








Original Research

Intake of fruit, vegetables and pulses, and all-cause, cardiovascular and cancer mortality: Results from a population-based prospective study



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ABSTRACT

Objectives: The aim of this study was to explore the association of fruit, vegetable, and pulses consumption with all-cause, cardiovascular, and cancer mortality.

Study design: This prospective study included 66,933 individuals from three Spanish health surveys linked to the national death registry up to December 2022.

Methods: Adjusted Poisson regression models were used to analyze the data, categorizing fruit, vegetable and pulses intake according to Spanish dietary recommendations and using splines to examine non-linear relationships.

Results: No clear association was found between pulses intake and mortality. Consuming fruits and vegetables ≥ 2 times/day reduced all-cause mortality risk by 20 % (95%CI = 10%–29 %) and 17 % (95%CI = 7%–26 %) respectively, compared with < 3 times/week. Combined intake of fruits and vegetables from 1 to 1.99 to ≥ 5 times/day showed reductions in all-cause and CVD mortality ranging from 16 % (95%CI = 5%–26 %) to 30 % (95%CI = 20%–39 %), and from 25 % (95%CI = 5%–41 %) to 35 % (95%CI = 14%–50 %), respectively, compared with < 1 time/day. No additional benefits against all-cause and CVD mortality for intakes of fruits over 2–3 times/day, but gradual reductions in mortality risk for vegetable intake of 2–5 times/day were observed. Combined intake showed protection up to intakes of 10 times/day, notably for CVD mortality. Associations were similar but weaker for cancer mortality.

Conclusions: This study suggests that significant benefits of fruits and, specially, vegetables intake might go beyond the recommended five servings a day. Confirmation of these results could lead to specific dietary recommendations to prevent chronic diseases.

1. Introduction

A recent systematic analysis that quantified the impact of a suboptimal intake of major food groups and nutrients across 195 countries on

non-communicable diseases, highlighted a low consumption of fruits, vegetables, and legumes as the third, fifth, and ninth dietary risks respectively, and concluded that diet improvements could delay one in five deaths worldwide.¹

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Specifically, several studies relate the intake of fruit and vegetables to cancer^{2–8} and cardiovascular disease (CVD)^{3–7,9,10} prevention, two of the main causes of death worldwide.¹¹ As for legume intake, its potential protective effect on all-cause,^{12,13} cancer¹³ and CVD^{13–15} mortality or disease is still controversial. Most of these studies use predefined consumption thresholds based on general or country-specific recommendations, which vary over time, and among countries or entities.^{16,17} Exploring the dose-response association between fruit, vegetable and legume intake and mortality might be a useful approach to evaluate the effect of these exposures on long-term health and formulate more standardized guidelines based on empirical evidence.

Some meta-analyses^{3–7,9,10,12–15} that compile the existing evidence aiming to define thresholds for the consumption of fruits and vegetables beyond which no further reduction in mortality risk is observed, report conflicting results. While some studies set this threshold at 5 servings/day for fruits and vegetables^{5,7} and at 50 grs/day for legumes,¹³ others argue benefits far beyond these limits.^{3,4,6,9,10,12,14} Some methodological issues might be partly behind these differences. Most of the included articles measure the intake categorically, that is posteriorly transformed to a continuous scale by assigning the median/midpoint of the interval. Non-linear dose-response analyses are afterwards carried out using these continuous variables, which inevitably introduces some sources of error in the estimates.

Spain, a Mediterranean country with one of the highest per capita fruit and vegetable consumption rates in Europe,¹⁸ provides a broad range of intake levels for study. It also has a nationwide population-based survey that collects dietary information since 2012 in the context of the Spanish^{19,20} and the European Health Surveys²¹ that can be linked with the national mortality registry from the Spanish National Institute of Statistics (INE, Instituto Nacional de Estadística).²² Some studies have explored the association between the intake of fruits, vegetables and/or legumes with mortality in Spain^{18,23–32} but none has exploited the potential of the data described and most of them explore these associations as a secondary objective,^{24–30} others are carried out over age-^{24–28,31,32} or sex-³⁰ specific populations, and only one explores non-linear dose-response associations.¹⁸

The aim of this study is to analyze the categorical and non-linear association of the intake of fruits, vegetables, fruits and vegetables and legumes with the risk of all-cause, cardiovascular, and cancer mortality in the adult population of Spain, in order to evaluate the validity of current recommendations and add evidence about thresholds for the potential benefits of fruits, vegetables and pulses intake.

2. Methods

2.1. Study design and population

The INE provided microdata of three Spanish National and European Health Surveys: Encuesta Nacional de Salud España 2012 (ENSE-2012, July 2011 to June 2012) and 2017 (ENSE-2017, January 2014 to January 2015) and Encuesta Europea de Salud 2014 en España (EESA-2014, October 2016 to October 2017) that followed a standardized protocol.^{19–21} Briefly, in a three-stage sampling design a sample of census tracts from each of the 52 Spanish provinces was selected, from which a random sample of households was drawn. Lastly, an adult ≥ 15 years of age was randomly selected from each of these households. Each participant answered a questionnaire on sociodemographic and economic factors, health status and health determinants. Information was collected in a computer-assisted personal interview, conducted at the participant's home. The number of completed interviews relative to the total number of eligible households was 66.5 % for the ENSE-2012, 71.3 % for EESA 2014 and 69.9 % for the ENSE-2017. The total sample included data on 66,938 individuals from 6689 census tracts.

2.2. Follow-up period and death ascertainment

Dates and causes of death for the period 2011–2022 were obtained from the mortality registry of the INE and linked to the three health surveys, using the identification document number.

The exact date of the interview was not provided by the INE due to privacy and ethical considerations. Therefore, we assigned the start of the follow-up period at the midpoint of the recruitment period of each survey. The follow-up ended at the date of death or the December 31, 2022 for those who did not die. For deaths occurred before the assigned recruitment date, this date was replaced with the midpoint between the start of the original recruitment period and date of death.

For the present study, we selected as outcomes all-cause mortality (dead; not dead) as well as circulatory system diseases (ICD10: I00–I99), and neoplasms (ICD10:C00–D48) mortality.

2.3. Measurements and assessment of confounders

Information on fruit, vegetables and pulses consumption was collected with a food frequency questionnaire (FFQ) that included one question about the frequency of intake for each of the following groups: Fresh fruits (excluding juices); vegetables, salads and greens; and pulses. The ENSE-2012 include five response options (daily; three or more times per week but less than once a day; once or twice a week; less than once a week; never or almost never). The EESA-2014 and ENSE-2017 surveys further distinguished between three times per week and four to six times per week. For fruits and vegetables, participants who responded “daily” were also asked to report the quantitative intake.

For the categorical analyses, variables were grouped in concordance with the dietary recommendations of the Spanish Agency of Food Safety and Nutrition (AESAN) (≥ 2 –3 servings of fruits/day of 120–200 g. per serving; ≥ 3 servings of vegetables/day of 150–200 g. per serving; ≥ 4 servings of legumes/week of 50–60 g. dry per serving)³³ and the distribution of the variables. Fruit intake was categorized as > 3 times/week, 3–6 times/week, 1 time/day, 2 times/day and ≥ 3 times/day. Due to the low consumption of vegetables (only 1.5 % of the sample presented intakes ≥ 3 times/day), a single category of intakes ≥ 2 times/day was created for this food group. Legume intake was grouped as < 1 time/week, 1–2 times/week and ≥ 3 times/week, since available information did not allow more detailed classification of intake. Additionally, after converting them into continuous variables as described below, fruit and vegetable intakes were added and classified as < 1 time/day, 1–1.99 times/day, 2–3.99 times/day, 4–4.99 times/day and ≥ 5 times/day.

Continuous analyses were only carried out over fruit and vegetable intake since information on quantitative daily intake was only collected for these groups. Categorical responses were transformed to daily intake by dividing the midpoint of the weekly frequency by seven, i.e., 1.5/7 for “once or twice a week”, 0.5/7 for “less than once a week”, and 0 for “never or almost never”. To assign the midpoint for the “three or more times per week but less than once a day” category, we took advantage of the more granular information provided by the EESA-2014 and ENSE-2017 which disaggregated this category as “4–6/week” and “3/week”. We calculated the weighted average of the categories 4–6/week (assigning a value of 5) and 3/week, and the resulting value (4.2/week) divided by 7 was assigned to the corresponding categories in the three surveys.

2.4. Statistical analyses

Sample characteristics were described for the whole sample and by all-cause, CVD and cancer mortality with mean and standard deviation (sd) for quantitative variables and number of cases and percentages for qualitative variables. The significance of the bivariate associations was tested with t-tests for quantitative variables and chi-squared tests for qualitative variables, excluding missing values. Since the distribution of

follow up time was not symmetric, it was described with the median and interquartile range (IQR).

Multivariable analyses with Poisson regression models were carried out to explore the following associations:

- a) Categorical intake of fruit, vegetables, fruits and vegetables and pulses and all-cause, cardiovascular and cancer mortality setting the reference as the lowest intake.
- b) Non-linear associations between all-cause, cardiovascular and cancer mortality and intake of fruits, vegetables and fruits and vegetables, using restricted cubic splines with knots at the 5th, 35th, 65th and 95th percentiles as recommended by Harrell,³⁴ setting the reference at intakes of fruit or vegetables of 1.5 times a week and 3 times a week for fruits and vegetables. Departure from linearity was tested with the Wald test.

All models were adjusted by mean-centered age and squared mean-centered age at recruitment, sex, education, country of birth, body mass index, physical activity, smoking, alcohol drinking, binge drinking, and number of severe comorbidities including heart attack, other heart diseases, stroke and chronic obstructive pulmonary disease (none; one; two; three or more). Models were also adjusted by the modified Mediterranean Diet Adherence Screener Score (MEDAS, 0–10 points)³⁵ excluding the specific recommendations on cooking fats and “sofrito” sauce which information was not collected, as well as the recommendation on alcohol intake that was included as an adjustment variable. Also, juices intake was not added to the total fruit consumption. Additionally, the specific recommendations on fruit and vegetables or pulses were excluded in the respective models. Models for fruits were additionally adjusted by vegetable intake and models for vegetables were additionally adjusted for fruit intake. Models for fruits, vegetables and fruits and vegetables were additionally adjusted by pulses intake and models for pulses were additionally adjusted for fruit and vegetable intake.

Heterogeneity of effects by sex, age and BMI groups was explored for all-cause mortality including in the models an interaction between each of the exposures and sex, age, and BMI.

Finally, we carried out two sensitivity analyses excluding subgroups that might have more delicate health conditions: 1) Individuals that self-reported to have a very bad health status ($n = 1481$); 2) Individuals who previously had a medical diagnosis of myocardial infarction, stroke, or cancer ($n = 5228$), 3) Individuals with severe comorbidities (heart attack and other heart diseases, embolism, stroke, cerebral hemorrhage, diabetes, cancer, chronic bronchitis, emphysema or EPOC, $n = 14709$).

This study was approved by the Carlos III Institute of Health Ethical Research Committee on the May 3, 2019 (CEI PI 28_2019). All participants signed an informed consent.

All analyses were performed using Stata/MP version 18 (Statacorp, College Station, TX).

3. Results

After excluding 5 participants with incongruent data of death, the final sample included 66,933 participants who were followed during a median of 8.4 (Min–Max: 0.03–11.0) years (522,754 person-years).

Participants who died during follow-up were older, had better adherence to the Mediterranean diet, consumed more fruits and pulses, were more likely to be male, born in Spain and less educated, had higher BMI, lower physical activity, and were more often never/former drinkers and smokers. They also had more comorbidities and poorer self-perceived health. The pattern was similar for cause-specific mortality, except for CVD, where there were more females among the deceased (Table 1). Description of sample characteristics by exposure groups can be found in Table S1 of the additional material.

The results of the association of fruit, vegetable, fruit and vegetable and pulses intake with all-cause, CVD and cancer mortality are

summarized in Table 2. Consuming fruit 2 or more times a day was associated with a 20 % lower risk of all-cause mortality compared to consuming fruit less than 3 times a week. This result was similar for CVD and cancer mortality but associations were weaker. Vegetable intake was also related with a decrease in all-cause mortality, showing a similar protection for intakes of 3–6 times a week and 1 time a day (between 10 and 12 % lower risk), that was slightly stronger for intakes of 2 or more times per day (17 % lower risk). The trend was similar for cause-specific mortality but the associations were not as strong. When considering the joint effect of fruit and vegetable intake, an increasing protection against all-cause mortality was observed, from 16 % for the intake of 1–1.99 times per day to 30 % for ≥ 5 per day, compared to intakes of < 1 portion per day. This association was also observed for CVD mortality, ranging from 25 % to 35 % for the same intakes, but was not as clear for cancer mortality. No association was found between pulses intake and all-cause or cause-specific mortality.

Although interaction tests were not significant, the protective effect of high fruit and vegetable consumption on all-cause mortality appeared to be stronger among women, older participants and those with a BMI below 25 kg/m² (Table 3).

Finally, the non-linear analyses (Fig. 1) revealed that, while fruits provide protection against all-cause and cause-specific mortality at low to moderate intake levels, the protective impact of vegetables strengthens as intake increases. More concretely, protection of fruit intake against all-cause and CVD mortality increased with intakes from 1.5 times a week to 2 times a day, with only a slight additional increase beyond this. The protection against all-cause and CVD mortality of vegetable intake also started at intakes of 1.5 times per week and kept increasing markedly up to intakes of 5 times per day, especially for CVD mortality. When considering the joint influence of fruit and vegetable intake on all-cause mortality, we observed a marked risk reduction with intakes up to 3 servings per day. Beyond this, the risk continues to decrease, though more gradually, up to a maximum explored of 10 servings per day. This effect was more marked for CVD mortality, with a steeper slope (Fig. 1). The associations for cancer mortality followed similar trends to that observed for all-cause mortality, but they were weaker and peaked at around intakes of 1.5 times per day for fruits and 4 times per day for fruits and vegetables. The specific risk estimates from the splines are provided in Table S2 of the Additional Material.

4. Discussion

Our findings based on National Health Survey data indicate that, while the association of pulses intake with all-cause, CVD and cancer mortality remains uncertain, a moderate to high consumption of fruit and vegetables appears to be associated with lower risks of all-cause and, notably, CVD mortality. Although no major additional benefits were observed for intakes of fruits over 2 times/day, the protection of vegetable intake gradually increased from 2 times/day to 5 times/day, especially for CVD mortality. Combined consumption of fruit and vegetables showed protection against all-cause and, notably, CVD mortality up to intakes of 10 times/day. Trends were similar for cancer mortality but associations were weaker.

The associations found support the current recommendations of the AESAN to consume around 5 servings of fruits and vegetables per day, coming from, at least 2 servings of fruits and 3 of vegetables per day.³³ However, results from the non-linear dose response analyses indicate that the benefits of the intake of vegetables might increase significantly with intake above these recommendations. Our data does not provide strong support for the recommendation to consume pulses 2 to 4 times per week with regard to mortality.

Systematic reviews and meta-analyses of prospective cohort studies have explored the association between fruit,^{2,3,5-7,9,10,12} vegetable^{2,3,5-7,9,10,12} and combined^{3-7,9} intake with the risk of all-cause,^{3-7,10,12,13} CVD^{3-7,9,10,13} and cancer²⁻⁷ mortality. In concordance with our results, most of them claim a protective effect of high

Table 1
 Basal characteristics of participants, overall and by outcome event (all-cause, cardiovascular and cancer mortality).

	Full Sample n = 66,933		General mortality				CVD ^a Mortality					Cancer Mortality					
			Alive n = 59,313		Dead n = 7620		Alive n = 64,682		Dead n = 2251			Alive n = 64893		Dead n = 2040			
	median	IQR ^d	median	IQR ^d	median	IQR ^d	median	IQR ^d	median	IQR ^d	median	IQR ^d	median	IQR ^d	median	IQR ^d	
	mean/ n	SD ^a / %	mean/ n	SD ^a / %	mean/ n	SD ^a / %	p- value	mean/ n	SD ^a / %	mean/ n	SD ^a / %	p- value	mean/ n	SD ^a / %	mean/ n	SD ^a / %	p- value
Time of follow up, median (IQR ^b)	8.4	5.3	8.4	5.3	4.5	4.5		8.4	5.3	4.3	4.4		8.4	5.3	4.2	4.2	
Age at recruitment, mean(sd ^b)	47.86	18.79	45.35	16.90	75.01	15.35	0.000	47.11	18.22	77.76	14.43	0.000	47.34	18.53	69.45	14.79	0.000
Sex, n(%)							0.000					0.047					0.000
Male	30,788	48.8	27,130	48.4	3658	52.3		29,843	48.8	945	46.2		29,607	48.4	1181	62.3	
Female	36,145	51.2	32,183	51.6	3962	47.7		34,839	51.2	1306	53.8		35,286	51.6	859	37.7	
Education, n(%)							0.000					0.000					0.000
University or more	11,588	17.8	11,137	18.8	451	6.9		11,483	18.1	105	5.4		11,402	18.0	186	10.2	
High school	17,451	28.3	16,732	29.9	719	10.8		17,284	28.8	167	8.6		17,179	28.6	272	14.8	
Secondary school	16,833	27.4	15,701	28.4	1132	15.9		16,521	27.7	312	16.2		16,449	27.5	384	20.5	
Primary school or less	21,061	26.5	15,743	22.8	5318	66.5		19,394	25.4	1667	69.9		19,863	25.8	1198	54.5	
Country of birth, n(%)							0.000					0.000					0.000
Spain	60,950	86.3	53,491	85.4	7459	96.4		58,750	86.1	2200	95.6		58,965	86.1	1985	95.0	
Other	5983	13.7	5822	14.6	161	3.6		5932	13.9	51	4.4		5928	13.9	55	5.0	
Fruit intake, n(%)							0.000					0.000					0.000
<3 times/week	9556	16.3	8880	16.8	676	9.9		9380	16.4	176	8.7		9341	16.4	215	12.1	
3–6 times/week	13,233	20.7	12,022	21.2	1211	15.5		12,873	20.9	360	15.4		12,894	20.8	339	16.1	
1 time/day	9562	14.7	8350	14.5	1212	16.6		9196	14.7	366	17.1		9256	14.7	306	15.5	
2 times/day	19,245	27.8	16,688	27.3	2557	33.6		18,487	27.7	758	34.1		18,610	27.8	635	30.5	
≥3 times/day	15,251	20.3	13,306	20.0	1945	24.2		14,668	20.2	583	24.5		14,709	20.2	542	25.5	
Unknown	86	0.1	67	0.1	19	0.3		78	0.1	8	0.3		83	0.1	3	0.2	
Vegetable intake, n(%)							0.001					0.319					0.379
<3 times/week	9675	15.1	8450	15.1	1225	15.9		9311	15.1	364	15.9		9379	15.1	296	14.7	
3–6 times/week	27,312	40.1	24,276	40.3	3036	38.5		26,415	40.2	897	38.2		26,495	40.2	817	38.5	
1 time/day	19,333	29.2	17,125	29.0	2208	30.8		18,684	29.2	649	30.7		18,734	29.1	599	31.0	
≥2 times/day	10,507	15.4	9380	15.5	1127	14.6		10,174	15.4	333	14.9		10,185	15.4	322	15.5	
Unknown	106	0.2	82	0.1	24	0.3		98	0.2	8	0.3		100	0.2	6	0.3	
Fruit and vegetable intake, n(%)							0.000					0.000					0.000
Less than once a day	9276	15.5	8532	16.0	744	10.3		9065	15.6	211	10.2		9062	15.6	214	10.9	
1–1.99 times/day	16,726	26.0	15,041	26.4	1685	22.0		16,241	26.1	485	20.9		16,271	26.1	455	22.3	
2–3.99 times/day	25,730	37.5	22,374	36.9	3356	44.0		24,720	37.3	1010	44.6		24,878	37.4	852	42.0	
4–4.99 times/day	8189	11.6	7180	11.4	1009	13.6		7894	11.5	295	14.1		7913	11.5	276	13.0	
≥5 times/day	6894	9.3	6093	9.2	801	9.8		6653	9.2	241	9.9		6657	9.2	237	11.5	
Unknown	118	0.2	93	0.2	25	0.3		109	0.2	9	0.3		112	0.2	6	0.3	
Legume intake, n(%)							0.000					0.204					0.035
Less once a week	8836	13.6	7789	13.6	1047	13.6		8505	13.6	331	14.5		8568	13.7	268	13.1	
1–2 times a week	40,324	59.0	35,917	59.2	4407	56.5		39,026	59.1	1298	56.4		39,144	59.1	1180	56.0	
≥3 times/week	17,657	27.2	15,514	27.0	2143	29.6		17,042	27.1	615	28.9		17,070	27.1	587	30.6	
Unknown	116	0.2	93	0.2	23	0.3		109	0.2	7	0.2		111	0.2	5	0.3	
MEDAS ^b , mean(sd)	4.92	1.94	4.86	1.92	5.60	1.87	0.000	4.90	1.93	5.62	1.86	0.000	4.91	1.94	5.61	1.91	0.000
Body Mass Index, n(%)							0.000					0.000					0.000
Insufficient weight (<18 kg/m ²)	1281	2.3	1150	2.4	131	1.7		1248	2.3	33	1.4		1245	2.3	36	2.0	
Normal Weight (18–24.99 kg/m ²)	27,111	43.0	25,013	44.4	2098	27.6		26,573	43.5	538	23.6		26,481	43.3	630	31.5	
Overweight (25–29.99 kg/m ²)	23,519	34.0	20,950	33.9	2569	35.0		22,813	34.1	706	32.5		22,772	33.9	747	37.8	
Obesity (≥30 kg/m ²)	10,958	15.8	9395	15.3	1563	21.2		10,422	15.6	536	25.2		10,546	15.7	412	20.3	
Unknown	4064	4.9	2805	4.0	1259	14.4		3626	4.6	438	17.3		3849	4.8	215	8.4	
Physical activity, n(%)							0.000					0.000					0.000
Several times a week	6945	11.9	6768	12.7	177	2.7		6898	12.1	47	2.8		6876	12.1	69	3.8	
Several times a month	7410	12.5	7264	13.5	146	2.2		7380	12.8	30	1.5		7352	12.7	58	3.2	

(continued on next page)

Table 1 (continued)

	Full Sample n = 66,933		General mortality				CVD ^a Mortality				Cancer Mortality			
			Alive n = 59,313		Dead n = 7620		Alive n = 64,682		Dead n = 2251		Alive n = 64893		Dead n = 2040	
	median	IQR ^b	median	IQR ^b	median	IQR ^b	median	IQR ^b	median	IQR ^b	median	IQR ^b	median	IQR ^b
Occasionally	25,764	35.9	23,352	36.4	2412	30.4	25,107	36.1	657	27.6	24,945	35.9	819	37.8
Sedentary	26,748	39.6	21,876	37.3	4872	64.5	25,236	38.9	1512	67.9	25,655	39.2	1093	55.0
Unknown	66	0.1	53	0.1	13	0.2	61	0.1	5	0.2	65	0.1	1	0.2
Smoking, n(%)														
Never Smoker	34,394	50.9	30,006	50.7	4388	53.5	32,949	50.7	1445	60.2	33,475	51.2	919	40.2
Former Smoker	16,238	23.4	14,054	22.7	2184	30.8	15,662	23.3	576	27.9	15,552	23.1	686	36.3
Current Smoker ≤14 cigarettes/day	10,104	16.1	9554	16.8	550	7.9	9977	16.3	127	6.0	9889	16.2	215	11.1
Current Smoker >14 cigarettes/day	6115	9.5	5636	9.6	479	7.5	6022	9.6	93	5.4	5899	9.4	216	12.0
Unknown	82	0.1	63	0.1	19	0.3	72	0.1	10	0.5	78	0.1	4	0.3
Alcohol intake, n(%)														
Non-Drinker	14,337	21.2	11,988	20.5	2349	29.3	13,565	21.0	772	32.0	13,875	21.2	462	21.4
Former drinker	9345	12.5	7341	11.3	2004	25.6	8782	12.2	563	24.3	8840	12.2	505	24.6
3 or less times per month	18,345	28.9	17,329	30.3	1016	13.6	18,044	29.3	301	14.1	18,037	29.2	308	15.1
Daily drinker 1–10 grs/day	13,880	21.1	12,708	21.5	1172	16.0	13,541	21.2	339	16.5	13,518	21.2	362	17.3
Daily drinker 11–20 grs/day	6905	10.4	6313	10.6	592	8.6	6749	10.5	156	7.3	6697	10.4	208	11.3
Daily drinker >20 grs/day	3920	5.6	3477	5.5	443	6.3	3810	5.6	110	5.3	3734	5.5	186	9.8
Unknown	201	0.3	157	0.2	44	0.6	191	0.3	10	0.4	192	0.3	9	0.5
Binge drinking, n(%)														
No	62,348	92.7	54,948	92.3	7400	96.9	60,153	92.5	2195	97.5	60,395	92.6	1953	95.5
Yes	4483	7.2	4274	7.6	209	3.0	4433	7.3	50	2.2	4397	7.2	86	4.4
Unknown	102	0.2	91	0.2	11	0.1	96	0.2	6	0.2	101	0.2	1	0.1
Number of severe comorbidities ^c , n(%)														
None	52,205	81.4	48,943	85.0	3262	42.3	51,358	82.5	847	37.4	51,237	82.2	968	46.8
1	11,335	14.5	8496	12.5	2839	36.7	10,451	13.9	884	38.0	10,596	14.0	739	35.9
2	2796	3.3	1587	2.1	1209	16.5	2375	2.9	421	19.6	2536	3.1	260	13.5
≥3	578	0.7	273	0.3	305	4.4	481	0.6	97	4.9	505	0.6	73	3.7
Unknown	19	0.0	14	0.0	5	0.0	17	0.0	2	0.1	19	0.0	0	0.0
Self-perceived health (last 12 months), n (%)														
Very good	12,140	21.3	11,849	22.9	291	4.1	12,068	21.7	72	3.2	12,018	21.7	122	6.3
Good	32,849	49.8	30,664	51.8	2185	28.2	32,238	50.4	611	27.1	32,149	50.2	700	33.7
Fair	15,490	20.7	12,575	19.1	2915	37.4	14,586	20.2	904	39.0	14,775	20.3	715	34.9
Bad	4973	6.3	3356	4.9	1617	21.8	4483	5.9	490	22.8	4608	6.0	365	18.2
Very bad	1481	1.9	869	1.3	612	8.5	1307	1.8	174	8.0	1343	1.8	138	6.9

^a Interquartile Range (IQR); Standard Deviation (SD); Cardiovascular Disease (CVD).

^b Mediterranean Diet Adherence Screener score (MEDAS) was missing for 340 (0.51 %) of individuals.

^c Severe comorbidities considered: heart attack, other heart diseases, stroke and chronic obstructive pulmonary disease.

Table 2

Association of all-cause, cardiovascular and cancer mortality with fruit, vegetable and pulses intake.

	All-cause mortality n = 62344					CVD ^a mortality n = 62344					Cancer mortality n = 62344				
	Alive	Dead	IRR ^b	95 % CI ^a		Alive	Dead	IRR ^b	95 % CI ^a		Alive	Dead	IRR ^b	95 % CI ^a	
				LL ^a	UL ^a				LL ^a	UL ^a				LL ^a	UL ^a
Fruit															
<3 times/week	8455	573	1.00			8886	142	1.00			8837	191	1.00		
3–6 times/week	11,243	959	0.89	0.78	1.01	11,927	275	0.90	0.69	1.16	11,915	287	0.88	0.70	1.11
1 time/day	7923	1004	0.93	0.82	1.06	8639	288	0.96	0.74	1.23	8657	270	0.89	0.70	1.13
2 times/day	15,816	2113	0.80	0.71	0.90	17,324	605	0.81	0.64	1.02	17,359	570	0.80	0.64	0.99
≥3 times/day	12,631	1627	0.80	0.71	0.90	13,785	473	0.84	0.66	1.08	13,771	487	0.84	0.67	1.05
p for trend			0.000				1783	0.082				1805	0.136		
Vegetable															
<3 times/week	7975	1011	1.00			8706	280	1.00			8716	270	1.00		
3–6 times/week	22,764	2461	0.88	0.80	0.96	24,513	712	0.91	0.77	1.08	24,524	701	0.90	0.75	1.07
1 time/day	16,329	1853	0.90	0.82	0.99	17,659	523	0.89	0.74	1.06	17,641	541	0.93	0.77	1.12
≥2 times/day	9000	951	0.83	0.74	0.93	9683	268	0.84	0.68	1.03	9658	293	0.89	0.72	1.10
p for trend			0.011					0.116					0.484		
Fruit and vegetable															
Less than once a day	8086	616	1.00			8539	163	1.00			8512	190	1.00		
1–1.99 times/day	14,104	1362	0.84	0.74	0.95	15,085	381	0.75	0.59	0.95	15,079	387	0.88	0.70	1.10
2–3.99 times/day	21,208	2761	0.78	0.70	0.88	23,175	794	0.70	0.56	0.88	23,211	758	0.86	0.71	1.06
4–4.99 times/day	6833	855	0.73	0.64	0.83	7438	250	0.71	0.55	0.91	7435	253	0.80	0.63	1.02
≥5 times/day	5837	682	0.70	0.61	0.80	6324	195	0.65	0.50	0.86	6302	217	0.84	0.66	1.08
p for trend			0.000					0.015					0.169		
Pulses															
<1 time/week	7322	823	1.00			7898	247	1.00			7911	234	1.00		
1–2 times/week	33,961	3623	0.96	0.87	1.04	36,559	1025	0.93	0.79	1.11	36,553	1031	0.90	0.76	1.08
≥3 times/week	14,785	1830	0.96	0.88	1.06	16,104	511	0.95	0.79	1.15	16,075	540	0.96	0.80	1.16
p for trend			0.789					0.887					0.698		

^a Cardiovascular disease (CVD); confidence interval (CI); lower limit (LL); upper limit (UL).

^b Incidence Rate Ratio (IRR) adjusted by mean-centered age and squared mean-centered age at recruitment; sex; BMI; place of birth; physical activity; smoking, alcohol intake; binge drinking; education; and severe comorbidities including previous severe circulatory or respiratory disease, tumors and/or diabetes. Models for fruits were additionally adjusted by vegetable al pulses intake and MEDAS diet quality index excluding the recommendations on fruit and vegetables. Models for vegetables were additionally adjusted by fruit and pulses intake and MEDAS diet quality index excluding the recommendations on fruit and vegetables. Models for fruit and vegetables were additionally adjusted by MEDAS diet quality index excluding the recommendations on fruit and vegetables. Models for pulses were additionally adjusted for fruit and vegetable intake and MEDAS diet quality index excluding the recommendation on legumes.

intakes against all-cause and CVD mortality, with the exception of Kwok et al.¹⁰ study. The absence of association with cancer was also claimed by Wang X et al.⁷ for the three food groups, Oyebo et al.³ for fruit intake and Wang DD et al.⁵ for vegetable intake. Additionally, some of these studies explore non-linear dose-response associations for fruits,^{5,6,9,12} vegetables^{5,6,9,12} and/or both combined.^{4,7,9} Thresholds for all-cause mortality^{4,7,12} were around 2–3 fruits per day^{5,6,9,12} and 3 vegetable portions/day,^{5,6,12} lower than our findings. For combined intake, some meta-analyses limit the protection to 5 servings/day^{5,7} while others claim benefits for higher intakes.^{4,6} As explained above, disagreements may stem from converting categorical to continuous data. Generally, fruit and vegetable intake showed stronger protective effects against CVD than all-cause or cancer mortality^{4,6} aligning with our results. Reviews on legume intake show mixed results, with some indicating protection against all-cause^{12,13} or CVD¹⁴ mortality and others questioning such protection against CVD^{13,15} or cancer mortality.¹³

Among the studies including Spanish data,^{18,23,25–27,29–32,36} only one explored non-linear dose-response associations,¹⁸ finding a protection for the intake of fruits and vegetables against all-cause mortality up to 600 g/day with a magnitude of the association similar to that we found in our work (around 25 %). From those exploring categorical associations, the study with the biggest sample size claimed benefits of fruit intake against all-cause mortality from around 1 serving/day,¹⁸ while others with more modest sample sizes set the reference at intakes close or over 2 and showed benefits over the fixed threshold^{26,27} or no benefits at all.²⁵ For vegetables, the largest study found benefits from 0.6 to 1 servings/day,¹⁸ while smaller studies set reference values too high to find clear associations.^{25–28} Studies exploring the association of legume intake with all-cause mortality^{25–27,31} did not report clear associations. Studies exploring the effect of fruits, vegetables and/or legumes against

CVD^{23,30,31} revealed that CVD mortality risk was associated with low intakes of fruits,²³ vegetables^{23,30} and high intakes of legumes.³¹ Association with cancer mortality was only explored for legumes^{29,31} and both studies claimed a protective potential of this food group.

One of the biological mechanisms behind the protective effect of fruits and vegetables consumption against mortality may be their rich content of micronutrients and bioactive compounds, vitamins, and minerals that prevent chronic diseases.^{36–38} Also, phytonutrients present in this type of foods enhance health by offering antioxidant, anti-inflammatory, antibacterial, antifungal, antiallergic, chemoprotective, neuroprotective, hypolipidemic, and/or hypotensive benefits.^{39,40} Additionally, their high fiber content might impact in hunger-satiety mechanisms,³⁸ promoting intake control and reducing weight gain, which is linked to all-cause mortality and, especially to CVD and cancer mortality.⁴¹ Vegetables may offer more benefits than fruits due to their lower calorie and higher fiber content, as well as being a better source of some nutrients like folate, iron, magnesium, calcium, or potassium.⁴² The lack of effect for legumes might be because, while high in fiber, they have fewer beneficial compounds like carotenoids, folate, or calcium compared to fruits and vegetables. Additionally, fruits and vegetables offer a greater variety of nutrients and have a lower energy density, helping maintain a healthy weight.⁴³ It is also possible that, given the limited range of legume intake in our study, the lack of a significant association between mortality and legume intake may reflect chance variation, and a weak inverse relationship might emerge when combined with findings from other studies.

The lower effect found for cancer mortality might be because cancer is a heterogeneous group of diseases with diverse risk factors. For example, while lung cancer (responsible for the highest number of cancer deaths in Spain⁴⁴) has not been clearly associated with the intake of fruits and vegetables,⁴⁵ colorectal cancer (second in the mortality

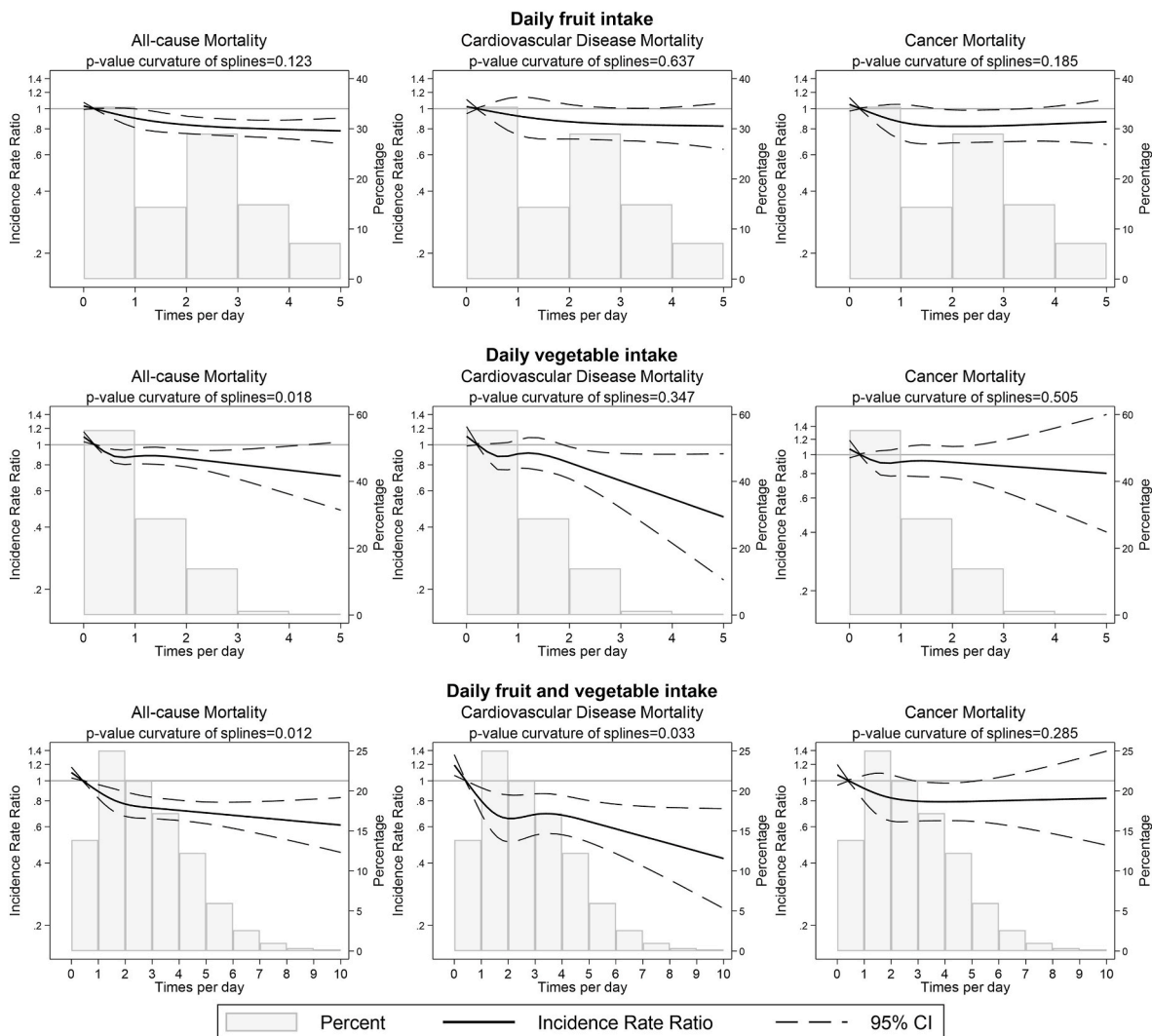


Fig. 1. Non-linear association between all-cause, cardiovascular and cancer mortality and fruit and vegetable intake. Incidence Rate Ratio (IRR) and 95 % confidence interval, adjusted by mean-centered age and squared mean-centered age at recruitment; sex; BMI; place of birth; physical activity; smoking, alcohol intake; binge drinking; education; and severe comorbidities including previous severe circulatory or respiratory disease, tumors and/or diabetes. Models for fruits were additionally adjusted by vegetable al pulses intake and MEDAS diet quality index excluding the recommendations on fruit and vegetables. Models for vegetables were additionally adjusted by fruit and pulses intake and MEDAS diet quality index excluding the recommendations on fruit and vegetables. Models for pulses were additionally adjusted for fruit and vegetable intake and MEDAS diet quality index excluding the recommendation on legumes. Percentages represent the distribution of the overall population across intake levels.

rank⁴⁴), has been related with low fiber intake.⁴⁶ Therefore, the beneficial influence of fruit and vegetable intake in preventing mortality from some types of cancer might be diluted when including tumors unaffected by such intake.

One of the main strengths of the present study is the large sample size and its high representativeness, since ENSE-2012, EESE-2014 and ENSE-2017 are population-based surveys that are representative of the Spanish population. The ENSE and EESE surveys are carried out through a whole year, which ensures the representation of seasonal changes in dietary habits. Furthermore, the individual-level data from the surveys were linked to the mortality registry of the Spanish National Institute of Statistics, whose coverage is almost exhaustive, minimizing classification errors. In addition, the results are adjusted by the most important factors related to all-cause, CVD and cancer mortality such as physical activity, alcohol and tobacco consumption, etc. Even if this adjustment does not completely rule out the possibility that a high fruit and vegetable intake represents a healthier general lifestyle, it significantly reduces the bias.

The main limitation is the potential for information bias in self-reported data, though this bias is likely non-differential since death occurs after exposure data collection. Information and recall bias could vary with health status, but sensitivity analyses excluding individuals with very poor health or severe comorbidities yielded similar conclusions (Additional Material [Tables S3–S11](#) and [Figs. S1–S3](#)). Additionally, the FFQ used does not detail specific fruits and vegetables and records intake by times/day rather than portions/servings. However, according to our results, for 2012, 2014 and 2017, fruits and vegetables were consumed in average 2.58, 2.59 and 2.53 times per day, which lies between the estimations of the Spanish Ministry of agriculture (MAPAMA)⁴⁷ that reports intakes of 2.72, 2.73 and 2.45 portions per day, and the data of the National Institute of Statistics (INE)⁴⁸ that estimates these intakes to be 2.21, 2.20 and 2.24 for the same years, suggesting minimal impact on estimations. Also, despite the considerable sample size, the relatively short follow-up period since the 2012 ENSE limits the power to detect clear associations for specific mortality, particularly for high vegetable intake, since only 1.5 % of the sample

consumed vegetables 3 or more times/day. For that reason we only showed here the results for the main specific mortality causes (CVD and cancer) but additional results for diseases of the respiratory system (n = 815 deaths), infectious and parasitic diseases (n = 421), diseases of the nervous system and sensory organs (n = 408), diseases of digestive system (n = 349), genitourinary diseases (n = 243), endocrine, nutritional, and metabolic diseases (n = 241) and external mortality causes (n = 218) can be found in Table S12 of the Additional material. Lastly, due to the lack of gender information in health surveys, we could not examine gender disparities.

4.1. Conclusions

This study suggests that the health benefits of consuming fruits and vegetables may be more significant than those of legumes. It also highlights that benefits of fruit and vegetable intake might be obtained for intakes over the recommended five servings a day, particularly due to the substantial protective effects of vegetable consumption beyond the recommended three servings a day. Confirmation of these results might allow to design more specific dietary recommendations to effectively prevent chronic diseases.

Author statements

Ethical approval

The study was approved by the Carlos III Institute of Health Ethical Research Committee on the 3rd of May (CEI PI 28_2019). All participants signed an informed consent.

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Competing interests

None declared.

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CRedit authorship contribution statement

Paloma Martínez-Castañeiras: Conceptualization, Methodology, Writing – original draft. **Cristina Ortiz:** Conceptualization, Methodology, Data curation, Writing – review & editing. **Nerea Fernandez de Larrea-Baz:** Conceptualization, Methodology, Writing – review & editing. **Virginia Lope:** Conceptualization, Writing – review & editing. **Gary Sánchez-Gordón:** Conceptualization, Writing – review & editing. **Emma Ruiz-Moreno:** Conceptualization, Writing – review & editing. **Isabel Alonso:** Conceptualization, Writing – review & editing. **Esther Garcia-Esquinas:** Conceptualization, Writing – review & editing. **Beatriz Pérez-Gómez:** Conceptualization, Writing – review & editing. **Roberto Pastor-Barriuso:** Conceptualization, Methodology, Writing – review & editing. **Iñaki Galán:** Conceptualization, Methodology, Writing – review & editing, Supervision, Funding acquisition. **Adela Castelló:** Conceptualization, Methodology, Formal analysis, Data

curation, Writing – original draft, Supervision, Project administration, Funding acquisition.

Availability of data

Anonymous data from the ENSE-2014, ENSE-2017 are available at the INE webpage: https://www.ine.es/dyngs/INEbase/es/operacion.htm?c=Estadistica_C&cid=1254736176783&menu=resultados&idp=1254735573175#_tabs-1254736195295.

Anonymous data from the EESE-2014 are available at the INE webpage:

https://www.ine.es/dyngs/INEbase/es/operacion.htm?c=Estadistica_C&cid=1254736176784&menu=resultados&idp=1254735573175#_tabs-1254736195298.

Anonymous data of mortality are available at the INE webpage:

https://www.ine.es/dyngs/INEbase/es/operacion.htm?c=Estadistica_C&cid=1254736176780&menu=resultados&idp=1254735573175#_tabs-1254736195294.

Linkage of all these databases should be required to the INE.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.puhe.2024.12.014>.

References

1. Afshin A, Sur PJ, Fay KA, et al. Health effects of dietary risks in 195 countries, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2019 May;393(10184):1958–1972.
2. Turati F, Rossi M, Pelucchi C, Levi F, La Vecchia C. Fruit and vegetables and cancer risk: a review of southern European studies. *Br J Nutr*. 2015 Apr;113(Suppl 2): S102–S110.
3. Oyebo O, Gordon-Dseagu V, Walker A, Mindell JS. Fruit and vegetable consumption and all-cause, cancer and CVD mortality: analysis of Health Survey for England data. *J Epidemiol Community Health*. 2014 Sep;68(9):856–862.
4. Aune D. Plant foods, antioxidant biomarkers, and the risk of cardiovascular disease, cancer, and mortality: a review of the evidence. *Adv Nutr*. 2019 Nov 1;10(Suppl 4): S404–S421.
5. Wang DD, Li Y, Bhupathiraju SN, et al. Fruit and vegetable intake and mortality: results from 2 prospective cohort studies of US men and women and a meta-analysis of 26 cohort studies. *Circulation*. 2021 Apr 27;143(17):1642–1654.
6. Aune D, Giovannucci E, Boffetta P, et al. Fruit and vegetable intake and the risk of cardiovascular disease, total cancer and all-cause mortality—a systematic review and dose-response meta-analysis of prospective studies. *Int J Epidemiol*. 2017 Jun 1;46(3):1029–1056.
7. Wang X, Ouyang Y, Liu J, et al. Fruit and vegetable consumption and mortality from all causes, cardiovascular disease, and cancer: systematic review and dose-response meta-analysis of prospective cohort studies. *BMJ*. 2014 Jul 29;349, g4490.
8. World Cancer Research Fund/American Institute for Cancer Research. Continuous Update Project Expert Report 2018. Wholegrains, vegetables and fruit and the risk of cancer. Available at: <https://www.wcrf.org/wp-content/uploads/2020/12/Who-legrains-veg-and-fruit.pdf>. Accessed 12 of June 2024.
9. Zhan J, Liu YJ, Cai LB, Xu FR, Xie T, He QQ. Fruit and vegetable consumption and risk of cardiovascular disease: a meta-analysis of prospective cohort studies. *Crit Rev Food Sci Nutr*. 2017 May 24;57(8):1650–1663.
10. Kwok CS, Gulati M, Michos ED, et al. Dietary components and risk of cardiovascular disease and all-cause mortality: a review of evidence from meta-analyses. *Eur J Prev Cardiol*. 2019 Sep 1;26(13):1415–1429.
11. World Health Organization. *The top 10 causes of death [Fact sheet]*; 2020, 2020 Dic 9. Available at: <https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death>. Accessed 12 of June 2024.
12. Schwingshackl L, Schwedhelm C, Hoffmann G, et al. Food groups and risk of all-cause mortality: a systematic review and meta-analysis of prospective studies. *Am J Clin Nutr*. 2017 Jun;105(6):1462–1473.
13. Zargarzadeh N, Mousavi SM, Santos HO, et al. Legume consumption and risk of all-cause and cause-specific mortality: a systematic review and dose-response meta-analysis of prospective studies. *Adv Nutr*. 2023 Jan;14(1):64–76.
14. Mendes V, Niforou A, Kasdagli M, Ververis E, Naska A. Intake of legumes and cardiovascular disease: a systematic review and dose-response meta-analysis. *Nutr Metabol Cardiovasc Dis*. 2023 Jan 1;33(1):22–37.
15. Thorisdottir B, Arnesen EK, Bärebring L, et al. Legume consumption in adults and risk of cardiovascular disease and type 2 diabetes: a systematic review and meta-analysis. *Food Nutr Res*. 2023;67.
16. European Commission. *Dietary recommendations for legumes and pulses intake | Knowledge for policy [Internet]*; 2024 Jan 29. Available at <https://knowledge4policy>.

- ec.europa.eu/health-promotion-knowledge-gateway/dietary-recommendations-legumes-pulses-intake_en. Accessed 12 of June 2024.
17. Food-Based Dietary Guidelines recommendations for fruit and vegetables | Knowledge for policy. Available at: https://knowledge4policy.ec.europa.eu/health-promotion-knowledge-gateway/food-based-dietary-guidelines-europe-table-3_en; 2024 Jan 29. Accessed 12 of June 2024.
 18. Leenders M, Sluijs I, Ros MM, et al. Fruit and vegetable consumption and mortality: European prospective investigation into cancer and nutrition. *Am J Epidemiol*. 2013 Aug 15;178(4):590–602.
 19. Ministerio de Sanidad e Instituto Nacional de Estadística. National health survey 2011–2012. (*Metodología*); 2013 Mar 14. Available at: https://www.ine.es/en/metodologia/t15/t153041912_en.pdf. Accessed 12 of June 2024.
 20. Ministerio de Sanidad e Instituto Nacional de Estadística. National health survey 2017. (*Methodology*); 2017. Available at: https://www.ine.es/en/metodologia/t15/t153041917_en.pdf. Accessed 12 of June 2024.
 21. Ministerio de Sanidad e Instituto Nacional de Estadística. *European Survey of Health in Spain 2014*. (*Methodology*); 2014. Available at: https://www.ine.es/en/metodologia/t15/t153042014_en.pdf. Accessed 12 of June 2024.
 22. Instituto Nacional de Estadística. Estadística de defunciones. Movimiento natural de la población. Available at: https://www.ine.es/dyngs/INEbase/es/operacion.htm?c=Estadistica_C&cid=1254736176780&menu=resultados&idp=1254735573175#_tabs-1254736195294. Accessed 2 Jul 2024.
 23. Crowe FL, Roddam AW, Key TJ, et al. Fruit and vegetable intake and mortality from ischaemic heart disease: results from the European Prospective Investigation into Cancer and Nutrition (EPIC)-Heart study. *Eur Heart J*. 2011 May;32(10):1235.
 24. Delgado-Velandia M, Maroto-Rodríguez J, Ortolá R, García-Esquinas E, Rodríguez-Artalejo F, Sotos-Prieto M. Plant-based diets and all-cause and cardiovascular mortality in a nationwide cohort in Spain: the ENRICA study. *Mayo Clin Proc*. 2022 Nov 1;97(11):2005–2015.
 25. Hershey MS, Fernandez-Montero A, Sotos-Prieto M, et al. The Association Between the Mediterranean Lifestyle Index and All-Cause Mortality in the Seguimiento Universidad de Navarra Cohort. *Am J Prev Med*. 2020 Dec 1;59(6):e239–e248.
 26. Alvarez-Alvarez I, Zazpe I, Pérez de Rojas J, et al. Mediterranean diet, physical activity and their combined effect on all-cause mortality: The Seguimiento Universidad de Navarra (SUN) cohort. *Prev Med*. 2018 Jan 1;106:45–52.
 27. Domínguez LJ, Bes-Rastrollo M, Toledo E, et al. Dietary fiber intake and mortality in a Mediterranean population: the “Seguimiento Universidad de Navarra” (SUN) project. *Eur J Nutr*. 2019 Dec 1;58(8):3009–3022.
 28. Martínez-González MA, Guillén-Grima F, De Irala J, et al. The Mediterranean diet is associated with a reduction in premature mortality among middle-aged adults. *J Nutr*. 2012 Sep;142(9):1672–1678.
 29. Lázaro-Sánchez AD, Juárez Marroquí A, Quesada Rico JA, Orozco-Beltrán D. Risk factors for cancer mortality in Spain: population-based cohort study. *Int J Environ Res Publ Health*. 2022 Jan;19(16):9852.
 30. Quesada JA, Bertomeu-González V, Ruiz-Nodar JM, López-Pineda A, Sánchez-Ferrer F. Hábitos de vida y mortalidad cardiovascular de las mujeres menopáusicas: estudio de cohortes de base poblacional. *Rev Española Cardiol*. 2022 Jul 1;75(7):576–584.
 31. Papandreou C, Becerra-Tomás N, Bulló M, et al. Legume consumption and risk of all-cause, cardiovascular, and cancer mortality in the PREDIMED study. *Clin Nutr*. 2019 Feb;38(1):348–356.
 32. Buil-Cosiales P, Zazpe I, Toledo E, et al. Fiber intake and all-cause mortality in the Prevención con Dieta Mediterránea (PREDIMED) study. *Am J Clin Nutr*. 2014 Dec; 100(6):1498–1507.
 33. Agencia Española de seguridad alimentaria y nutrición. *Healthy and sustainable dietary recommendations supplemented with physical activity recommendations for the Spanish population*; December 2022. Available at: https://www.aesan.gob.es/AECO SAN/docs/documentos/nutricion/RECOMENDACIONES_DIETETICAS_EN.pdf. Accessed 12 of June 2024. 2022.
 34. Harrell FE. *Regression Modeling Strategies: With Applications to Linear Models, Logistic Regression, and Survival Analysis [Internet]*. New York, NY: Springer; 2001. Springer Series in Statistics). Available from: <http://link.springer.com/10.1007/978-1-4757-3462-1>. Accessed November 22, 2023.
 35. Schröder H, Fitó M, Estruch R, et al. A short screener is valid for assessing Mediterranean diet adherence among older Spanish men and women. *J Nutr*. 2011 Jun;141(6):1140–1145.
 36. Agudo A, Cabrera L, Amiano P, et al. Fruit and vegetable intakes, dietary antioxidant nutrients, and total mortality in Spanish adults: findings from the Spanish cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC-Spain). *Am J Clin Nutr*. 2007 Jun;85(6):1634–1642.
 37. WHO FAO, ed. *Diet, Nutrition, and the Prevention of Chronic Diseases: Report of a WHO-FAO Expert Consultation ; [Joint WHO-FAO Expert Consultation on Diet, Nutrition, and the Prevention of Chronic Diseases, 2002, Geneva, Switzerland]*. Geneva: World Health Organization; 2003:149 (WHO technical report series).
 38. Flood-Obbagy JE, Rolls BJ. The effect of fruit in different forms on energy intake and satiety at a meal. *Appetite*. 2009 Apr;52(2):416–422.
 39. Gupta C, Prakash D. Phytonutrients as therapeutic agents. *J Compl Integr Med*. 2014 Sep;11(3):151–169.
 40. Wallace TC, Bailey RL, Blumberg JB, et al. Fruits, vegetables, and health: a comprehensive narrative, umbrella review of the science and recommendations for enhanced public policy to improve intake. *Crit Rev Food Sci Nutr*. 2020 Jul 19;60(13):2174–2211.
 41. Abdelaal M, le Roux CW, Docherty NG. Morbidity and mortality associated with obesity. *Ann Transl Med*. 2017 Apr;5(7):161.
 42. Offringa LC, Stanton MV, Hauser ME, Gardner CD. Fruits and vegetables versus vegetables and fruits: rhyme and reason for word order in health messages. *Am J Lifestyle Med*. 2018 May 2;13(3):224–234.
 43. Slavin JL, Lloyd B. Health benefits of fruits and Vegetables1. *Adv Nutr*. 2012 Jul 6;3(4):506–516.
 44. Sociedad Española de Oncología Médica. *Las cifras del cáncer en España 2024*. Sociedad Española de Oncología Médica (SEOM); 2024. ISBN: 978-84-09-58445-1. © https://www.seom.org/images/LAS_CIFRAS_2024.pdf. Accessed 12 of June 2024.
 45. World Cancer Research Fund/American Institute for Cancer Research. *Continuous Update Project Expert Report 2018. Diet, Nutrition, Physical Activity and Lung Cancer*; 2017;71. Available at: dietandcancerreport.org. Accessed 12 of June 2024.
 46. World Cancer Research Fund/American Institute for Cancer Research. *Continuous Update Project Expert Report 2018. Diet, Nutrition, Physical Activity and Colorectal Cancer*; 2017;111. Available at: dietandcancerreport.org. Accessed 12 of June 2024.
 47. Panel de consumo alimentario. Ministerio de agricultura, pesca y alimentación. Series de datos de consumo alimentario en hogares. <https://www.mapa.gob.es/va/alimentacion/temas/consumo-tendencias/panel-de-consumo-alimentario/series-anauales/default.aspx>. Accessed 12 of June 2024.
 48. Instituto Nacional de Estadística. *Encuesta de presupuestos familiares. Cantidades físicas consumidas, gasto y valor unitario*; 2024. <https://www.ine.es/jaxiT3/Tabla.htm?t=25168>, 12 of June 2024.