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Consumption of fruit and vegetables and risk of frailty: a dose-response analysis of 3 prospective cohorts of community-dwelling older adults[1,2]

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ABSTRACT

Background: Consuming fruit and vegetables (FVs) may protect against frailty, but to our knowledge no study has yet assessed their prospective dose-response relation.

Objective: We sought to examine the dose-response association between FV consumption and the risk of frailty in older adults.

Design: Data were taken from 3 independent cohorts of community-dwelling older adults: the Seniors-ENRICA (Study on Nutrition and Cardiovascular Risk Factors in Spain) cohort (n = 1872), Three-City (3C) Bordeaux cohort (n = 581), and integrated multidisciplinary approach cohort (n = 473). Baseline food consumption was assessed with a validated computerized diet history (Seniors-ENRICA) or with a food-frequency questionnaire (3C Bordeaux and AMI). In all cohorts, incident frailty was assessed with the use of the Fried criteria. Results across cohorts were pooled with the use of a random-effects model.

Results: During a mean 2.5-y follow-up, 300 incident frailty cases occurred. Fully adjusted models showed that the pooled ORs (95% CIs) of incident frailty comparing participants who consumed 1, 2, or ≥3 portions of fruit/d to those with no consumption were, respectively, 0.59 (0.27, 0.90), 0.58 (0.29, 0.86), and 0.48 (0.20, 0.75), with a P-trend of 0.04. The corresponding values for vegetables were 0.69 (0.42, 0.97), 0.56 (0.35, 0.77), and 0.52 (0.13, 0.92), with a P-trend < 0.01. When FVs were analyzed together, the pooled ORs (95% CIs) of incident frailty were 0.41 (0.21, 0.60), 0.47 (0.25, 0.68), 0.36 (0.18, 0.53), and 0.31 (0.13, 0.48), with a P-trend < 0.01 for participants who consumed 2, 3, 4, or ≥5 portions/d, respectively, compared with those who consumed ≤1 portion/d. An inverse dose-response relation was also found between the baseline consumption of fruit and risk of exhaustion, low physical activity, and slow walking speed, whereas the consumption of vegetables was associated with a decreased risk of exhaustion and unintentional weight loss.

Conclusions: Among community-dwelling older adults, FV consumption was associated with a lower short-term risk of frailty in a dose-response manner, and the strongest association was obtained with 3 portions of fruit/d and 2 portions of vegetables/d. *Am J Clin Nutr* doi: 10.3945/ajcn.115.125781.

Keywords: fruits, vegetables, elderly, frailty, exhaustion, slow walking speed

INTRODUCTION

Consuming fruit and vegetables (FVs)[10] offers life-long health benefits. Evidence from numerous meta-analyses has revealed that the intake of these foods during adulthood is associated with a reduced risk of several chronic diseases, such as ischemic heart

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[2] Supplemental Tables 1 and 2 are available from the "Online Supporting Material" link in the online posting of the article and from the same link in the online table of contents at http://ajcn.nutrition.org.

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[10] Abbreviations used: AMI, Aging Multidisciplinary Investigation; ENRICA, Study on Nutrition and Cardiovascular Risk Factors in Spain; FV, fruit and vegetable; IADL, instrumental activities of daily living; MMSE, Mini-Mental State Examination; 3C, Three-City.

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disease (1, 2), stroke (3), and certain cancers (4–7), as well as a decreased mortality risk, particularly from cardiovascular disease (8). In addition, some data suggest that midlife consumption of FVs is associated with better functional health (9–12).

Population aging, one of the major challenges of modern societies, comes along with an increase in the prevalence and burden of many chronic diseases and geriatric conditions. Despite the extensive evidence showing that FV consumption improves the health of young adults, the extent to which these benefits apply to older adults has received relatively little attention. The few existing prospective data suggest that consuming FVs during old age may help prevent the onset of depression (13), cognitive decline (14), mobility limitations, and disability (15–18) while positively influencing muscle strength (19, 20) and bone mineral status (21, 22). In addition, the consumption of FVs in older adults has shown to decrease the risk of disease-specific and all-cause mortality (23–25).

Frailty is a geriatric syndrome characterized by reduced physiologic reserve resulting from affectation in multiple biological systems, which is manifested by increased risk of falls, disability, institutionalization, and death after exposure to even minor stressors (26). Moreover, the frailty syndrome is a common disorder that affects ~10% of individuals aged ≥65 y and reaches 25% in those aged >85 y (27). In view of the serious consequences of this condition and its increasing prevalence, extensive research is currently being conducted to identify its modifiable risk factors. There is some evidence that FV consumption is inversely associated with frailty. One study, published in 2013 as part of the Whitehall II prospective cohort study, showed that not consuming FVs during adulthood (45–60 y) was associated with an increased risk of prefrailty and frailty after 10.5 y of follow-up (28). Another investigation, a cross-sectional analysis published in 2014, showed an inverse dose-response association between consuming FVs and the prevalence of frailty among women aged ≥65 y (29). However, no study to our knowledge has yet examined the prospective dose-response relation between FV consumption and frailty. This information might prove useful in elaborating recommendations on the specific amounts of FVs to be consumed by older adults.

The main objective of this study was to evaluate the dose-response association between FV consumption and the risk of frailty with the use of 3 independent cohorts of community-dwelling older adults: the Seniors-ENRICA (Study on Nutrition and Cardiovascular Risk Factors in Spain) cohort, Three-City (3C) Bordeaux cohort, and integrated multidisciplinary approach (AMI) cohort.

METHODS

Study population and design

Seniors-ENRICA cohort

From 2008 to 2010, 2614 men and women were selected through stratified random sampling from the noninstitutionalized Spanish population aged ≥60 y (30, 31). At baseline, computer-assisted telephone interviews were used to obtain information on sociodemographic factors, lifestyle behaviors, and morbidity. In addition, home visits were performed to conduct a physical examination, collect blood and urine samples, and record usual diet and prescribed medication. Participants were followed up until 2012 (mean follow-up time: 3.5 y), when a second wave of data was collected. Ninety-five participants (3.6%) died during that period. From the remaining 2519 subjects, we excluded 154 who lacked information on frailty, 55 who were frail, 11 with no information on FV consumption at baseline, and 36 with missing information on potential confounders at baseline. In addition, 391 who were lost during follow-up or had incomplete information on frailty in 2012 were excluded, leading to a final sample size of 1872 participants. All participants provided written informed consent, and the Clinical Research Ethics Committee of La Paz University Hospital approved the study.

3C Bordeaux cohort

The 3C study is a prospective cohort of vascular risk factors of dementia. Its methodology has been described in detail elsewhere (32). At baseline (1999–2000) and at each visit, information was collected on sociodemographic factors, lifestyle behaviors, and medical history. A physical examination also included anthropometric data, blood pressure, information on frailty and disability, and neuropsychological testing. The sample herein included those participants (n = 1214) seen at the 10-y follow-up (2009–2010) and re-examined 2 y later (2011–2012) at the Bordeaux center, the only center of the 3C study where the standard data collection was completed with a comprehensive dietary survey. During this 2-y follow-up period, 141 participants (11.6%) died and 169 (13.9%) were lost. Among the 904 remaining participants, we excluded 102 who lacked information on frailty, 153 who were frail, 18 with no information on FV consumption, and 37 with missing information on potential confounders at baseline. In addition, 13 individuals with incomplete information on frailty between 2011 and 2012 were excluded, leading to a final sample size of 581 participants. All participants provided written informed consent, and the Consultative Committee for the Protection of Persons Participating in Biomedical Research of the Kremlin-Bicêtre University Hospital approved the study.

AMI cohort

The AMI cohort is an epidemiologic prospective study on health and aging among 1002 farmers aged ≥65 y living in rural areas in Gironde, France (33). At baseline (2007), home visits were conducted to obtain information on sociodemographic factors, lifestyle behaviors, medications, material and social living environment, disability, and frailty. The sample herein consisted of 695 participants who were followed up 2 y later. During follow-up, 52 participants (7.5%) died and 74 (10.7%) were lost. Among the 569 remaining participants, we excluded 16 who lacked information on frailty, 40 who were frail, 6 who had no information on FV consumption, and 20 with missing information on potential confounders at baseline. Finally, 14 individuals with incomplete information on frailty at follow-up were excluded, leading to a final sample size of 473 participants. All participants provided written informed consent, and the Ethics Committee of the University Hospital of Bordeaux approved the study.

Study variables

Frailty

In all cohorts, frailty was assessed with the use of a slight modification of the phenotypic criteria proposed by Fried et al.

(34). Individuals meeting ≥3 of the following 5 criteria were considered as frail: *1*) self-reported exhaustion, based on a response of ≥3–4 d/wk to any of the following questions from the Center for Epidemiologic Studies Depression Scale (35)—"I felt that anything I did was a big effort" or "I felt that I could not keep on doing things"; *2*) low physical activity, defined as walking ≤2.5 h/wk in men and ≤2 h/wk in women in Seniors-ENRICA or as <1 h of exercise/wk or <3.5 h of leisure activities/wk in 3C Bordeaux and AMI; *3*) weakness, defined as the lowest quintile of grip strength measured with a Jamar dynamometer and adjusted for sex and BMI (in kg/m^2) in Seniors-ENRICA (36) or as having difficulty rising from a chair without using armrests in 3C Bordeaux and AMI (37); *4*) weight loss, defined as the unintentional loss of ≥4.5 kg (Seniors-ENRICA) in the preceding year or ≥3 kg (3C Bordeaux, AMI) in the previous 3 mo; and *5*) slow walking speed, defined as the worst quintile in a 3-m walking speed test and adjusted for sex and height in Seniors-ENRICA and AMI (38) or as using the Rosow test in 3C Bordeaux. Results from the Rosow test have shown to be strongly associated with the walking performance domain (39).

FV consumption

At baseline, information on food consumption in the Seniors-ENRICA cohort was assessed with a validated computerized diet history that was developed from that used in the European Prospective Investigation into Cancer and Nutrition cohort study in Spain (40, 41). This tool registered the consumption of foods in the preceding year, and the quantification of food portions was aided by a set of photographs that allowed classification in 7 different sizes. In the 3C Bordeaux and AMI studies, baseline food consumption was evaluated by a trained research assistant with the use of a semiquantitative food-frequency questionnaire (42). When foods and vegetables were eaten daily, the number of portions was asked. For those participants who reported a frequency of consumption of <1 portion/d, the intake of fruit and/or vegetables was considered to be 0 portions/d. A portion of fruit was defined as 120 g, and a portion of vegetables was defined as 150 g (43). At baseline of the 3C Bordeaux study, the food-frequency questionnaire was validated against a 24-h dietary recall, and a good concordance between both instruments was observed for weekly servings of foods and nutrient intakes (44, 45).

Other variables

Self-reported information was obtained on age, sex, educational status, and tobacco consumption at baseline in all 3 cohorts. Participants also reported whether they had previously suffered from any of the following physician-diagnosed diseases (31–33): cardiovascular disease (ischemic heart disease, stroke, or heart failure), cancer, chronic respiratory disease (chronic bronchitis or asthma), osteoarthritis, arthritis, or hip fracture.

TABLE 1
Characteristics of the Seniors-ENRICA population at baseline according to baseline daily portions of fruit and vegetables consumed (2008–2010)[1]

		Fruit		Vegetables		Fruit and vegetables	
	Overall	0	≥3	0	≥3	≤1	≥5
n	1872	183	563	659	207	244	422
Women	51.6	43.7	53.8	56.3	39.1	53.3	47.4
Age, y	68.7 ± 6.4[2]	67.7 ± 6.4	68.8 ± 5.7	69.6 ± 6.4	67.6 ± 5.7	68.7 ± 6.7	68.1 ± 5.8
Education							
≤Primary	53.4	48.1	51.0	58.1	52.2	53.3	47.9
Secondary	25.2	31.1	24.9	23.8	24.1	28.7	26.3
University	21.4	20.8	24.1	18.1	23.7	18.0	25.8
Tobacco use							
Never	57.6	45.9	62.0	58.7	50.8	54.5	59.5
Former	30.7	33.9	30.5	27.8	39.1	27.9	32.0
Current	11.7	20.2	7.5	13.5	11.1	17.6	8.5
BMI, kg/m^2							
<25	19.3	19.1	21.1	18.5	19.8	19.7	20.6
25–29.9	49.2	46.5	48.5	48.4	49.3	48.0	50.5
≥30	31.5	34.4	30.4	33.1	30.9	32.3	28.9
Comorbidities							
Cardiovascular disease[3]	5.1	3.8	5.7	4.4	3.4	4.9	6.2
Diabetes	15.0	14.2	13.0	15.3	13.5	15.6	12.6
Cancer	1.9	2.7	1.6	1.7	2.9	2.1	2.6
Asthma or chronic bronchitis	7.6	7.1	8.2	8.2	6.8	5.7	6.6
Osteomuscular disease[4]	47.4	43.7	49.0	49.3	49.3	46.7	50.5
Depression	7.4	7.7	7.3	9.6	5.8	9.0	6.2
Treatments, *n*	1.8 ± 1.7	1.6 ± 1.6	1.8 ± 1.7	1.8 ± 1.6	1.9 ± 1.7	1.6 ± 1.7	1.8 ± 1.7
Modified Trichopoulou index[5]	3.4 ± 1.4	3.2 ± 1.4	3.4 ± 1.5	3.1 ± 1.4	3.7 ± 1.3	3.0 ± 1.3	3.6 ± 1.4
Energy intake, kcal/d	2033 ± 567	2055 ± 666	2044 ± 561	1905 ± 542	2200 ± 578	1944 ± 576	2131 ± 550

[1]Values are percentages unless otherwise indicated. ENRICA, Study on Nutrition and Cardiovascular Risk Factors in Spain.
[2]Mean ± SD (all such values).
[3]Ischemic heart disease, stroke, and heart failure.
[4]Osteoarthritis, arthritis, and hip fracture.
[5]Mediterranean diet excluding fruit and vegetables.

TABLE 2
Characteristics of the Three-City Bordeaux population at baseline according to baseline daily portions of fruit and vegetables consumed (2009–2010)[1]

		Fruit		Vegetables		Fruit and vegetables	
	Overall	0	≥3	0	≥3	≤1	≥5
n	581	47	147	135	27	77	98
Women	63.5	66.0	67.4	63.0	59.3	66.2	64.3
Age, y	81.8 ± 4.1[2]	80.6 ± 3.4	82.1 ± 4.3	81.5 ± 4.0	81.5 ± 4.3	80.9 ± 3.8	82.0 ± 4.2
Education							
≤Primary	26.5	34.0	27.9	28.9	22.2	29.8	22.4
Secondary	29.3	27.7	28.6	25.9	18.5	28.6	30.6
University	44.2	38.3	43.5	45.2	59.3	41.6	47.0
Tobacco use							
Never	66.4	65.9	73.5	66.7	63.0	68.8	71.4
Former	28.9	27.7	23.8	29.6	33.3	24.7	25.5
Current	4.7	6.4	2.7	3.7	3.7	6.5	3.1
BMI, kg/m^2							
<25	45.4	51.0	51.0	48.9	51.9	48.0	52.0
25–29.9	40.1	36.2	32.0	41.5	44.4	41.6	29.6
≥30	14.5	12.8	17.0	9.6	3.7	10.4	18.4
Comorbidities							
Cardiovascular disease[3]	13.8	17.0	12.2	14.8	18.5	15.6	13.3
Diabetes	14.1	10.6	17.0	9.6	7.4	9.1	14.3
Cancer	8.6	10.6	9.5	8.2	14.8	6.5	8.2
Asthma	8.8	4.3	13.6	8.2	11.1	5.2	14.3
Osteomuscular disease[4]	5.2	4.3	8.8	6.7	3.7	6.5	8.2
Depression	4.6	6.4	4.1	5.2	3.7	5.2	4.1
MMSE[5] score	27.7 ± 2.12	27.5 ± 2.3	27.4 ± 2.2	27.8 ± 1.9	28.2 ± 2.4	27.7 ± 2.0	27.7 ± 2.0
Treatments, *n*	5.4 ± 3	5.1 ± 2.9	5.6 ± 2.9	5.3 ± 2.8	5.3 ± 3.2	5.2 ± 2.5	5.4 ± 2.6
Modified Trichopoulou index[6]	27.7 ± 2.1	4.0 ± 1.2	4.0 ± 1.2	4.0 ± 1.2	4.4 ± 1.3	4.0 ± 1.2	4.1 ± 1.2

[1]Values are percentages unless otherwise indicated.
[2]Mean ± SD (all such values).
[3]Ischemic heart disease, stroke, and heart failure.
[4]Osteoarthritis, arthritis, and hip fracture.
[5]MMSE, Mini-Mental State Examination.
[6]Mediterranean diet excluding fruit and vegetables.

Drug treatments were checked by the study staff against drug packages (31–33).

Baseline weight and height were measured with the use of standard methods. Normal weight was defined as a BMI <25, overweight as a BMI between 25 and 29.9, and obesity as a BMI ≥30.

Adherence to the Mediterranean diet was summarized with the use of the Mediterranean diet score, also known as the Trichopoulou index (46), excluding FV consumption. In addition, in the Seniors-ENRICA study energy intake was calculated with the use of Spanish food composition tables (41).

Limitations in instrumental activities of daily living (IADLs) were measured with the use of the Lawton IADL Scale (47); the questions on subjects' ability to prepare meals, do household chores, and care for clothing were not considered in men. The presence of limitation in ≥1 IADL was considered a disability.

Finally, in the 3C Bordeaux and AMI studies, the Mini-Mental State Examination (MMSE) test (48) was administered at baseline to assess the global cognitive performance of participants.

Statistical analysis

Among participants without frailty at baseline, the association between the baseline intake of FVs and risk of frailty was evaluated with ORs and their 95% CIs obtained from logistic regression. Food intake was classified into categories according to the number of portions of fruit (0, 1, 2, or ≥3), vegetables (0, 1, 2, or ≥3), or FVs together (≤1, 2, 3, 4, or ≥5) consumed per day. To maximize the statistical power, the 2 first categories of FV consumption (0 and 1) were added up into a single category (≤1) because the number of individuals who consumed 0 portions of fruit and 0 portions of vegetables was very low. The lowest category was used as reference in the analysis. Two multiple logistic models were built. Model 1 adjusted for age, sex, and educational status. Model 2 further adjusted for BMI, behavioral risk factors (tobacco consumption and Trichopoulou index), chronic diseases, and drug treatments. In addition, model 2 in the Seniors-ENRICA adjusted for total energy intake, whereas in 3C Bordeaux and AMI it adjusted for the MMSE score. *P* values for linear trend were estimated by modeling the FV categories as a continuous variable.

Next, we estimated the association between baseline FV intake and the onset of each frailty criterion among robust adults (free of all 5 criteria) at baseline. These analyses were adjusted as in model 2.

Between-study heterogeneity was assessed with the chi-square-based Q statistic and quantified with the use of the I^2 statistic. Given that the results in the 3 cohorts were generally consistent (I^2 <30%), they were pooled with the use of random-effects meta-analysis as implemented in Stata version 13 with the use of the *metan* command. Linear trends were tested with use of the *glst* command, which uses the generalized least squares for trend estimation of summarized dose-response data.

TABLE 3
Characteristics of the AMI population at baseline according to baseline daily servings of fruit and vegetables (2007)[1]

		Fruit		Vegetables		Fruit and vegetables	
	Overall	0	≥3	0	≥3	≤1	≥5
n	473	88	54	53	29	48	49
Women	37.8	30.68	50	39.6	24.1	27.1	42.9
Age, y	74.5 ± 5.8[2]	73.8 ± 5.2	74.1 ± 6.5	74.7 ± 5.8	75.7 ± 6.3	74.3 ± 6.1	74.1 ± 6.5
Education							
≤Primary	78.0	76.2	77.8	81.1	86.2	75.0	83.7
Secondary	8.7	10.2	9.3	5.7	6.9	8.3	8.2
≥High school	13.3	13.6	12.9	13.2	6.9	16.7	8.2
Tobacco use							
Never	65.8	70.4	70.4	62.3	55.2	66.7	67.4
Former	29.8	23.9	27.8	32.1	37.9	29.2	30.6
Current	4.4	5.7	1.8	5.6	6.9	4.2	2.0
BMI, kg/m^2							
<25	25.8	29.6	25.9	26.4	24.1	33.3	22.5
25–29.9	47.8	47.7	59.3	39.6	48.3	39.6	65.3
≥30	26.4	22.7	14.8	34.0	27.6	27.1	12.2
Comorbidities							
Cardiovascular disease[3]	26.2	27.6	24.1	24.5	34.5	22.9	26.5
Diabetes	10.6	10.2	13.0	7.6	6.9	2.1	12.2
Cancer	12.3	18.2	9.3	5.7	6.9	12.5	8.2
MMSE score	26.2 ± 2.7	26.1 ± 2.9	26.5 ± 2.2	26.2 ± 3.2	26.1 ± 2.9	26.0 ± 3.0	25.7 ± 2.7
Treatments, *n*	4.8 ± 3.2	4.6 ± 2.9	4.5 ± 3.3	5.1 ± 3.1	4.7 ± 3.1	4.5 ± 3.4	4.2 ± 3.2
Modified Trichopoulou index[4]	3.6 ± 1.1	3.7 ± 1.1	3.5 ± 1.0	3.4 ± 0.9	3.8 ± 0.9	3.8 ± 1.0	3.8 ± 0.9

[1]Values are percentages unless otherwise indicated. AMI, integrated multidisciplinary approach; MMSE, Mini-Mental State Examination.
[2]Mean ± SD (all such values).
[3]Ischemic heart disease, stroke, and heart failure.
[4]Mediterranean diet excluding fruit, vegetables, and olive oil consumption.

To assess the robustness of results, we followed different strategies. First, because IADL limitation can overlap with frailty, the analyses were repeated after excluding individuals with baseline limitations in IADL. Second, because reduced physical activity is a risk factor of frailty, we ran analyses that included sedentary behavior and recreational activity as additional covariates in model 2. Because data on sedentary behavior and recreational activity were not available in the 3C Bordeaux or AMI studies, this second analysis was performed using only information from Seniors-ENRICA.

Analyses from the Seniors-ENRICA cohort and the meta-analysis were performed with the use of Stata version 13, whereas analyses performed on the 3C and AMI cohorts used SAS version 9.2 (IBM).

RESULTS

Tables 1–3 present the main baseline sociodemographic, lifestyle, and clinical characteristics of participants included in the Seniors-ENRICA, 3C Bordeaux, and AMI studies, respectively. Participants in Seniors-ENRICA were generally younger and showed a lower prevalence of chronic conditions and medication use than those in the 3C Bordeaux and AMI studies. In addition, participants in the 3C Bordeaux study were less frequently men and showed the lowest prevalence of smoking and obesity, whereas those in the AMI study presented the lowest levels of educational attainment.

Table 4 shows the main results of the study. In total, 136 individuals with incident frailty in Seniors-ENRICA, 91 in 3C Bordeaux, and 73 in AMI were identified during follow-up. Given that results in analyses adjusted for sociodemographic variables (model 1) and those with full adjustment for potential confounders (model 2) were similar, we have emphasized the fully adjusted results throughout. A dose-response association between FV consumption and the risk of frailty was observed: the greater the consumption, the lower the risk of incident frailty. The pooled ORs (95% CIs) of incident frailty comparing participants who consumed 1, 2, or ≥3 portions of fruit/d to those with no consumption were, respectively, 0.59 (0.27, 0.90), 0.58 (0.29, 0.86), and 0.48 (0.20, 0.75), with a *P*-trend of 0.04. The corresponding values for vegetables were 0.69 (0.42, 0.97), 0.56 (0.35, 0.77), and 0.52 (0.13, 0.92), with *P*-trend < 0.01. When FVs were analyzed together, the pooled ORs (95% CIs) of incident frailty were 0.41 (0.21, 0.60), 0.47 (0.25, 0.68), 0.36 (0.18, 0.53), and 0.31 (0.13, 0.48) for participants who consumed 2, 3, 4, or ≥5 portions, respectively, compared with those who consumed ≤1 (*P*-trend < 0.01).

Table 5 displays the results for the association between the consumption of FVs and risk of each of the 5 components of the frailty syndrome. Results from pooled analyses showed a significantly decreased risk of exhaustion (*P*-trend = 0.03), low physical activity (*P*-trend < 0.01), and slow walking speed (*P*-trend = 0.03) with increasing portions of fruits consumed per day. Finally, a higher consumption of vegetables was associated with a significantly decreased risk of exhaustion (*P*-trend = 0.04) and unintentional weight loss (*P*-trend = 0.05). When FVs were analyzed together, a higher consumption of FVs was significantly associated with a decreased risk of exhaustion (*P*-trend = 0.02), low physical activity (*P*-trend <0.01), and unintentional weight

TABLE 4
Association between fruit and vegetable consumption (portions/d) at baseline and risk of frailty in 3 independent cohorts of community-dwelling older adults[1]

	Fruit					Vegetables					Fruit and vegetables					
Study cohort	0	1	2	≥3	*P*-trend	0	1	2	≥3	*P*-trend	≤1	2	3	4	≥5	*P*-trend
Seniors-ENRICA																
Events/total, *n*	15/183	31/308	64/818	26/563		71/659	24/314	33/692	8/207		34/244	32/375	30/388	23/443	17/422	
Model 1																
OR	1.00	1.02	0.73	0.46	<0.01	1.00	0.69	0.54	0.51	<0.01	1.00	0.43	0.48	0.35	0.29	<0.01
95% CI		0.51, 2.01	0.39, 1.36	0.23, 0.91			0.42, 1.15	0.34, 0.84	0.23, 1.10			0.25, 0.75	0.28, 0.83	0.20, 0.63	0.16, 0.55	
Model 2																
OR	1.00	1.03	0.71	0.46	0.02	1.00	0.68	0.52	0.50	<0.01	1.00	0.39	0.45	0.34	0.27	<0.01
95% CI		0.51, 2.07	0.38, 1.35	0.23, 0.94			0.40, 1.15	0.32, 0.83	0.22, 1.12			0.22, 0.68	0.25, 0.79	0.18, 0.62	0.14, 0.53	
Three-City Bordeaux																
Events/total, *n*	10/47	23/150	33/237	25/147		24/135	35/219	29/200	3/27		17/77	16/128	22/138	21/140	15/98	
Model 1																
OR	1.00	0.57	0.47	0.57	0.34	1.00	0.83	0.70	0.58	0.21	1.00	0.42	0.59	0.47	0.50	0.22
95% CI		0.24, 1.36	0.21, 1.09	0.24, 1.35			0.46, 1.50	0.38, 1.30	0.15, 2.19			0.19, 0.93	0.28, 1.23	0.22, 1.00	0.22, 1.14	
Model 2																
OR	1.00	0.50	0.39	0.43	0.13	1.00	0.79	0.61	0.51	0.12	1.00	0.39	0.49	0.35	0.43	0.08
95% CI		0.20, 1.26	0.16, 0.96	0.17, 1.10			0.41, 1.49	0.32, 1.18	0.12, 2.25			0.17, 0.91	0.22, 1.08	0.16, 0.78	0.18, 1.03	
AMI																
Events/total, *n*	15/88	20/158	30/173	8/54		11/53	18/146	39/245	5/29		8/48	22/126	14/144	23/106	6/49	
Model 1																
OR	1.00	0.57	0.92	0.73		1.00	0.55	0.73	0.73		1.00	0.99	0.49	1.33	0.63	
95% CI		0.27, 1.21	0.45, 1.87	0.28, 1.94	0.99		0.24, 1.30	0.34, 1.59	0.22, 2.48	0.85		0.40, 2.52	0.18, 1.29	0.52, 3.37	0.19, 2.05	0.88
Model 2																
OR	1.00	0.50	0.94	0.78		1.00	0.59	0.74	0.71		1.00	0.91	0.51	1.42	0.55	
95% CI		0.22, 1.12	0.44, 2.00	0.27, 2.20	0.79		0.23, 1.48	0.32, 1.74	0.19, 2.65	0.82		0.33, 2.50	0.18, 1.46	0.54, 4.03	0.15, 1.97	0.99
Random-effects meta-analysis																
Events/total, *n*	40/318	74/616	127/1228	59/764		106/847	77/679	101/1137	16/263		59/369	70/629	66/670	67/689	38/569	
Model 1																
OR	1.00	0.65	0.64	0.52		1.00	0.69	0.59	0.54		1.00	0.45	0.51	0.39	0.33	
95% CI		0.33, 0.98	0.35, 0.94	0.24, 0.79	0.05		0.43, 0.95	0.39, 0.80	0.17, 0.92	<0.01		0.24, 0.65	0.29, 0.72	0.21, 0.58	0.16, 0.51	<0.01
Model 2																
OR	1.00	0.59	0.58	0.48		1.00	0.69	0.56	0.52		1.00	0.41	0.47	0.36	0.31	
95% CI		0.27, 0.90	0.29, 0.86	0.20, 0.75	0.04		0.42, 0.97	0.35, 0.77	0.13, 0.92	<0.01		0.21, 0.60	0.25, 0.68	0.18, 0.53	0.13, 0.48	<0.01

[1]Results from the 3 cohorts were pooled with the use of random-effects meta-analysis. ORs and their 95% CIs were obtained from multiple logistic regression models. Model 1 was adjusted for age, sex, and educational status (≤primary, secondary, or university). Model 2 was additionally adjusted for BMI (in kg/m^2), tobacco (never smoker, former smoker, or current smoker), cardiovascular disease, diabetes mellitus, cancer, asthma or chronic bronchitis, osteomuscular disease, MMSE score, depression, number of drug treatments, modified Trichopoulou index, and energy intake (kcal/d). Note that in the Seniors-ENRICA no adjustment was made for the MMSE score, whereas in the Three-City Bordeaux study no adjustment was made for energy intake. In the AMI study, no adjustment was made for depression, asthma, chronic bronchitis, or energy intake. AMI, integrated multidisciplinary approach; ENRICA, Study on Nutrition and Cardiovascular Risk Factors in Spain; MMSE, Mini-Mental State Examination.

TABLE 5
Association between fruit and vegetable consumption (portions/d) at baseline and risk of each frailty criterion in 3 independent cohorts of community-dwelling older adults[1]

	Fruit					Vegetables					Fruit and vegetables					
Study cohort	0	1	2	≥3	*P*-trend	0	1	2	≥3	*P*-trend	≤1	2	3	4	≥5	*P*-trend
Seniors-ENRICA																
Exhaustion																
Events/total, *n*	29/183	44/308	121/818	61/563		117/659	35/314	84/692	19/207		43/244	68/375	45/388	56/443	43/422	
OR	1.00	0.80	0.79	0.58		1.00	0.61	0.83	0.67		1.00	0.91	0.60	0.77	0.62	
95% CI		0.46, 1.39	0.49, 1.27	0.35, 0.97	0.03		0.40, 0.95	0.60, 1.16	0.39, 1.16	0.15		0.58, 1.43	0.37, 0.98	0.48, 1.22	0.38, 1.01	0.04
Low physical activity	35/183	57/308	130/818	75/563		110/659	55/314	104/692	28/207		52/244	55/375	65/388	65/443	60/422	
Events/total, *n*																
OR	1.00	0.93	0.77	0.63		1.00	1.08	0.96	0.86		1.00	0.59	0.72	0.65	0.64	
95% CI		0.58, 1.51	0.50, 1.17	0.40, 0.99	0.02		0.75, 1.55	0.71, 1.31	0.54, 1.37	0.56		0.38, 0.91	0.48, 1.10	0.43, 0.98	0.42, 0.98	0.15
Slow walking speed																
Events/total, *n*	30/183	62/308	126/818	61/563		95/659	51/314	109/692	24/207		42/244	55/375	72/388	62/443	48/422	
OR	1.00	1.22	0.88	0.59		1.00	1.14	1.19	0.82		1.00	0.76	1.10	0.79	0.62	
95% CI		0.74, 1.99	0.56, 1.37	0.37, 0.96	<0.01		0.78, 1.66	0.87, 1.63	0.50, 1.35	0.87		0.48, 1.19	0.71, 1.69	0.51, 1.22	0.39, 0.99	0.08
Weight loss																
Events/total, *n*	16/183	29/308	66/818	35/563		67/659	25/314	47/692	7/207		27/244	41/375	29/388	28/443	21/422	
OR	1.00	0.98	0.84	0.65		1.00	0.74	0.70	0.32		1.00	0.91	0.64	0.56	0.43	
95% CI		0.51, 1.90	0.47, 1.52	0.34, 1.23	0.10		0.45, 1.22	0.47, 1.06	0.14, 0.74	<0.01		0.53, 1.55	0.36, 1.13	0.32, 0.99	0.23, 0.80	<0.01
Weakness																
Events/total, *n*	53/183	110/308	298/818	186/563		250/659	116/314	221/692	60/207		84/244	148/375	141/388	142/443	132/422	
OR	1.00	1.25	1.24	1.10		1.00	1.04	1.02	0.93		1.00	1.06	1.12	1.02	1.00	
95% CI		0.80, 1.95	0.83, 1.83	0.73, 1.66	0.98		0.76, 1.42	0.79, 1.32	0.64, 1.36	0.87		0.72, 1.54	0.76, 1.63	0.70, 1.48	0.69, 1.47	0.86
Three-City Bordeaux																
Exhaustion																
Events/total, *n*	12/44	31/137	42/214	34/141		24/122	58/201	33/188	4/25		19/69	24/118	28/125	31/130	17/94	
OR	1.00	0.66	0.50	0.56		1.00	1.67	0.68	0.65		1.00	0.56	0.66	0.57	0.37	
95% CI		0.29, 1.49	0.22, 1.10	0.24, 1.28	0.19		0.93, 2.97	0.36, 1.27	0.18, 2.30	0.07		0.27, 1.19	0.32, 1.37	0.28, 1.17	0.16, 0.84	0.05
Low physical activity																
Events/total, *n*	33/44	94/137	112/214	85/141		74/122	129/201	108/188	4/25		50/69	73/118	69/125	76/130	56/94	
OR	1.00	0.66	0.26	0.34		1.00	1.15	0.66	0.74		1.00	0.57	0.41	0.38	0.39	
95% CI		0.29, 1.50	0.12, 0.58	0.15, 0.78	<0.01		0.69, 1.91	0.39, 1.11	0.28, 1.94	0.08		0.28, 1.15	0.21, 0.82	0.19, 0.76	0.19, 0.82	<0.01
Slow walking speed																
Events/total, *n*	11/44	24/137	32/214	28/141		20/122	39/201	33/188	3/25		15/69	20/118	18/125	25/130	17/94	
OR	1.00	0.50	0.36	0.47		1.00	1.06	0.79	0.59		1.00	0.55	0.49	0.49	0.52	
95% CI		0.20, 1.23	0.15, 0.86	0.19, 1.16	0.18		0.55, 2.04	0.40, 1.55	0.13, 2.60	0.32		0.24, 1.27	0.21, 1.14	0.22, 1.10	0.22, 1.24	0.19
Weight loss																
Events/total, *n*	3/44	15/137	27/214	9/141		11/122	22/201	18/188	3/25		7/69	12/118	15/125	13/130	7/94	
OR	1.00	2.19	3.82	1.32		1.00	1.56	1.20	2.04		1.00	1.08	1.22	1.35	0.86	0.94
95% CI		0.41, 11.71	0.74, 19.82	0.24, 7.39	0.95		0.58, 3.19	0.43, 3.83	0.36, 11.57	0.62		0.30, 3.99	0.35, 4.32	0.37, 4.95	0.22, 3.37	

(Continued)

TABLE 5 (*Continued*)

	Fruit					Vegetables					Fruit and vegetables					
Study cohort	0	1	2	≥3	*P*-trend	0	1	2	≥3	*P*-trend	≤1	2	3	4	≥5	*P*-trend
Weakness																
Events/total, *n*	10/44	25/137	31/214	25/141		22/122	35/201	30/188	4/25		15/69	20/118	18/125	23/130	15/94	
OR	1.00	0.65	0.45	0.53		1.00	0.87	0.75	0.94		1.00	0.59	0.52	0.55	0.52	0.20
95% CI		0.27, 1.61	0.18, 1.07	0.21, 1.33	0.16		0.46, 1.65	0.39, 1.44	0.26, 3.39	0.47		0.26, 1.35	0.23, 1.18	0.25, 1.22	0.22, 1.24	
AMI																
Exhaustion																
Events/total, *n*	10/78	19/138	26/155	6/43		9/44	22/131	28/212	2/27		10/44	14/107	15/127	18/94	4/42	
OR	1.00	0.98	1.34	1.08		1.00	0.81	0.56	0.28		1.00	0.41	0.40	0.72	0.30	
95% CI		0.41, 2.30	0.59, 3.06	0.34, 3.37	0.53		0.32, 2.01	0.23, 1.37	0.05, 1.49	0.06		0.16, 1.09	0.16, 1.03	0.28, 1.82	0.08, 1.11	0.48
Low physical activity																
Events/total, *n*	15/78	18/138	24/155	10/43		4/44	21/131	36/212	6/27		7/44	13/107	20/127	19/94	8/42	
OR	1.00	0.44	0.69	1.21		1.00	2.24	2.51	3.32		1.00	0.63	0.92	1.38	1.28	
95% CI		0.19, 0.99	0.32, 1.51	0.43, 3.42	0.68		0.67, 7.45	0.78, 8.08	0.74, 14.80	0.12		0.21, 1.90	0.33, 2.61	0.48, 3.99	0.36, 4.48	0.15
Slow walking speed																
Events/total, *n*	18/78	24/138	34/155	11/43		12/44	27/131	41/212	7/27		11/44	25/107	17/127	25/94	9/42	
OR	1.00	0.50	0.86	1.09		1.00	0.66	0.60	0.89		1.00	0.70	0.34	1.04	0.68	
95% CI		0.23, 1.07	0.42, 1.80	0.39, 3.02	0.59		0.27, 1.60	0.26, 1.42	0.26, 3.08	0.57		0.27, 1.81	0.13, 0.91	0.40, 2.69	0.21, 2.20	0.99
Weight loss																
Events/total, *n*	8/78	13/138	10/155	3/43		5/44	10/131	17/212	2/27		7/44	8/107	9/127	8/84	2/42	
OR	1.00	0.94	0.71	0.48		1.00	0.72	0.50	0.46		1.00	0.29	0.32	0.46	0.12	
95% CI		0.32, 2.74	0.24, 2.16	0.10, 2.32	0.30		0.20, 2.59	0.15, 1.70	0.07, 3.17	0.22		0.08, 1.07	0.09, 1.07	0.13, 1.61	0.02, 0.79	0.11
Weakness																
Events/total, *n*	26/78	65/138	63/155	18/43		19/44	48/131	92/212	13/27		18/44	39/107	54/127	45/94	16/42	
OR	1.00	1.63	1.40	1.65		1.00	0.77	1.10	1.26		1.00	0.79	1.03	1.43	0.96	
95% CI		0.89, 3.00	0.76, 2.55	0.72, 3.75	0.34		0.37, 1.60	0.55, 2.20	0.46, 3.46	0.30		0.36, 1.70	0.49, 2.18	0.66, 3.10	0.38, 2.44	0.25
Random-effects meta-analysis																
Exhaustion																
Events/total, *n*	51/305	94/275	189/1187	101/747		150/825	115/646	145/922	25/259		72/357	106/600	88/640	105/667	24/558	
OR	1.00	0.78	0.70	0.59		1.00	0.69	0.76	0.59		1.00	0.64	0.56	0.69	0.47	
95% CI		0.44, 1.12	0.41, 0.98	0.33, 0.86	0.03		0.44, 0.95	0.54, 0.98	0.27, 0.91	0.04		0.38, 0.90	0.33, 0.78	0.43, 0.96	0.26, 0.69	0.02
Low physical activity																
Events/total, *n*	83/305	169/275	266/1187	170/747		188/825	205/646	248/922	38/259		109/357	141/600	154/640	160/667	124/558	
OR	1.00	0.65	0.45[2]	0.51		1.00	1.12	0.84	0.84		1.00	0.59	0.58	0.53	0.54	
95% CI		0.38, 0.92	0.27, 0.63	0.30, 0.72	<0.01		0.78, 1.45	0.61, 1.07	0.47, 1.21	0.16		0.37, 0.81	0.36, 0.79	0.33, 0.73	0.33, 0.75	<0.01
Slow walking speed																
Events/total, *n*	59/305	110/275	192/1187	100/747		127/825	117/646	183/922	34/259		68/357	100/600	107/640	112/667	74/558	
OR	1.00	0.65[2]	0.62[2]	0.58		1.00	1.00	0.96	0.80		1.00	0.69	0.59	0.69	0.60	
95% CI		0.37, 0.94	0.37, 0.87	0.33, 0.82	0.03		0.68, 1.34	0.68, 1.24	0.42, 1.19	0.51		0.42, 0.97	0.34, 0.85	0.42, 0.96	0.35, 0.85	0.07
Weight loss																
Events/total, *n*	27/305	57/275	103/1187	47/747		83/825	57/646	82/922	12/259		41/357	51/600	53/640	49/667	30/558	
OR	1.00	0.98	0.82	0.64		1.00	0.80	0.69	0.33		1.00	0.61	0.53	0.56	0.33	
95% CI		0.39, 1.58	0.36, 1.28	0.23, 1.05	0.22		0.45, 1.15	0.42, 0.96	0.04, 0.61	0.05		0.26, 0.96	0.23, 0.83	0.26, 0.86	0.11, 0.56	0.01

(Continued)

TABLE 5 (*Continued*)

	Fruit					Vegetables					Fruit and vegetables					
Study cohort	0	1	2	≥3	*P*-trend	0	1	2	≥3	*P*-trend	≤1	2	3	4	≥5	*P*-trend
Weakness																
Events/total, *n*	89/305	200/275	392/1187	229/747		291/825	199/646	343/922	77/259		117/357	207/600	213/640	210/667	163/558	
OR	1.00	1.09[2]	0.87[2]	0.91[2]		1.00	0.96	0.98	0.95		1.00	0.87	0.89	0.87	0.83	
95% CI		0.69, 1.49	0.56, 1.18	0.56, 1.26	0.46		0.70, 1.22	0.75, 1.20	0.61, 1.29	0.82		0.58, 1.17	0.60, 1.17	0.58, 1.17	0.54, 1.13	0.42

[1]Results from the 3 cohorts were pooled with the use of random-effects meta-analysis. ORs and their 95% CIs were obtained from multiple logistic regression models. All models were adjusted for age, sex, educational status (≤primary, secondary, or university), BMI (in kg/m^2), tobacco (never smoker, former smoker, or current smoker), cardiovascular disease, diabetes mellitus, cancer, asthma or chronic bronchitis, osteomuscular disease, MMSE score, depression, number of drug treatments, modified Trichopoulou index, and energy intake (kcal/d). Note that in the Seniors-ENRICA no adjustment was made for the MMSE score, whereas in the Three-City Bordeaux study no adjustment was made for energy intake. In the AMI study no adjustment was made for depression, osteomuscular disease, asthma or chronic bronchitis, or energy intake. AMI, integrated multidisciplinary approach; ENRICA, Study on Nutrition and Cardiovascular Risk Factors in Spain; MMSE, Mini-Mental State Examination.

[2]$I^2 \geq 30\%$; data should be interpreted with caution.

loss (*P*-trend = 0.01). The consumption of fruits, vegetables, or FVs was not significantly associated with the risk of weakness in the pooled adjusted analysis. In sensitivity analyses, results were consistent after excluding individuals with baseline IADL limitations or after adjusting for sedentary behavior and recreational activity (**Supplemental Tables 1** and **2**).

DISCUSSION

Results from the Seniors-ENRICA, 3C Bordeaux, and AMI cohorts of community-dwelling older adults support that consuming FVs decreases the short-term risk of frailty in a dose-response manner. To our knowledge, only one longitudinal study (28) has so far reported an inverse association between FV consumption and the risk of frailty, but the participants in that study were younger than those in our study, and the follow-up was conducted during a mean of 10.5 y. Our study broadens the knowledge in the field because this is the first study to our knowledge to observe that FV intake provides short-term, dose-dependent protection against frailty risk even at a late stage of life.

Our results also show an inverse dose-response relation between fruit intake and risk of exhaustion, low physical activity, and slow walking speed and between vegetable intake, exhaustion, and reduced risk of unintentional weight loss. To our knowledge, no previous study has found an inverse association between fruit intake and the risk of exhaustion or between vegetable intake and the risk of unintentional weight loss. However, a protective link between FV intake and slow walking speed has already been reported (12, 16, 17, 49). Indeed, in the Women's Health and Aging Study I, mean total serum carotenoids, mainly proceeding from FVs, were directly associated with mean walking speed over 3 y of follow-up (17), whereas low serum carotenoids were predictors of the progression from moderate toward severe walking disability (16). In the Whitehall II Prospective Cohort Study, consuming <2 portions FVs/d during midlife was associated with slower walking speed in old age (12). Finally, in the InCHIANTI (Invecchiare in Chianti, aging in the Chianti region) study, high-plasma carotenoids protected against declines in walking speed and the development of a severe walking disability in adults aged 65–102 y (49).

Unexpectedly, we did not find any association between FV consumption and muscle strength. The InCHIANTI study previously showed that older adults with lower plasma carotenoid concentrations were at an increased risk of decline in skeletal muscle strength over time (20). Similarly, in a randomized controlled trial, participants who increased FV consumption to ≥5 portions/d showed improvements in grip strength compared with those with an intake of ≤2 portions/d (19). More recently, results from the Fourth Korea National Health and Nutrition Examination Survey indicated that consuming FVs during old age was inversely associated with the prevalence of sarcopenia (50).

FVs can influence the risk of frailty through several mechanisms. First, whereas oxidative stress (51, 52) plays an important role in frailty development, FVs are natural sources of antioxidants (e.g., vitamin C, vitamin E, β-carotene) and contain trace minerals that are needed for antioxidant enzymes to act correctly (53). Second, phytochemicals (e.g., polyphenols) contained in FVs have strong anti-inflammatory properties (54), and several studies have shown a heightened inflammatory state in frail older adults (55). Third, FVs are an important source of certain

nutrients that are themselves protective against conditions that in turn act as risk factors of frailty. [Dietary fiber, for example, is linked to a lower incidence of cardiovascular disease and obesity (56), whereas potassium favors the preservation of muscle mass (57), and this is associated with greater bone mineral density in older men and women (22).] Finally, whereas frailty is associated with alterations in the immune system, including an impaired antibody response to pneumococcal and influenza immunization (55), FV consumption has been associated with stimulating the immune system (53). In a 2012 clinical trial (58), older participants who increased their intake of FVs to ≥5 portions/d showed an improvement in the Pneumovax II vaccination antibody response compared with those with an intake of ≤2 portions/d.

Strengths of this study include its prospective design and the consistency of the results across 3 heterogeneous populations. In addition, in the 3 studies frailty was defined according to standard criteria, analyses were adjusted for an extensive list of potential confounders, and results were robust to sensitivity analyses. Limitations of this study should also be noted. First, because food consumption was self-reported, some recall and desirability bias may have affected our results; however, it should be noted that habitual diet was assessed with standard and validated instruments. Second, although there is evidence that FV consumption throughout adulthood is associated with a reduced risk of certain frailty components as well as with comorbid conditions that are linked with frailty in old age, we could not account for the influence of early dietary patterns on the study association. Third, despite adjusting for many variables, we cannot rule out some residual confounding caused by unmeasured factors. Finally, we could not adjust for MMSE in the Seniors-ENRICA cohort, energy intake in the 3C Bordeaux study, and depression, asthma, chronic bronchitis, or energy intake in the AMI study.

In conclusion, FV consumption in community-dwelling older adults is associated with a lower short-term risk of frailty in a dose-response manner, and the strongest association was obtained with 3 portions of fruit/d and 2 portions of vegetables/d.

The authors' responsibilities were as follows—EG-E and FR-A: conceptualized the study; KP, J-FD, SB, CF, and FR-A; acquired the data; EG-E, BR, and MC: conducted the statistical analyses; EG-E, KP, SB, CF, and FR-A: interpreted the results and drafted the initial manuscript; and all authors: reviewed and approved the final manuscript. None of the authors reported a conflict of interest related to the study.

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