Secondary	23.9	22.6	24.4	30.6	28.8	28.3
University	20.2	18.9	18.4	57.7	61.7	64.6 ⁵
Current smoker, %	14.7	13.1	8.2 ⁵	5.9	5.2	3.8 ⁵
Heavy drinker ^a , %	10.5	7.6	5.9 ⁴	19.1	16.6	15.7 ⁴
BMI, kg/m ²	28.4 (4.4)	28.4 (4.3)	28.9 (4.6)*	26.7 (4.2)	26.4 (3.9)	26.7 (4.4)
Physical activity, METs-h/wk	22.0 (15.8)	21.7 (14.8)	21.1 (15.0)	43.3 (50.2)	42.6 (50.7)	43.7 (45.5)
Sleep duration, h/d	6.9 (1.4)	6.9 (1.4)	6.8 (1.4)	7.3 (1.0)	7.3 (0.9)	7.3 (0.9)
Energy intake, kcal/d	1900 (562)	2049 (673)	2109 (749)**	2043 (479)	2088 (464)	2206 (499)**
Intake of calcium, mg/dl	615 (167)	843 (158)	1182 (342)**	848 (261)	970 (245)	1141 (292)**
Intake of protein, g/d	84.1 (25.0)	90.2 (24.7)	98.6 (28.0)**	78.4 (18.2)	81.4 (17.8)	87.9 (19.6)**
Intake of saturated fat, g/d	20.6 (8.9)	24.1 (9.9)	28.4 (12.9)**	28.6 (10.1)	29.4 (10.2)	31.8 (10.8)*
MEDAS score	7.0 (1.7)	6.7 (1.9)	6.8 (1.7)*	4.3 (1.5)	4.4 (1.6)	4.6 (1.6)**
Diagnosed diseases, %						
Hypertension	63.2	64.6	65.3	35.3	33.8	33.2
Diabetes	17.0	16.4	15.7	5.2	4.1	4.4
Osteomuscular disease	48.2	49.8	49.9	22.1	21.7	23.0
Use of sleeping pills, %	13.6	14.1	16.3	0.5	0.4	0.5
Muscle mass in %, year 2013	49.4 (8.9)	49.0 (9.2)	48.8 (9.0)	-	-	-
Exhaustion, %, year 2013	4.5	5.9	5.3	-	-	-
Slow walking speed, %, year 2013	9.8	10.1	10.2	-	-	-

Note: MET: Metabolic Equivalent. BMI: Body Mass Index.

For continuous variables, the mean (standard deviation) is reported.

^a Heavy drinker: ≥40 g/d of alcohol in men and ≥24 g/d in women.

^b Serving sizes in Seniors-ENRICA study (1 serving): 200 ml of milk, 125 g of yogurt, and 40 g of cheese.

^c Serving sizes in UK Biobank study (1 serving): 250 ml of milk, 125 g of yogurt, and 40 g of cheese.

*p<0.05; **p<0.001.

Table 2. Dairy consumption in the Seniors-ENRICA and UK Biobank study.

	Seniors-ENRICA study (N=2,981)	UK Biobank study (N=8,927)
	Mean (SD) servings/d	Mean (SD) servings/d
Total dairy products	2.28 (1.36)	0.92 (0.64)
Milk	1.03 (0.80)	0.18 (0.30)
Whole milk	0.23 (0.53)	0.01 (0.09)
Part-skim milk	0.41 (0.65)	0.12 (0.26)
Skim milk	0.39 (0.72)	0.05 (0.16)
Yogurt	0.59 (0.66)	0.41 (0.45)
Full-fat yogurt	0.25 (0.49)	0.08 (0.23)
Low-fat yogurt	0.34 (0.57)	0.33 (0.43)
Cheese	0.66 (0.87)	0.33 (0.31)

Table 3. Hazard ratios (95% confidence interval) for the association between dairy consumption and the risk of ≥ 1 falls in the Seniors-ENRICA study (N=2,981).

	Dairy consumption, servings/d			P-trend	Continuous per 1 serving/d increment
	Tertile 1	Tertile 2	Tertile 3		
Total dairy					
Tertile range	0-1.62	1.63-2.62	2.63-12.01		
Person-years	5014	4961	4952		
Cases, n	261	257	283		
Age- and sex-adjusted model	1.00	0.99 (0.83-1.17)	1.09 (0.92-1.29)	0.32	1.04 (0.96-1.14)
Multivariable ¹	1.00	0.99 (0.83-1.17)	1.03 (0.86-1.22)	0.75	1.01 (0.93-1.11)
Multivariable ²	1.00	0.99 (0.83-1.18)	1.03 (0.87-1.23)	0.72	1.02 (0.93-1.11)
Milk					
Tertile range	0-0.68	0.69-1.21	1.22-7.84		
Person-years	4932	5115	4880		
Cases, n	275	279	247		
Age- and sex-adjusted model	1.00	0.88 (0.75-1.04)	0.89 (0.75-1.06)	0.19	0.94 (0.86-1.03)
Multivariable ¹	1.00	0.86 (0.72-1.01)	0.84 (0.71-1.01)	0.06	0.92 (0.84-1.00)
Multivariable ²	1.00	0.85 (0.72-1.01)	0.85 (0.71-1.02)	0.08	0.92 (0.84-1.01)
Multivariable ³	1.00	0.86 (0.73-1.02)	0.86 (0.72-1.03)	0.10	0.93 (0.85-1.01)
Yogurt					
Tertile range	0	0.01-0.92	0.93-7.00		
Person-years	5390	4916	4621		
Cases, n	274	256	271		
Age- and sex-adjusted model	1.00	0.96 (0.81-1.14)	1.11 (0.94-1.32)	0.22	1.06 (0.97-1.15)
Multivariable ¹	1.00	0.97 (0.82-1.16)	1.09 (0.92-1.30)	0.32	1.05 (0.96-1.14)
Multivariable ²	1.00	0.96 (0.81-1.14)	1.09 (0.92-1.30)	0.34	1.04 (0.96-1.14)
Multivariable ³	1.00	0.97 (0.81-1.16)	1.10 (0.92-1.31)	0.29	1.05 (0.96-1.15)
Cheese					
Tertile range	0-0.15	0.16-0.68	0.69-9.43		
Person-years	5002	4904	5021		
Cases, n	277	255	269		
Age- and sex-adjusted model	1.00	0.93 (0.78-1.10)	0.97 (0.82-1.15)	0.74	0.99 (0.91-1.07)
Multivariable ¹	1.00	0.93 (0.78-1.11)	0.93 (0.78-1.11)	0.41	0.96 (0.88-1.05)
Multivariable ²	1.00	0.92 (0.78-1.10)	0.92 (0.77-1.10)	0.36	0.96 (0.88-1.05)
Multivariable ³	1.00	0.93 (0.78-1.11)	0.93 (0.78-1.11)	0.42	0.96 (0.88-1.05)

¹ Cox model adjusted for age, sex, educational level (\leq primary, secondary, university), smoking status (never smoker, former smoker, current smoker), alcohol consumption (abstainer, moderate, heavy drinker), BMI (tertiles of kg/m²), physical activity (tertiles of MET-h/wk), sleep duration (tertiles of h/d), energy intake (tertiles of kcal/d), MEDAS score (tertiles), hypertension, diabetes, and use of sleeping pills.

² Cox model additionally adjusted for osteomuscular disease.

³ Cox model additionally adjusted for the other types of dairy products.

Table 4. Hazard ratios (95% confidence interval) for the association between dairy consumption and the risk of ≥ 1 falls in the UK Biobank study (N=8,927).

	Dairy consumption, servings/d			P-trend	Continuous per 1 serving/d increment
	Tertile 1	Tertile 2	Tertile 3		
Total dairy					
Tertile range	0-0.60	0.61-1.12	1.13-6.50		
Person-years	12168	9920	10184		
Cases, n	64	68	69		
Age- and sex-adjusted model	1.00	1.32 (0.93-1.86)	1.51 (1.07-2.13)	0.02	1.23 (1.04- 1.45)
Multivariable ¹	1.00	1.31 (0.93-1.86)	1.44 (1.01-2.06)	0.04	1.20 (1.01-1.43)
Multivariable ²	1.00	1.31 (0.93-1.85)	1.41 (0.99-2.01)	0.06	1.19 (1.00-1.41)
Milk					
Consumption (yes vs no)	No		Yes		
Person-years	22581		9692		
Cases, n	135		66		
Age- and sex-adjusted model	1.00	-	1.57 (1.16-2.11)		
Multivariable ¹	1.00	-	1.57 (1.16-2.13)		
Multivariable ²	1.00	-	1.54 (1.14-2.09)		
Multivariable ³	1.00	-	1.53 (1.13-2.08)		
Yogurt					
Tertile range	0	0.25-0.50	0.60-3.00		
Person-years	13942	8434	9896		
Cases, n	69	68	64		
Age- and sex-adjusted model	1.00	1.47 (1.04-2.06)	1.22 (0.87-1.73)	0.23	1.11 (0.94-1.31)
Multivariable ¹	1.00	1.49 (1.05-2.10)	1.22 (0.86-1.75)	0.24	1.11 (0.93-1.31)
Multivariable ²	1.00	1.48 (1.05-2.09)	1.21 (0.85-1.73)	0.27	1.10 (0.93-1.31)
Multivariable ³	1.00	1.45 (1.02-2.06)	1.21 (0.85-1.73)	0.28	1.10 (0.93-1.31)
Cheese					
Tertile range	0-0.20	0.30-0.40	0.50-2.60		
Person-years	16167	7552	8553		
Cases, n	100	44	57		
Age- and sex-adjusted model	1.00	1.00 (0.70-1.42)	1.18 (0.85-1.64)	0.35	1.08 (0.92-1.27)
Multivariable ¹	1.00	0.95 (0.66-1.36)	1.05 (0.75-1.47)	0.82	1.02 (0.86-1.21)
Multivariable ²	1.00	0.98 (0.68-1.40)	1.09 (0.78-1.53)	0.65	1.04 (0.88-1.23)
Multivariable ³	1.00	1.01 (0.70-1.45)	1.07 (0.76-1.50)	0.70	1.03 (0.87-1.22)

¹ Cox model adjusted for age, sex, educational level (\leq primary, secondary, university), smoking status (never smoker, former smoker, current smoker), alcohol consumption (abstainer, moderate, heavy drinker), BMI (tertiles of kg/m²), physical activity (tertiles of MET-h/wk), sleep duration (tertiles of h/d), energy intake (tertiles of kcal/d), MEDAS score (tertiles), hypertension, diabetes, and use of sleeping pills.

² Cox model additionally adjusted for osteomuscular disease.

³ Cox model additionally adjusted for the other types of dairy products.