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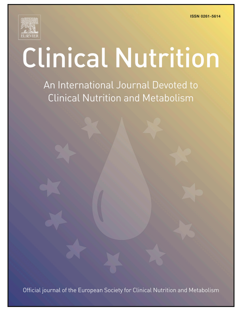

Adherence to a mediterranean diet is associated with lower prevalence of osteoarthritis: Data from the osteoarthritis initiative

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ADHERENCE TO A MEDITERRANEAN DIET IS ASSOCIATED WITH LOWER PREVALENCE OF OSTEOARTHRITIS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

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ABSTRACT

Background & Aims: The Mediterranean diet appears to be beneficial for several medical conditions, but data regarding osteoarthritis (OA) are not available. The aim of this study was to investigate if adherence to the Mediterranean diet is associated with a lower prevalence of OA of the knee in a large cohort from North America.

Methods: 4,358 community-dwelling participants (2,527 females; mean age: 61.2 years) from the Osteoarthritis Initiative were included. Adherence to the Mediterranean diet was evaluated through a validated Mediterranean diet score (aMED) categorized into quartiles (Q). Knee OA was diagnosed both clinically and radiologically. The strength of the association between aMED (divided in quartiles) and knee OA was investigated through a logistic regression analysis and reported as odds ratios (OR) with 95% confidence intervals (CIs), adjusted for potential confounders.

Results: Participants with a higher adherence to Mediterranean diet had a significantly lower prevalence of knee OA compared to those with lower adherence (Q4: 25.2% vs. Q1: 33.8%; p<0.0001). Using a logistic regression analysis, adjusting for 10 potential confounders with those in the lowest quartile of aMED as reference, participants with the highest aMED had a significant reduction in presence of knee OA (OR,0.83; 95% CIs: 0.69-0.99, p=0.04). Among the individual components of Mediterranean diet, only higher use of cereals was associated with lower odds of having knee OA (OR: 0.76; 95% CI: 0.60-0.98; p=0.03).

Conclusions: Higher adherence to a Mediterranean diet is associated with lower prevalence of knee OA. This remained when adjusting for potential confounders.

Keywords : osteoarthritis; Mediterranean diet; aged; healthy ageing; lifestyle.

INTRODUCTION

The term 'Mediterranean diet' encompasses the traditional dietary habits of people from across the Mediterranean region and is usually depicted as a food pyramid[1]. The Mediterranean-style diet is an established healthy-eating diet pattern that has consistently demonstrated to have beneficial effects on musculoskeletal[2], cardiovascular[3], metabolic[4], and cognitive[5] diseases.

Recent global surveys of disease surveys have demonstrated that whilst average life expectancy is increasing[6,7], the number of years people that live with chronic conditions is also rising. One of the most common causes of years lived with disability are chronic musculoskeletal disorders [8,9]. Osteoarthritis (OA) of the knee is the 11th highest contributor to global disability[10]. The worldwide prevalence of OA has been estimated as 10% in men and 20% in women over the age of 60 years [11].

To the best of the author's knowledge, no analyses have investigated the relationship between Mediterranean diet and OA[12]. The Framingham Osteoarthritis Cohort study previously reported that participants with higher vitamin C and E and β-carotene intake may be less likely to have progressive knee OA[13]. However this is only one of the few studies investigating the effect of diet on OA in humans. In mice, the use of olive oil, an essential component of Mediterranean diet, appears to be associated with a lower articular cartilage degradation[14] suggesting a potential role of diets rich in this component for OA.

Given the potential benefits of the Mediterranean diet on several diseases and the absence of data on OA, this study aimed to investigate whether adherence to a Mediterranean diet is associated with lower prevalence of knee OA in a large cohort of North American people from the Osteoarthritis Initiative dataset. We hypothesized that higher adherence to Mediterranean diet was associated with lower prevalence of knee OA.

MATERIALS AND METHODS

Data source and subjects

Data were gathered from the Osteoarthritis Initiative (OAI) database. The OAI is a publically available database open at http://www.oai.ucsf.edu/. Within the OAI, potential participants were recruited across four clinical sites in the United States of America (USA) (Baltimore, MD; Pittsburgh, PA; Pawtucket, RI; and Columbus, OH) between February 2004 and May 2006. People were eligible in the OAI who either: (1) had knee OA with knee pain for a 30-day period in the past 12 months or (2) were at high risk of developing knee OA [15]. For the current paper, we used the data recorded during baseline and screening evaluations (November 2008).

All participants provided informed written consent. The OAI study was given full ethical approval by the institutional review board of the OAI Coordinating Center, at University of California in San Francisco.

Adherence to the Mediterranean diet (exposure)

Dietary pattern was analysed using a validated tool, the Block Brief 2000 food frequency (FFQ) questionnaire during the baseline visit [16]. Seventy items were assessed for checking the usual food and beverage consumption over the past year. The frequency of consumption was reported at nine levels of intake from “never” to “every day”. In addition, were seven dietary behavior questions were available regarding food preparation methods and fat intake, one question on fiber intake, and 13 questions on vitamin and mineral intakes.

Adherence to the Mediterranean diet was evaluated using the Mediterranean diet score (aMED) as proposed by Panagiotakos et al.[17]. This score is based on a food frequency questionnaire which was recorded during the baseline OAI visit. The aMED takes into consideration several foods commonly consumed within the Mediterranean diet. Each food has a score from 0 (less adherent) to 5 (better adherence); the total score ranges from 0 to 55, with higher values indicating higher adherence to a Mediterranean diet. Cereals (e.g. bread, pasta, rice), potatoes, fruits, vegetables, legumes (e.g. peas, beans), fish were categorized according to servings/month in: 0=never; 1=1 to 4 servings for month; 2=5 to 8; 3=9 to 12; 4=13 to 18; 5= more than 18 servings/month. Since there was no information regarding the consumption of whole cereals vs. refined cereals as this was collected, all types of grains were considered in the present analyses under the same heading. The consumption of red meat, poultry and full fat dairy products (e.g. milk cheese, yogurt) were categorized as: 0=more than 18 servings/month; 1=13 to 17 servings for month; 2=9 to 12; 3=5 to 8; 4=1 to 4; 5= never). The use of olive oil was categorised as the times used in a week in: 0=never; 1=rare; 2 ≤1/weekly; 3= 2 times/weekly; 4=3 to 6; 5=daily. Finally, alcoholic beverages were categorised as: 0≥700 ml/day or 0; 1600 to 699 ml/day; 2=500 to 599 ml/day; 3=400 to 499 ml/day; 4=300 to 399 ml/day; 5=< 300 ml/day.

Since there are no agreed cut-offs scores for higher aMED adherence, we divided the population in to quartiles using 25, 28 and 32 points in: aMED<25, 26-28, 29-32, and >33.

Outcome

The primary analysis was to determine the presence of knee OA, defined as the combination in the clinical reporting and assessment of pain and stiffness (i.e. pain, aching or stiffness in or around the knee on most days during the last year), and radiographical OA on the baseline fixed flexion radiograph based on the presence of tibiofemoral osteophytes (correspondent to Osteoarthritis Research Society International atlas grades 1-3, clinical center reading). In the OAI, the presence of pain, stiffness, and physical functioning (or disability) due to OA was assessed through the WOMAC (Western Ontario and McMaster Universities Arthritis Index). Briefly, the responses for each subscale (pain, stiffness, disability) are categorized on a five-point Likert scale ranging from none (0 points) to extreme (4 points) [18]. The maximum possible score is 68, and the final score was normalized to 100 (range 0–100), with higher scores reflecting greater activity limitations. [18]

Covariates

We identified 10 potential self-reported confounders that we considered when assessing the relationship between aMED and knee OA. These included body mass index (BMI); physical activity evaluated using the Physical Activity Scale for the Elderly scale (PASE);[19] race; smoking habit, educational attainment level and yearly income (< or ≥ $50,000 and missing data).

Validated general health measures of self-reported comorbidities were assessed through the modified Charlson comorbidity score[20]. Among the medical morbidities assessed through the Charlson co-morbidity score, we reported descriptively the prevalence of some common diseases in North American people, namely fractures, heart attack and failure, stroke, chronic obstructive pulmonary disease, diabetes and cancer. [21]

Statistical analyses

For continuous variables, normal distributed data assumptions were tested using the Kolmogorov-Smirnov test. The data were shown as means ±standard deviations (SD) for quantitative measures, and frequency and percentages for all discrete variables. For continuous variables, differences between the means of the covariates by aMED quartiles were calculated using an Analysis of Variance (ANOVA); chi-square test was applied for discrete variables. Levene's test was used to test the homoscedasticity of variances and, if its assumption was violated, then Welch's ANOVA was used. Post-hoc analyses and Bonferroni adjustment were applied to compare data.

Next, in order to consider the relationship between knee OA and aMED scores, a logistic regression was conducted with the presence of knee OA considered as the outcome and the aMED as the exposure and categorized in quartiles and taking in Q1 (=lowest aMED) as the reference group. The basic model was not adjusted for any confounders, whilst the fully adjusted model included the following adjustments: age (as continuous); sex; race (whites vs. others); BMI (as continuous); education (degree vs. others); smoking habits (current and previous vs. others); yearly income (categorized as $\geq$ or < 50,000$ and missing data); Charlson comorbidity index; PASE score (as continuous), total energy intake (as continuous). Multi-collinearity among covariates was assessed through variance inflaction factor (VIF), taking a cut-off of two as reason of exclusion, but no covariate was excluded for this reason. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were finally calculated to estimate the strength of the associations between aMED (categorised as quartiles) and knee OA. Similarly, we performed the same analyses taking individual components of Mediterranean diet as exposure and dividing the adherence in low (score 0-1-2 points over 5 available) and high (4-5).

The analyses for the paper were undertaken with the SPSS software version 21.0 for Windows (SPSS Inc., Chicago, Illinois). All of the statistical tests were two-tailed and a level of <0.05 was considered as significant. .

RESULTS

Sample selection

The OAI dataset includes a total of 4,796 North American participants. After excluding 109 participants with hip or knee replacement, 175 participants due to missing aMED data and 62 with unreliable caloric intake (<500 or >5000 Kcal/day), 4,358 participants were finally included in the current analyses.

Descriptive characteristics

Among the final sample of 4,358 participants, 1,831 were males and 2,527 females. Mean age was 61.2 years (±9.1 years; range: 45-79). Mean aMED score was 28.1 points (5.1 points; range: 5-44). The prevalence of OA (diagnosed according to the presence of pain, stiffness and radiographical tibiofemoral osteophytes) in this cohort was 29.1%.

Table 1 illustrates the baseline characteristics by aMED quartiles. Those in the highest quartile (reflecting higher adherence to Mediterranean diet) were older, more likely to be female, white, with higher educational level and income than those within the other quartiles. Those in the highest quartile of aMED had a lower BMI values) and had fewer medical morbidities, even if these participants reported a higher prevalence of cancer (**Table 1**).

Adherence to Mediterranean diet and osteoarthritis

As shown in **Table 2**, there was a significant lower presence of knee OA in those with higher aMED scores compared to other quartiles (Q4: 25.2% vs. Q1: 33.8%; p<0.0001). Using a logistic regression analysis adjusting for 10 potential confounders, and taking those with the lowest adherence to Mediterranean diet as reference (=Q1), participants with the highest adherence to Mediterranean diet had a significantly reduced probability of knee OA (OR=0.83; 95% CI: 0.69-0.99, p=0.04; **Table 2**). Other factors significantly associated with knee OA in the multivariate analysis were: BMI (for each increase in one Kg/m^2: OR=1.08; 95%CI: 1.06-1.10, p<0.0001), non-white ethnicity (OR=1.60, 95%CI: 1.35-1.90, p<0.0001) and below college level education (OR=1.23; 95%CI: 1.04-1.44; p=0.03), while age was marginally significant (for each year: OR=1.008; 95%CI: 1.00-1.02, p=0.05).

Table 3 illustrates the effect of individual components of Mediterranean diet and their association with the presence of knee OA. After adjusting for potential confounders, only higher use of cereals was associated with a significantly reduced probability of knee OA (OR=0.76; 95%CI: 0.60-0.98; p=0.03).

DISCUSSION

In this large cross-sectional study, we found evidence to suggest that North American people who are more adherent to a Mediterranean diet had a significantly lower presence of knee OA. After adjusting for 10 potential confounders, those with the highest aMED score (i.e. more adherent to the Mediterranean diet) had a significant lower prevalence of knee OA by approximately 17%.

Participants with a higher adherence to a Mediterranean diet had significantly lower BMI values and fewer medical morbidities (particularly diabetes), higher education level and greater income than other participants. This suggests that these factors may also influence the prevalence of knee OA in individuals with higher adherence to Mediterranean diet. At the same time, such participants had a significantly higher presence of two important risk factors for knee OA, namely being female and older in age [22]. The apparent paradox of higher prevalence of cancer among those with higher aMED score could be due to a change toward a healthier diet among those diagnosed with cancer.[23] This discrepancy, however, indirectly confirmed a significant and independent association between higher adherence to this dietary pattern and lower prevalence of knee OA. After adjusting for potential confounders (including severity of comorbidity and social and economic factors), the association between aMED and knee OA remained statistically significant. The multivariate analysis suggests that obesity, education and race are associated with prevalent OA, also taking in account other potential confounders. Thus, since our research suggests that Mediterranean diet is associated with a lower risk of knee OA, obese, less educated and non-white people should be monitored in order to encourage them to follow a healthier diet.

Whilst our data is cross sectional and causality cannot be determined, there may be a number of mechanisms that might explain the relationship we observed. Firstly, a higher adherence to a Mediterranean diet is linked to a decrease in inflammation.[24] Inflammation is acknowledged as an important pathway in the development of knee OA.[25] Therefore the anti-inflammatory properties derived from the phytochemicals in a Mediterranean diet may modify this pathway.[14] Secondly, a Mediterranean diet may influence a reduction in oxidative stress markers.[26] These have been purported to influence the onset of OA though providing increasing levels of collagen type II and aggrecan expression whilst inhibiting apoptosis-related proteins expression, providing a chondroprotective effect.[27,28] Finally, Mediterranean diet could play a role in the remodeling of extracellular matrix (ECM)[29] promoting effective repair of the ECM which is frequently defective in those who develop and present with OA. All factors could play an important role in the development of knee OA, and provide a physiological rationale for these findings.[30]

Previous literature on Mediterranean diet and rheumatic diseases has largely focused on population with rheumatoid arthritis. In this case, several observational[31–34] and interventional[35–37] studies suggest a protective role for some components of Mediterranean diet on rheumatoid arthritis indirectly suggesting a potential role also for OA. However the pathogenesis of this condition is very different to OA, thereby making these finding important. Whilst a subset of people with OA may present with an inflammatory phenotype to their disease process, this is not uniform[38]. Accordingly, these results suggest that the protective mechanism which a Mediterranean diet is suggestive to confer may not be solely attributed to the inflammatory pathway[37], but to some other pathophysiological or epigenetic mechanism.

Previously there had been limited investigating into the impact of Mediterranean diet on knee OA. Animal models have shown that the supplementation of olive oil, an essential component of Mediterranean diet, may preserve the articular cartilage, particularly when prescribed in combination with physical activity[14]. From our analyses, there was no independent association between the use of olive oil and knee OA. Conversely, on assessing the individual components of a Mediterranean diet, only higher use of cereals was associated with lower probability of knee OA. There is limited evidence around the consumption of cereals and the relationship to knee OA.

However it could hypothesized that a higher intake of cereals could contribute to a lower prevalence of knee OA through anti-inflammatory and anti-oxidative stress action, but also due to these being good sources of vitamins and minerals (such as magnesium[39,40]) which may play a role in lower prevalence of knee OA. However it should be noted that pasta and rice are often consumed in association with olive oil and vegetables and, as supported in previous studies[1,41], not the single components, but the combination of the different ingredients of the Mediterranean diet is responsible for the protective effect and the health benefit observed with this dietary pattern.

The analysis suggests a negative association between Mediterranean diet and knee OA, suggesting a possible a protective effect on knee OA. Clinically, these findings indicate that for those at higher risk of developing knee OA, recommendation and promotion of such a diet may be warranted. Further investigation to identify which types of individuals are most to benefit from this recommendation and what the mechanisms and contexts should be in which to implement such dietary advice, should be undertaken.

The findings of our research should be considered within its limitations. The main is the cross-sectional nature of our research therefore precluding any consideration of a potential causal relationship between Mediterranean diet and knee OA, making residual confounding very likely. Second, we were not able to see the influence of bio-humoral markers (e.g. inflammation) in the association between Mediterranean diet and knee OA, but these markers could be of importance. A third limitation is that the medical conditions are self-reported and this could introduce a bias. Finally, we have used a slight modified version of a previous Mediterranean diet adherence[17] and also this choice could introduce another bias. On the contrary, among the strengths of our work, we could say the large sample size included and the fact this is the first epidemiological study reporting data on the impact of this dietary pattern on a frequent condition, like knee OA.

To conclude, the results from our paper indicate that a higher adherence to a Mediterranean diet is associated with lower prevalence of knee OA, even after adjusting for several important confounders. Further longitudinal research is required to confirm/ refute our findings and explore potential pathophysiological mechanisms.

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Conflict of interest: none.

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Table 1. Descriptive findings of the participants by adherence to Mediterranean diet.

	Q1 (n=1328) aMED<25	Q2 (n=939) aMED 26-28	Q3 (n=1236) aMED 29-32	Q4 (n=856) aMED >33	P value[*]
aMED score	22.1 (2.8)	27.1 (0.9)	30.4 (1.1)	35.0 (2.0)	<0.0001
Energy intake (Kcal/day)	1399.7 (600.7)[a,b,c]	1409.9 (566.7)[a,d,e]	1436.3 (577.0)[b,d,f]	1419.3 (518.7)[c,e,f]	0.43
Age (years)	59.3 (8.9)	61.3 (9.1)[g]	62.0 (9.2)[g,h]	62.9 (9.1) [h]	<0.0001
PASE (points)	161.1 (89.9) [i,l.m]	160.9 (80.3) [i,n,o]	160.9 (81.0) [l,n,p]	163.7 (82.2)[m,o,p]	0.86
Females (n, %)	714 (53.8)	552 (58.8)	731 (59.1)	325 (62.0)	0.001
White race (n, %)	949 (71.5)	756 (80.5)	1048 (84.8)	750 (87.6)	<0.0001
Smoking (previous/current)	713 (53.7)	473 (50.4)	664 (53.7)	437 (51.1)	0.27
Graduate degree (n, %)	323 (24.3)	284 (30.2)	391 (31.6)	327 (38.2)	<0.0001
Yearly income (< 50,000 $)	718 (54.1)	560 (59.6)	750 (60.7)	554 (64.7)	<0.0001
Medical conditions					
BMI (Kg/m^2)	29.6 (4.9)	28.9 (4.7)	28.2 (4.7)	27.4 (4.5)	<0.0001
Fractures (n, %)	208 (15.7)	181 (19.3)	223 (18.2)	154 (18.0)	0.14
Heart attack (n, %)	34 (2.6)	14 (1.5)	13 (1.1)	24 (2.8)	0.007

	Q1 (n=1328) aMED<25	Q2 (n=939) aMED 26-28	Q3 (n=1236) aMED 29-32	Q4 (n=856) aMED >33	P value*
Heart failure (n, %)	37 (2.8)	14 (1.5)	16 (1.3)	17 (2.0)	0.03
Stroke (n, %)	44 (3.4)	30 (3.2)	28 (2.3)	26 (3.1)	0.41
COPD (n, %)	34 (2.6)	20 (2.2)	24 (2.0)	18 (2.1)	0.72
Diabetes (n, %)	128 (9.9)	87 (9.4)	72 (5.9)	41 (4.9)	<0.0001
Cancer (n, %)	32 (2.5)	40 (4.4)	43 (3.5)	47 (5.5)	0.002
Presence of one or more disease (n, %)	347 (26.3)	247 (26.5)	259 (21.1)	211 (24.7)	0.03

Notes: The data are presented as mean (with standard deviations) for continuous variables and number (with percentage).

[*] P values were calculated using the Analysis of Variance for continuous and chi-square test for categorical ones, respectively.

[a-p] Means not sharing a superscript letter are significantly different at a Bonferroni corrected P value of 0.05/6 (=0.0083).

Abbreviations: aMED: adherence to Mediterranean diet score; PASE: Physical Activity Scale for the Elderly; BMI: body mass index; OA: osteoarthritis; COPD: chronic obstructive pulmonary disease.

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Table 2. Association between adherence to Mediterranean diet and presence of knee osteoarthritis.

	Number of Events/number of participants	Prevalence (%)	Unadjusted OR (95%CI)	Unadjusted P value	Fully-adjusted OR (95%CI)	Fully-adjusted P value
Q1 (aMED<25)	448/1328	33.8	1 [reference]		1 [reference]	
Q2 (aMED 26-28)	276/939	29.4	0.82 (0.68-0.98)	0.03	0.90 (0.75-1.09)	0.28
Q3 (aMED 29-32)	330/1236	26.7	0.70 (0.59-0.83)	<0.0001	0.85 (0.70-1.05)	0.13
Q4 (aMED>33)	216/856	25.2	0.66 (0.55-0.80)	<0.0001	**0.83 (0.69-0.99)**	**0.04**

Notes:

All the data are presented as odds ratios (ORs) with their 95% confidence intervals.

*Fully-adjusted model included as covariates: age (as continuous); sex; race (whites vs. others); body mass index (as continuous); education (degree vs. others); smoking habits (current and previous vs. others); yearly income (categorized as ≥ or < 50,000$ and missing data); Physical Activity Scale for Elderly score (as continuous); Charlson co-morbidity index; daily energy intake.

Abbreviations: CI: confidence intervals; OR: odds ratio.

Table 3. Singular components of Mediterranean diet and presence of knee osteoarthritis.

	Number of events/number of participants (=prevalence, %) [higher adherence; 4-5 points]	Number of events/number of participants (=prevalence, %) [higher adherence; 0-3 points]	Unadjusted OR (95%CI)	P value	Fully-adjusted OR (95%CI)	P value
Cereals	1152/4009 (=28.7%)	118/349 (=33.8%)	0.82 (0.64-1.03)	0.09	**0.76 (0.60-0.98)**	**0.03**
Potatoes	127/465 (=27.3%)	1142/3891 (=29.3%)	0.90 (0.72-1.12)	0.34	0.82 (0.65-1.04)	0.10
Fruits	886/3170 (=27.9%)	383/1187 (=32.3%)	0.81 (0.70-0.94)	0.005	0.89 (0.76-1.04)	0.13
Vegetables	1208/4172 (=29.0%)	61/184 (=33.2%)	0.84 (0.61-1.15)	0.27	0.97 (0.69-1.35)	0.84
Legumes	293/871 (=33.6%)	976/3485 (=28.0%)	1.33 (1.13-1.56)	0.001	1.17 (0.98-1.38)	0.08
Fish	126/371 (=34.0%)	1137/3962 (=28.7%)	1.30 (1.04-1.64)	0.02	1.29 (0.99-1.64)	0.06
Meat	154/587 (=26.2%)	1116/3771 (=29.6%)	0.83 (0.68-1.01)	0.07	0.99 (0.80-1.23)	0.95
Poultry	525/1879 (=27.9%)	738/2454 (=30.1%)	0.89 (0.78-1.02)	0.10	1.05 (0.90-1.21)	0.55
Dairy	71/223 (=31.8%)	1198/4134 (=29.0%)	1.13 (0.84-1.52)	0.42	0.97 (0.71-1.33)	0.86
Alcohol	508/1988 (=25.6%)	758/2355 (=32.2%)	0.72 (0.63-0.82)	<0.0001	0.88 (0.77-1.02)	0.09
Oil	147/558 (=26.3%)	1107/3759 (=29.4%)	0.87 (0.71-1.07)	0.19	0.99 (0.80-1.21)	0.88

Notes:

All the data are presented as odds ratios (ORs) with their 95% confidence intervals.

In all the analyses, we considered higher adherence to a component (as 4 or 5 points) vs. lower (0 to 3; reference).

*Fully-adjusted model included as covariates: age (as continuous); sex; race (whites vs. others); body mass index (as continuous); education (degree vs. others); smoking habits (current and previous vs. others); yearly income (categorized as ≥ or < 50,000$ and missing data); Physical Activity Scale for Elderly score (as continuous); Charlson co-morbidity index; daily energy intake.

Abbreviations: CI: confidence intervals; OR: odds ratio.