

Supplementary Table S1. Adherence to the Mediterranean Lifestyle (MEDLIFE) index at baseline among participants in the Seniors-Enrica-2 cohort ($N = 2,504$).

Index items	Components (serving size)	Criteria for 1 point	% scoring 1 point
Block 1: Mediterranean food consumption			
1. Sweets	Cookies, chocolate cookies, pastries, donuts, homemade baked goods, store-bought baked goods, muffins (50 g), chocolates (30 g), churros (100 g), turrón and mazapán (35 g)	≤ 2 servings/wk	34.58
2. Red meat	Beef, pork, lamb (100-150 g)	< 2 servings/wk	75.84
3. Processed meat	Sausage, soft spicy sausage, bacon (50 g), cured ham (60 g), cooked ham (30 g), hamburger (150 g), liver, organ meats (100-150 g), pâté (25 g)	≤ 1 serving/wk	9.27
4. Eggs	Eggs (1 unit)	2-4 servings/wk	41.01
5. Legumes	Lentils, beans, chickpeas, peas (150 g cooked)	≥ 2 servings/wk	39.58
6. White meat	Chicken/turkey with skin, chicken/turkey without skin, rabbit (100-150 g)	2 servings/wk	31.55
7. Fish/seafood	White fish, fatty fish, codfish, salted or smoked fish, shrimp, octopus, calamari (100-150 g), oysters and shellfish (6 units)	≥ 2 servings/wk	84.54
8. Potatoes	Baked or boiled potatoes (150 g)	≤ 3 servings/wk	91.01
9. Low-fat dairy products	Skim milk, low-fat milk (200 cc), low fat yogurt (125 g), fresh soft cheese (50 g)	2 servings/d	19.05
10. Nuts and olives	Almonds, peanuts, hazelnuts, walnuts (30 g), olives (10 units)	1-2 servings/d	16.53
11. Sofrito	Sauce of olive oil with onion, pepper, other vegetables (250 g) and tomato (150 g)	$> 2/4$ ingredients above the median	39.66
12. Fruit	Orange, banana, apple, pear, kiwi, mango, avocado, peach, apricot, nectarine (1 unit), clementine (2 units), strawberry (6 units), cherries, plums, figs, grapes (1 dessert plate), watermelon, melon (200-250 g), dates and dried fruits (150 g)	3-6 servings/d	12.38
13. Vegetables	Spinach, cauliflower, broccoli, lettuce, carrot, squash, green beans, eggplant, zucchini, cucumber, pepper, asparagus, gazpacho, garden salad, other vegetables (250 g), tomato (150 g) (<i>excludes potatoes</i>)	≥ 2 servings/d	29.39
14. Olive oil	Olive oil (1 Tbsp = 13.5 g) cutoff >36 g	≥ 3 servings/d	5.39
15. Cereals	White bread, whole-grain bread (50g), white or whole grain rice, pasta (150g cooked), pizza dough (200g), breakfast cereal (30g)	3-6 servings/d	65.85
Block 2: Dietary Habits			
16. Wine	Red/white wine (1 glass 100 cc)	Women: > 0 and ≤ 0.5 serving/d; Men: > 0 and ≤ 1 serving/d	14.86
17. Limit salt at meals	Do you add salt to foods (eggs, potatoes, fish, fried food)? Do you add salt to vegetables? Do you add salt to salads?	No	97.20
18. Preference for whole grain products	Fiber from whole grain cereals	> 6 g/d fiber from cereals	14.06
19. Snacks	Potato chips, popcorn, or other chips (1s = 50g)	≤ 1 serving/wk	94.73

20. Limit snacking between meals	Do you tend to snack in between meals or before going to bed?	No	77.32
21. Limited consumption of sugar-sweetened beverages	Sugar-sweetened beverages + juice (200 cc)	< 1/wk	80.03

Block 3 Physical activity, rest social habits and conviviality

22. Physical activity	Brisk walking, jogging, running, climbing stairs, bicycling, stationary cycling, swimming, dance, aerobic exercise, martial arts, gymnastics, gardening, tennis, soccer, skiing, ice skating, team sports, and other physical activities or sports	≥ 150 min/wk moderate or ≥ 60 min/wk vigorous	56.99
23. Nap	Napping throughout the week	> 0 - 30 min/d	72.44
24. Hours of sleep	Sleeping throughout the week	6-8 h/d	73.68
25. Watching TV	Watching TV/videos throughout the week	≤ 2 h/d	32.23
26. Eating in company	Do you have lunch or dinner with friends, family, or others?	Yes	63.70
27. Collective and non-collective sports	Playing soccer, tennis, squash, basketball or other team sports, running, jogging; etc.	≥ 1 h/wk	42.77

Abbreviations: min, minutes; h, hours; d, day; wk, week; cc, cubic centimeter; g, grams; Tbsp, tablespoons; TV, television.

Supplementary Table S2. Differences in participant's characteristics by inclusion status in the Seniors-Enrica-2 cohort.

	Included participants	Excluded participants due to missing GDF-15 data
<i>n</i> (%)	2504	684
Sex, women, <i>n</i> (%)	1326 (52.96)	368 (53.80)
Age, years, mean (SD)	71.56 (4.38)	72.93 (4.64)
Education, <i>n</i> (%) ^a		
≤ Primary	1590 (63.50)	474 (69.40)
Secondary	469 (18.73)	113 (16.54)
University	445 (17.77)	96 (14.06)
Smoking status, <i>n</i> (%)		
Current	233 (9.31)	65 (9.50)
Former	951 (37.98)	251 (36.70)
Never	1320 (52.72)	368 (53.80)
BMI, kg/m ² , mean (SD)	27.76 (4.47)	29.40 (4.96)
Energy intake, kcal/day, mean (SD)	1948.53 (351.43)	1978.63 (365.39)
Cardiovascular disease, <i>n</i> (%) ^b	85 (3.39)	66 (9.65)
Type 2 diabetes, <i>n</i> (%)	458 (18.29)	139 (20.32)
Systolic blood pressure	134.54 (18.09)	131.67 (20.85)
Blood biomarkers, mean (SD)		
Glucose, mg/dL	99.84 (23.72)	104.57 (35.84)
LDL, mg/dL	113.73 (29.04)	109.07 (41.67)
MEDLIFE index, 0-27 p, mean (SD)	13.71 (2.62)	10.39 (2.32)
Block 1: Mediterranean food consumption, 0-15 p, mean (SD)	5.97 (1.77)	4.56 (1.31)
Block 2: Mediterranean eating habits, 0-6 p, mean (SD)	4.33 (0.76)	3.22 (0.63)
Block 3: Physical activity, rest, social habits, and conviviality; 0-6 p, mean (SD)	3.42 (1.38)	2.61 (1.32)

Abbreviations: p, points; SD, standard deviation; BMI, body mass index.

a 1 participant with missing data.

b Including myocardial infarction, stroke, and heart failure.

Supplementary Table S3. Secondary analyses. Mean (95% CI) percentage differences for the association of MEDLIFE index quintiles and GDF-15 ($N = 2,504$).

	Quintile 1 4 – 10 p	Quintile 2 11 – 12 p	Quintile 3 13 p	Quintile 4 14 – 15 p	Quintile 5 16 – 21 p	<i>p</i> -trend	Per 2-point increase
<i>n</i>	405	605	363	641	490		
Model 1 ^a	Ref.	-4.1 (-9.6, 1.7)	-9.5 (-15.3, -3.3)**	-12.0 (-17.0, -6.7)***	-14.1 (-19.2, -8.5)***	< 0.001	--3.9 (-5.3, -2.6)***
Model 2 ^b	Ref.	-2.9 (-8.0, 2.5)	-8.2 (-13.6, -2.5)**	-8.5 (-13.3, -3.5)**	-10.2 (-15.2, -4.9)***	< 0.001	-2.7 (-4.0, -1.5)***
Model 3 ^c	Ref.	-3.0 (-8.0, 2.3)	-8.0 (-13.4, -2.3)**	-9.0 (-13.7, -4.1)***	-10.1 (-15.0, -4.9)***	< 0.001	-2.8 (-4.0, -1.5)***

Abbreviations: p, points; Ref., reference. GDF-15 = Growth Differentiation Factor 15 * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

a Model 1: Adjusted for sex (male, female), age, educational level (primary, secondary, university).

b Model 2: As Model 1 + for tobacco status (current, former, never), body mass index (kg/m^2), energy intake (kcal/day), type 2 diabetes mellitus, cardiovascular disease [myocardial infarction, stroke, or heart failure].

c Model 3: As Model 2 + for systolic blood pressure (mmHg), blood glucose (mg/dL), and blood LDL-cholesterol (mg/dL).

Supplementary Table S4. Secondary analyses. Mean (95% CI) percentage differences for the association of MEDLIFE index quartiles and GDF-15 by different subgroups ($n = 2,504$).

	Quartile 1 4 - 11 p	Quartile 2 12 - 13p	Quartile 3 14-15 p	Quartile 4 16 - 21 p	<i>p</i> -trend	<i>p</i> for interaction
Sex						
Men ($n = 1178$)	Ref.	-6.5 (-13.9, 1.5)	-12.1 (-18.5, -5.2)**	-14.2 (-21.2, -6.5)***	< 0.001	0.187
Women ($n = 1326$)	Ref.	0.1 (-6.6, 7.3)	-5.3 (-11.2, 1.1)	-6.0 (-12.9, 1.3)	0.029	
Age						
< 75 ($n = 1889$)	Ref.	-2.8 (-8.7, 3.6)	-7.6 (-12.9, -2.1)**	-8.4 (-14.1, -2.2)**	0.001	0.016
≥ 75 ($n = 615$)	Ref.	-1.2 (-10.8, 9.4)	-9.5 (-17.7, -0.5)*	-13.8 (-23.5, -2.8)*	0.003	
Educational level						
Primary ($n = 1590$)	Ref.	-4.6 (-10.4, 1.6)	-8.9 (-14.1, -3.4)**	-11.8 (-17.6, -5.6)***	< 0.001	0.891
Secondary ($n = 469$)	Ref.	2.5 (-10.8, 17.6)	-7.1 (-18.0, 5.4)	-8.5 (-21.0, 6.1)	0.072	
University ($n = 445$)	Ref.	1.4 (-11.9, 16.8)	-5.6 (-17.4, 7.8)	-2.5 (-15.7, 12.8)	0.418	
Smoking status						
Current ($n = 233$)	Ref.	-7.0 (-21.4, 10.2)	-14.8 (-27.5, 0.2)	-20.6 (-35.8, -1.8)*	0.013	0.084
Former ($n = 951$)	Ref.	0.1 (-8.8, 9.9)	-6.9 (-14.2, 1.0)	-8.0 (-16.1, 0.9)	0.017	
Never ($n = 1320$)	Ref.	-1.6 (-8.4, 5.6)	-6.5 (-12.6, 0.1)	-7.8 (-14.6, -0.4)*	0.010	
BMI						
< 25 ($n = 672$)	Ref.	-12.9 (-21.9, -2.7)*	-15.5 (-23.5, -6.6)**	-13.2 (-22.6, -2.8)*	0.013	0.218
25-29.9 ($n = 1179$)	Ref.	2.9 (-4.7, 11.1)	-4.4 (-11.0, 2.6)	-7.9 (-15.1, -0.1)*	0.005	
≥ 30 ($n = 653$)	Ref.	-1.8 (-11.0, 8.3)	-6.7 (-15.0, 2.5)	-8.9 (-18.1, 1.4)	0.043	
Cardiovascular disease						
No ($n = 2419$)	Ref.	-2.8 (-8.0, 2.6)	-8.4 (-12.9, -3.7)**	-9.4 (-14.4, -4.0)**	< 0.001	0.076
Yes ($n = 85$)	Ref.	-10.7 (-33.4, 19.9)	-14.7 (-35.9, 13.6)	-31.8 (-51.3, -4.5)*	0.032	
Type 2 Diabetes						
No ($n = 2046$)	Ref.	-3.8 (-9.0, 1.6)	-8.1 (-12.7, -3.3)**	-10.3 (-15.4, -5.0)***	0.004	0.831
Yes ($n = 458$)	Ref.	2.3 (-11.6, 18.5)	-10.9 (-22.5, 2.5)	-12.4 (-25.8, 3.5)	0.026	

Abbreviations: p, points; Ref., reference. BMI.; body mass index.

Adjusted for sex (male/female), age, educational level (primary, secondary, university), tobacco status (current, former, never), BMI, energy intake, type 2 diabetes mellitus, cardiovascular disease [myocardial infarction, stroke, or heart failure], systolic blood pressure, blood glucose and blood LDL levels. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Supplementary Table S5. Mean (95% CI) percentage differences for the association of MEDLIFE index quartiles and GDF15 excluding participants with cardiovascular disease, type 2 diabetes ($N = 1,985$) and/or BMI > 30.

	Quartile 1 4 - 11 p	Quartile 2 12 - 13p	Quartile 3 14-15 p	Quartile 4 16 – 21 p	<i>p</i> -trend
Participants without CVD and diabetes ($n = 1985$)					
<i>n</i>	390	508	570	517	
Model 1 ^a	Ref.	-5.0 (-10.3, 0.6)	-9.4 (-14.0, -4.6)***	-11.9 (-16.9, -6.5)***	< 0.001
Model 2 ^b	Ref.	-3.9 (-9.2, 1.7)	-8.2 (-12.8, -3.3)**	-9.9 (-15.1, -4.4)**	< 0.001
Model 3 ^c	Ref.	-3.8 (-9.0, 1.8)	-8.0 (-12.7, -3.2)**	-9.6 (-14.7, -4.1)**	< 0.001
Participants without BMI ≥ 30 ($n = 1851$)					
<i>n</i>	364	489	537	461	
Model 1 ^a	Ref.	-6.0 (-12.3, 0.8)	-12.6 (-18.0, -6.9)***	-15.0 (-20.9, -8.6)***	< 0.001
Model 4 ^d	Ref.	-3.1(-9.1, 3.3)	-8.2(-13.5, -2.7)**	-10.1(-16.0, -3.9)**	< 0.001
Model 5 ^e	Ref.	-2.9 (-8.9, 3.4)	-8.7 (-13.8, -3.2)**	-10.3 (-16.1, -4.1)**	< 0.001
Participants without CVD, diabetes, and BMI ≥ 30 ($n = 1518$)					
<i>n</i>	284	391	448	395	
Model 1 ^a	Ref.	-5.2 (-11.4, 1.4)	-10.3 (-15.7, -4.7)**	-13.6 (-19.4, -7.4)***	< 0.001
Model 2 ^b	Ref.	-3.3 (-9.6, 3.4)	-8.2 (-13.6, -2.4)**	-10.8 (-16.8, -4.4)**	< 0.001
Model 3 ^c	Ref.	-2.8 (-9.1, 3.9)	-8.1 (-13.5, -2.3)**	-10.6 (-16.6, -4.3)**	< 0.001

Abbreviations: p, points; Ref., reference. BMI.; body mass index * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

a Model 1: Adjusted for sex (male, female), age, educational level (primary, secondary, university).

b Model 2: As Model 1 + for tobacco status (current, former, never), BMI (kg/m²), energy intake (kcal/day).

c Model 3: As Model 2 + for systolic blood pressure (mmHg), blood glucose (mg/dL), and blood LDL levels (mg/dL).

d Model 4: As Model 1 + for tobacco status (current, former, never), BMI (kg/m²), energy intake (kcal/day), type 2 diabetes mellitus, cardiovascular disease [myocardial infarction, stroke, or heart failure].

e Model 5: As Model 2 + for systolic blood pressure (mmHg), blood glucose (mg/dL), and blood LDL levels (mg/dL).

Supplementary Table S6. Secondary analyses. Mean (95% CI) percentage differences for the association of MEDLIFE blocks quartiles, MEDLIFE quartiles and GDF-15 ($N = 2,504$).

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	<i>p</i> -trend	Per 2-point increase
<i>Block 1: Mediterranean food consumption</i>						
Excluding legumes	Ref.	-0.5 (-4.4, 3.6)	-5.0 (-9.8, 0.1)	-0.8 (-6.3, 5.0)	0.295	-1.6 (-3.5, 0.4)
Excluding low-fat dairy	Ref.	1.7 (-2.6, 6.2)	-3.9 (-8.4, 0.8)	-0.7 (-5.5, 4.3)	0.358	-1.3 (-3.3, 0.7)
Excluding legumes and low-fat dairy	Ref.	-1.2 (-5.6, 3.5)	-1.7 (-6.2, 2.9)	-3.9 (-8.1, 0.6)	0.096	-2.1 (-4.1, -0.0)*
MEDLIFE index						
Excluding legumes	Ref.	-7.0 (-10.9, -3.0)**	-10.1 (-14.1, -5.9)***	-10.4 (-14.9, -5.6)***	< 0.001	-3.1 (-4.4, -1.9)***
Excluding low-fat dairy	Ref.	-7.9 (-11.8, -3.8)***	-7.7 (-11.8, -3.4)**	-11.7 (-16.1, -7.1)***	< 0.001	-3.0 (-4.3, -1.7)***
Excluding legumes and low-fat dairy	Ref.	-7.7 (-11.4, -3.8)***	-8.4 (-13.2, -3.3)**	-11.0 (-14.9, -6.8)***	< 0.001	-3.4 (-4.7, -2.1)***

Adjusted for sex, age, educational level (primary, secondary, university), tobacco status (current, former, never), body mass index (kg/m²), energy intake (kcal/day), type 2 diabetes mellitus, cardiovascular disease [myocardial infarction, stroke, or heart failure], systolic blood pressure (mmHg), blood glucose (mg/dL), and blood LDL levels (mg/dL) and the item excluded from the general score in each case. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Supplementary Figure S1. Flow diagram of included participants from the Seniors ENRICA-2 cohort.

