Lipids in Health and Disease

RESEARCH

Open Access

Association of omega-3, omega-6 fatty acids intakes and omega-6: omega-3 ratio with the prevalence of suicidal ideation: mediating role of C-reactive protein

Hao Lin[1†], Zhibin Bai[1†], Daoke Wu[2], Qi Yang[1] and Shuangshuang Qu[3*]

Abstract

Background Although dietary omega fatty acids have been recognized for positive effects on mental health, the specific association between omega fatty acids intake and suicidal ideation remains ambiguous. This study aims to explore the potential association between the prevalence of suicidal ideation and dietary omega fatty acids intake in American adults.

Methods The data of 27,944 American adults collected from National Health and Nutrition Examination Survey (NHANES) were analyzed in this study. To assess the association between dietary omega fatty acids intake and suicidal ideation as measured by Item 9 of PHQ-9, logistic regression, restricted cubic spline regression, and stratified analyses, mediation analyses were employed.

Results Logistic regression analyses indicate that the intakes of omega-3 and omega-6 fatty acids were inversely associated with the prevalence of suicidal ideation, and dietary omega-6/omega-3 ratio was positively associated with the prevalence of suicidal ideation. Subgroup analyses further revealed a stronger association between suicidal ideation and omega fatty acids intake in individuals with a history of stroke. Furthermore, a saturation effect and non-linear association were identified between omega-3 and omega-6 fatty acids intake and the prevalence of suicidal ideation, characterized by an L-shaped curve with an inflection point at 1.36 g/d, 13.69 g/d, respectively. Notably, C-reactive protein (CRP) partially mediated the association between omega-6, omega-3 fatty acids intake and suicidal ideation by a proportion of 3.8% and 4.0%.

Conclusion The findings of this study suggest that higher omega-3 and omega-6 fatty acids intake and lower omega-6/omega-3 ratio is associated with a declined prevalence of suicidal ideation.

Clinical trial number Not applicable.

Keywords Dietary omega fatty acids intake, Suicidal ideation, Chronic inflammation, PHQ-9, Depression

[†]Hao Lin and Zhibin Bai contributed equally to this work.

*Correspondence:
Shuangshuang Qu
2670123661@qq.com

[1]Department of Gastroenterology, Pingyang Hospital of Wenzhou Medical University, Wenzhou City, China
[2]Digestive Endoscopy Center, Pingyang Hospital of Wenzhou Medical University, Wenzhou City, China
[3]Department of Nursing, Pingyang Hospital of Wenzhou Medical University, Wenzhou City, China

Introduction

Globally, suicide represents a major public health issue accounting for over 700,000 deaths annually [1]. In response, World Health Organization (WHO) has enacted a strategic initiative with the objective of declining suicide mortality by 33% across each member state from 2013 to 2030 [2]. According to ideation-to-action models of suicide, suicidal ideation can serve as a pivotal precursor to both suicide attempts and completed suicides [3]. Empirical studies have demonstrated that the probability of committing suicide in the first year following the onset of suicidal ideation is approximately 1.40% in psychiatric patients [4]. Consequently, the identification of modifiable risk factors associated with suicidal ideation is crucial for the effective prevention of suicide. Although existing literature has identified various risk factors, such as personality traits, mood disorders, and sociodemographic characteristics [5, 6], many of which are frequently unmodifiable.

Epidemiologic studies have shown that depression is related to genetic and environmental factors, especially dietary factors [7–9]. Moreover, specific dietary interventions may be employed as routine treatments, potentially exerting beneficial effects on psychiatric conditions [10, 11]. Studies have shown that the consumption of nutrients including polyunsaturated fatty acids (PUFAs), folic acid, vitamin B12, zinc, and vitamin D may mitigate the prevalence of psychiatric disorders such as depression [12–14].

PUFAs are essential lipids that must be acquired from dietary sources [15]. Within this category, omega-6 and omega-3 fatty acids constitute the two primary families of PUFAs, each playing vital roles in neurodevelopment and function, cardiovascular health, immune system enhancement, inflammation modulation, cancer prevention, and mental health maintenance, in other physiological processes [16, 17]. Some studies with limited sample sizes suggest that omega-3 fatty acids intake may reduce the prevalence of suicidal ideation in individuals with depression [18–20]. Nevertheless, the association between dietary intake of omega-3 and omega-6 fatty acids and the prevalence of suicidal ideation in the general population has not been inadequately explored. Furthermore, there is a lack of research that clearly delineates the specific intake levels of omega-3 and omega-6 fatty acids and their association with the prevalence of suicidal ideation.

There is research evidence that suicidal ideation is significantly associated with chronic systemic inflammation [21]. Chronic inflammation can mediate a permanent reorganization of inflammatory neurotransmitter pathways, resulting in the transition from acute to chronic pain and promoting depression, anxiety, and suicidal ideation [22–24]. Furthermore, there is a strong relationship between diet and chronic systemic inflammation; dietary omega-3 fatty acids have been shown to effectively reduce inflammation by decreasing levels of inflammatory biomarkers such as interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-α), and CRP [25, 26].

Consequently, this study aims to explore the association between dietary omega-3 and omega-6 fatty acids, along with their ratio, and the prevalence of suicidal ideation, utilizing data from NHANES. Additionally, the secondary goal was to analyze whether dietary omega fatty acids intake mediated the intended association through the CRP. The results may provide valuable insights for the clinical management and prevention of suicidal ideation.

Methods

Research subjects and design

NHANES, administered by National Center for Health Statistics (NCHS) [27], is an extensive study to assess the association between nutrition, disease prevention, and health promotion. This survey is conducted biennially by taking physical examinations, interviews, with a variety of sections encompassing demographic, dietary, laboratory data, and examinations. Further details about the NHANES database can be accessed at http://www.cdc.gov/nhanes.

In this study, the data from ten cycles of the NHANES dataset during the period from 1999 to 2018 were analyzed through a retrospective analysis. Subjects aged 18 years old or older ($n = 59204$) were included in this study. And according to the exclusion criteria, subjects lacking the data of suicidal ideation ($n = 27880$), those without the data of dietary omega fatty acids intake ($n = 1016$), pregnant females ($n = 599$), those without the data of body mass index (BMI) and other covariable ($n = 1765$) were excluded. Consequently, the final samples were comprised of 27,944 subjects, as illustrated in Fig. 1.

Assessment of dietary Omega fatty acids intake

Data on the unsaturated fatty acid and total energy intake of the subjects in this study were obtained from the dietary module in the NHANES. Dietary omega fatty acids and total energy intake were assessed on two distinct occasions: The first assessment was conducted in person, while the second was conducted by call. Owing to substantial data deficiencies encountered during the second round of interviews, the analysis in this study exclusively utilized the dietary information collected during the initial session [28].

This study also aims to comprehensively identify the various components of omega-3 and omega-6 fatty acids. The dietary omega-3 fatty acids examined included eicosapentaenoic acid (EPA, 20:5), alpha-linolenic acid (ALA, 18:3), docosahexaenoic acid (DHA, 22:6), and docosapentaenoic acid (DPA, 22:5), as well as additional

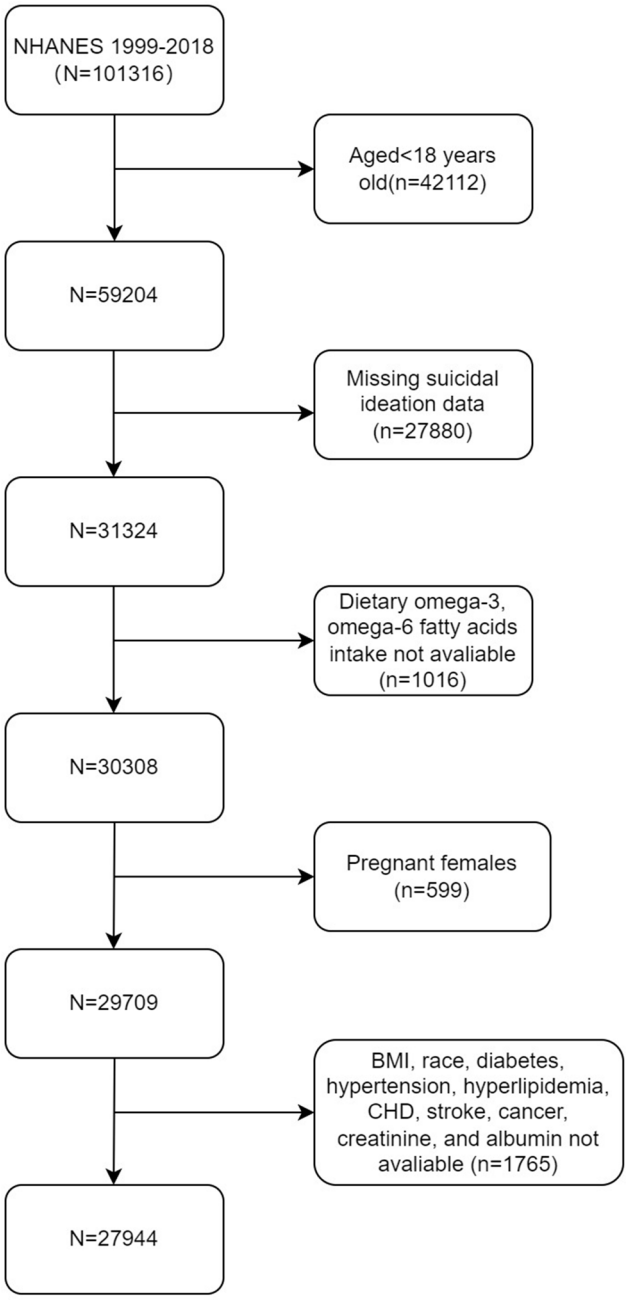

Fig. 1 Flowchart of the sample selection from the 1999–2018 NHANES

forms such as stearidonic acid (SDA, 18:4). The dietary omega-6 fatty acids analyzed comprised arachidonic acid (AA, 20:4) and linoleic acid (LA, 18:2) [29].

Assessments on suicidal ideation

Suicidal ideation was assessed by analyzing responses to Item 9 of Patient Health Questionnaire-9 (PHQ-9), a questionnaire which inquires: "How often have you engaged in self-harm or considered that it would be preferable to die over the past two weeks?" Subjects scored from 1 to 3 were classified as experiencing suicidal ideation, whereas those scored zero were classified as not experiencing suicidal ideation [30].

Covariable

Based on previous studies [30] and variables provided by NHANES, covariable of interest including self-reported health information, physical examination results, and sociodemographic variables were identified as potential confounding factors. Trained interviewers collected self-reported health information and sociodemographic variables, including smoking status, past medical history, and alcohol abuse during Mobile Examination Center (MEC) and household interviews. Sociodemographic variables included education level, age, marital status, gender, family poverty income ratio (PIR), and race. Physical examination results, including blood pressure and BMI, were collected by trained health technicians at MEC. Additionally, blood samples were collected at MEC for the assessment of albumin, CRP, creatinine, total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-C). The definitions for diabetes mellitus, hypertension, and hyperlipidemia were consistent with those previously reported [31]. The incidence of cancers, stroke, and coronary heart disease (CHD) was determined through self-reported diagnoses. Alcohol abuse was characterized by the intake at least 12 alcoholic beverages within one year. Smoking was defined by the consumption of a minimum of 100 cigarettes over an individual's lifetime. According to the 2018 Physical Activity Guidelines from the United States, moderate to vigorous aerobic physical activity (MVPA) has been classified into categorical variables: low (< 150 min per week) and high (≥ 150 min per week) [32].

Boruta algorithm

The outcomes of feature screening utilizing Boruta's algorithm are presented in Fig. 2. Following 500 iterations, it was identified that the fifteen variables most closely linked with suicidal ideation included gender, age, race, alcohol abuse, BMI, smoking status, CHD, hyperlipidemia, education level, PIR, albumin, marital status, creatinine, dietary omega-3 and omega-6 fatty acids intake and cancers. Despite the omission of certain key characteristics, such as physical activities and stroke due to their low z-values relative to the most strongly associated characteristics, these factors were still incorporated into subsequent analyses based on clinical experience and prior research.

Statistical analysis

Dietary omega-3, omega-6 or omega-6/3 ratio fatty acids intake was stratified into quartiles as follows: Q1: <0.90 g/d, Q2: 0.90–1.45 g/d, Q3: 1.45–2.27 g/d, Q4: >2.27 g/day for omega-3 intake. Q1: <8.61 g/d, Q2:

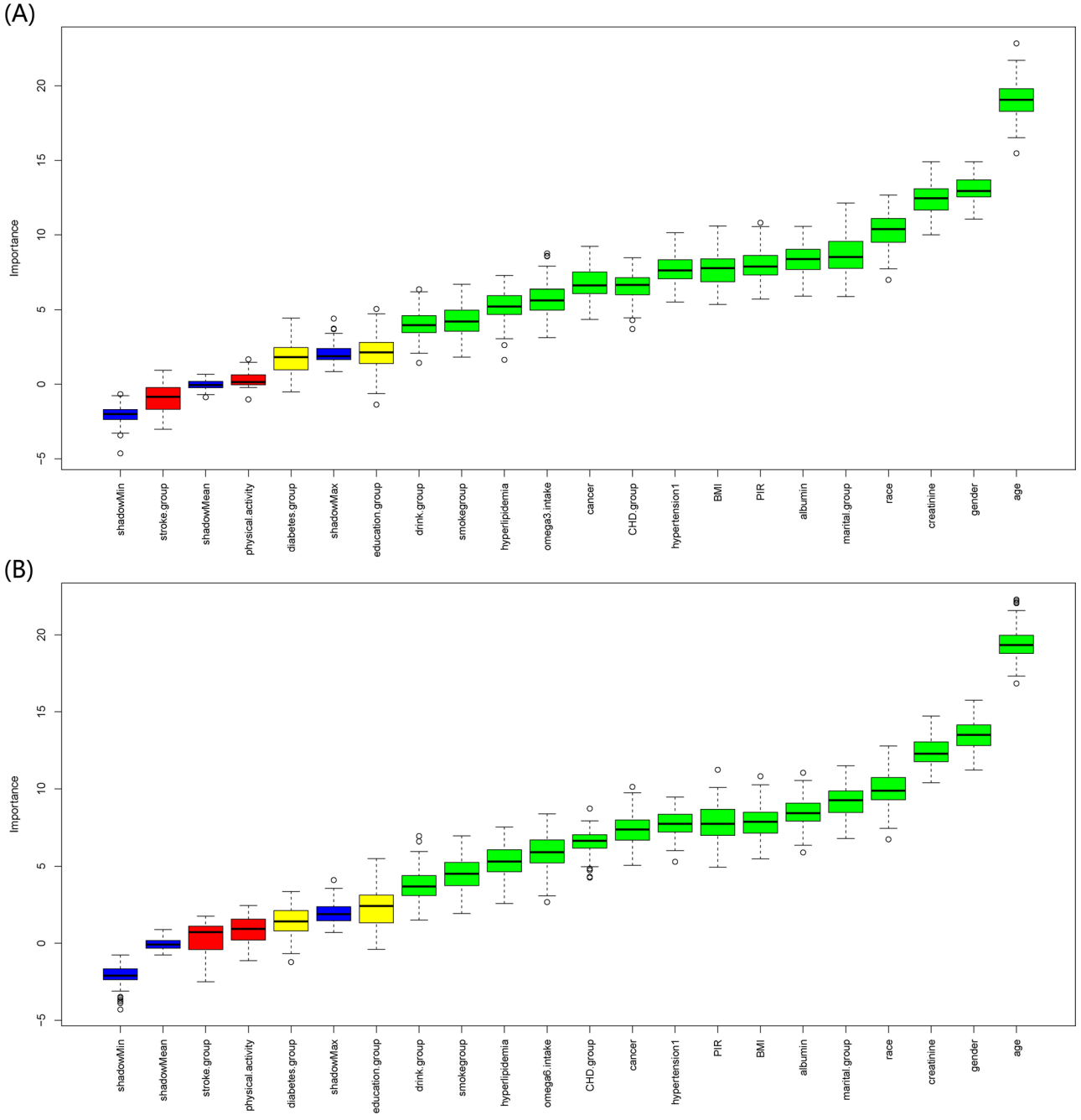

Fig. 2 (**A**)Feature selection process for suicidal ideation based on Boruta's algorithm, including dietary omega-3 intake. (**B**) Feature selection process for suicidal ideation based on Boruta's algorithm, including diet omega-6 intake

8.61–13.79 g/d, Q3: 13.79–20.95 g/d, Q4: >20.95 g/day for omega-6 intake. Q1: <7.53, Q2:7.53–9.10, Q3:9.10-11.41, and Q4:>11.41 for omega-6/3 ratio. The normality of continuous variables was assessed by presenting them as either the median with interquartile range or mean ± SD. The association between dietary omega intake and the prevalence of suicidal ideation was examined by ORs and 95% CI derived from multivariable logistic regression models. Boruta algorithm was utilized in this study for variable selection, resulting in the construction of three distinct models: Model 1, unadjusted; Model 2, adjusted for gender and age; and Model 3, comprehensively adjusted for a range of factors, including gender, age, race, alcohol abuse, BMI, total energy intake, smoking status, hypertension, physical activities, CHD, hyperlipidemia, stroke, PIR, education level, marital status, albumin, creatinine and cancers. Heterogeneity between dietary omega intake and the prevalence of

suicidal ideation was assessed through interaction and subgroup analyses across various variables. Additionally, the non-linear association between suicidal ideation and dietary omega fatty acids intake was explored through restricted cubic spline (RCS) curves.

Finally, "mediation" package in R 4.2.2. was utilized to perform Mediation analysis assessing the mediating effects of CRP on the associations of dietary omega fatty acids intake with suicidal ideation, adjusted by Model3. The presence of a mediating effect was defined as satisfying all of the following conditions having a significant indirect effect, a significant total effect, and a positive proportion of the mediator effect. Related data were analyzed with Free Statistics software and R software.

Results

Subjects' characteristics

Table 1 delineates the principal characteristics of the study cohort. Out of 27,944 subjects, 1037 (3.7%) reported experiencing suicidal ideation, at the mean age of 47.8 years old, with females representing 49.6%. Subjects reporting suicidal ideation were more likely to live alone. Moreover, subjects with suicidal ideation demonstrate a lower education level, albumin, and PIR. This group also exhibited a higher prevalence of comorbid conditions, including stroke, diabetes mellitus, CHD, hypertension, and hyperlipidemia, in addition to increased BMI, CRP and omega-6/3 ratio levels. Furthermore, dietary omega-3 and omega-6 fatty acids intake was significantly lower in subjects with suicidal ideation (Fig. 3) (all $p < 0.05$).

Association between suicidal ideation and dietary Omega fatty acids intake

Table 2 illustrates the findings from the logistic regression analysis for the association between dietary omega fatty acids intake and suicidal ideation. When dietary omega-3 and omega-6 fatty acids intake was stratified into quartiles, the fully adjusted model (Model 3) indicates that compared to subjects in the lowest Q1, the risk reduction in Q2, Q3 and Q4 were 25%, 32% and 40% for omega-3 fatty acids intake, and 25%, 25%, 30% for omega-6 fatty acids intake, respectively.

The omega-6/3 ratio was further categorized into quartiles. In the fully adjusted Model 3, individuals in the fourth quartile (Q4) exhibited a 25% increase in the prevalence of suicidal ideation compared to those in the first quartile (Q1), as shown in Table 2.

Non-linear association between dietary omega-3 and omega-6 fatty acids intake and suicidal ideation

After controlling for all variables, a non-linear association between dietary omega-3 and omega-6 fatty acids intake and suicidal ideation was identified, as depicted in Fig. 4A-B. Specifically, an L-shaped association was observed, with an inflection point at 1.36 g/d for omega-3 fatty acids intake, and 13.69 g/d for omega-6 fatty acids intake, respectively. Below this threshold, dietary omega-3 and omega-6 fatty acids intake demonstrates a significant effect value of 0.54, 0.94, respectively, whereas above this level, the effect value was not statistically significant (see Table 3). In addition, RCS analyses demonstrate a linear association between omega-6/3 ratio and suicidal ideation (as shown in Fig. 4C).

Subgroup analyses

A stratified multivariate logistic regression analysis was conducted to explore the association between dietary omega fatty acids intake and suicidal ideation among various subgroups (Fig. 5). The interaction test revealed no statistically significant differences in the association between suicidal ideation and dietary omega fatty acids intake with respect to gender, age, diabetes mellitus, BMI, hypertension, CHD, hyperlipidemia, and cancers. Additionally, the association between dietary omega-3 and omega-6 fatty acids intake and suicidal ideation was more pronounced in subjects with a history of stroke.

Mediation analysis

The mediation model and its associated pathways are depicted in Fig. 6. The analysis revealed a significant indirect effect of dietary omega-3 and omega-6 fatty acids intake on suicidal ideation, mediated by CRP. These findings indicate that CRP partially mediates the association between dietary omega-3 and omega-6 fatty acids intake and suicidal ideation, explaining approximately 4.0% and 3.8% of the total effect, respectively.

Discussion

In this cross-sectional study comprising 27,944 subjects, it was observed that the intake of omega-3 and omega-6 fatty acids was inversely associated with the prevalence of suicidal ideation, whereas dietary omega-6/3 ratio exhibited a positive association with this risk. The association between dietary omega-3 and omega-6 consumption and the prevalence of suicidal ideation was characterized by an L-shaped curve, with identified thresholds at 1.36 g/d and 13.69 g/d, respectively. This association was particularly pronounced among individuals with a history of stroke. Additionally, mediation analysis reveals that CRP partially mediated the association between dietary omega-3 and omega-6 fatty acids intake and suicidal ideation.

To the best of our knowledge, this study represents the first exploration into the association between dietary intake of omega fatty acids and the prevalence of suicidal ideation in the general population. Omega-3 fatty acids are regarded as essential nutrients and are

Table 1 Characteristics of the study population based on suicidal ideation

Characteristic	Total ($n=27944$)	Non-suicidal ideation ($n=26907$)	Suicidal ideation ($n=1037$)	*P* value
Age	47.8 ± 18.6	47.8 ± 18.7	47.8 ± 18.0	0.981
Gender, %				< 0.001
Male	14,092 (50.4)	13,630 (50.7)	462 (44.6)	
Female	13,852 (49.6)	13,277 (49.3)	575 (55.4)	
Race, %				< 0.001
Mexican American	4651 (16.6)	4446 (16.5)	205 (19.8)	
Other Hispanic	2681 (9.6)	2513 (9.3)	168 (16.2)	
Non-Hispanic White	12,343 (44.2)	11,943 (44.4)	400 (38.6)	
Non-Hispanic Black	5805 (20.8)	5611 (20.9)	194 (18.7)	
Other Race	2464 (8.8)	2394 (8.9)	70 (6.8)	
Education level, %				< 0.001
Less than high school	6488 (24.7)	6106 (24.1)	382 (39.3)	
High school or above	19,812 (75.3)	19,221 (75.9)	591 (60.7)	
Marital, %				< 0.001
Married/living with partner	16,716 (62.5)	16,213 (62.9)	503 (50.8)	
Separated/divorced/widowed	4943 (18.5)	4689 (18.2)	254 (25.6)	
Never married	5094 (19.0)	4860 (18.9)	234 (23.6)	
MVPA, %				0.142
Low (< 150 min per week)	23,165 (82.9)	22,306 (82.9)	859 (84.3)	
High (≥ 150 min per week)	4779 (17.1)	4601 (17.1)	178 (15.7)	
Alcohol status, n%				0.267
Current or ever, %	19,952 (71.4)	19,238 (71.5)	714 (69.9)	
Never	7992 (28.6)	7669 (28.5)	323 (30.1)	
Smoking status, n%				< 0.001
Current or ever, %	12,630 (45.2)	12,054 (44.8)	576 (55.3)	
Never	15,314 (54.8)	14,853 (55.2)	461 (44.7)	
Hypertension, %				< 0.001
Yes	9561 (34.2)	9123 (33.9)	438 (42.2)	
No	18,383 (65.8)	17,784 (66.1)	599 (57.8)	
Diabetes, %				< 0.001
Yes	3880 (13.9)	3669 (13.6)	211 (20.3)	
No	24,064 (86.1)	23,238 (86.4)	826 (79.7)	
Hyperlipidemia, %				0.002
Yes	19,576 (70.1)	18,805 (69.9)	771 (74.3)	
No	8368 (29.9)	8102 (30.1)	266 (25.7)	
CHD, %				< 0.001
Yes	1064 (4.1)	993 (3.9)	71 (7.3)	
No	25,158 (95.9)	24,260 (96.1)	898 (92.7)	
Stroke				< 0.001
Yes	929 (3.5)	853 (3.4)	76 (7.8)	
No	25,356 (96.5)	24,460 (96.6)	896 (92.2)	
Cancer, %				0.057
Yes	2490 (9.5)	2381 (9.4)	109 (11.2)	
No	23,802 (90.5)	22,940 (90.6)	862 (88.8)	
Body mass index, kg/m^2	29.0 ± 6.9	29.0 ± 6.9	29.8 ± 7.8	< 0.001
Albumin, g/dl	42.7 ± 3.3	42.7 ± 3.3	42.2 ± 3.7	< 0.001
Creatinine, umol/L	80.3 ± 38.7	80.3 ± 38.9	79.2 ± 34.5	0.354
PIR	2.51 ± 1.63	2.54 ± 1.63	1.71 ± 1.38	< 0.001
CRP	0.19 (0.07, 0.44)	0.19 (0.07, 0.44)	0.21 (0.08, 0.60)	0.008
Total energy intake, kcal/d	2124.7 ± 1004.0	2127.0 ± 1001.5	2065.3 ± 1066.9	0.053
Omega-3 fatty acids intake, g/d	1.45 (0.90, 2.27)	1.46 (0.90, 2.28)	1.23 (0.74, 2.03)	< 0.001

Table 1 (continued)

Characteristic	Total ($n=27944$)	Non-suicidal ideation ($n=26907$)	Suicidal ideation ($n=1037$)	*P* value
Omega-6 fatty acids intake, g/d	13.79 (8.61, 20.95)	13.83 (8.66, 21.01)	12.30 (7.11, 19.70)	< 0.001
Omega-6/3 fatty acids intake ratio	9.10 (7.53, 11.41)	9.10 (7.53, 11.40)	9.28 (7.58, 12.00)	0.020

Values are mean±SD or number (%). $P < 0.05$ was deemed significant. CHD, coronary heart disease; PIR, family income-to-poverty ratio; CRP, c-reactive protein; MVPA, moderate to vigorous aerobic physical activity

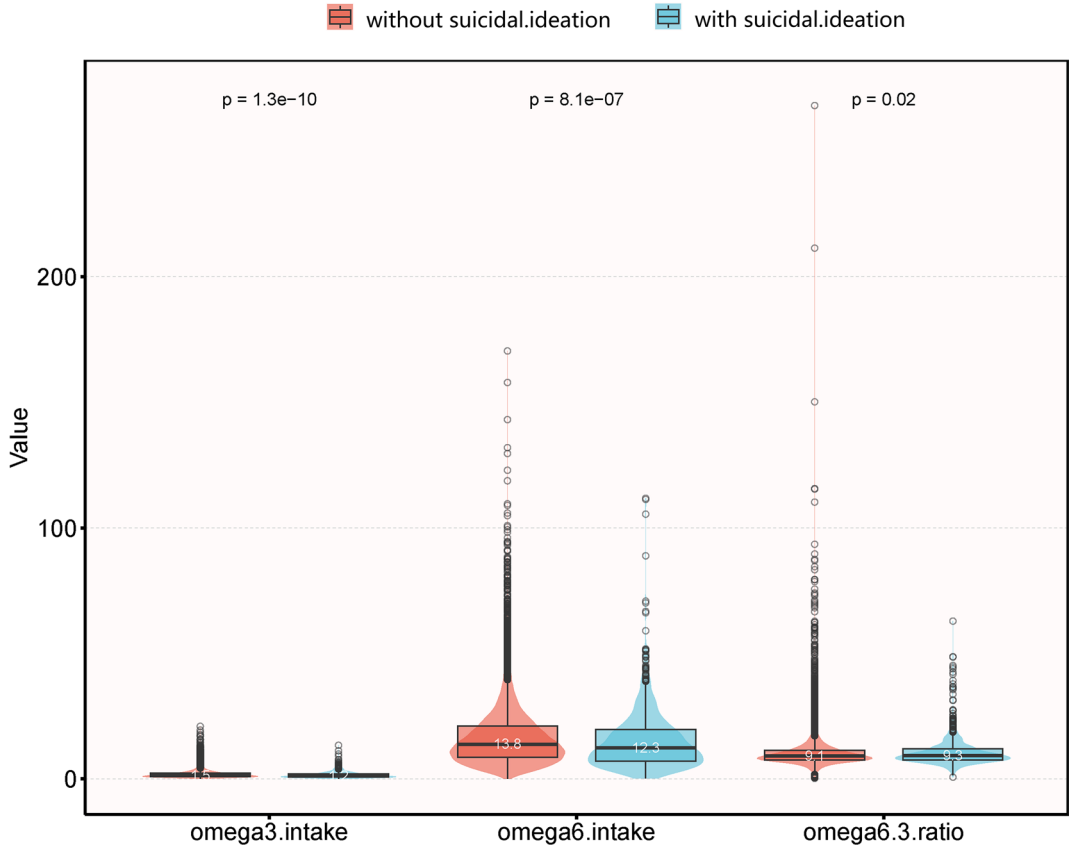

Fig. 3 Dietary omega intake levels in participants with or without suicidal ideation

predominantly acquired from external sources, such as seafood, due to the limited efficiency of endogenous synthesis from precursors [33]. The significant antioxidant and anti-inflammatory properties of omega-3 fatty acids have been shown to confer beneficial effects in various chronic inflammatory conditions, including diabetes mellitus, CVD, hypertension, cancers, and even rheumatoid arthritis [34]. In particular, several studies have identified an association between omega-3 deficiency and conditions such as catatonia and benign depression, with omega-3 supplementation reportedly alleviating symptoms of depression, irritability, and anxiety [35–37]. In the elderly population, omega-3 supplementation has been demonstrated to be an effective and low-cost preventive strategy against depression [38]. The research of Chika Horikawa et al. [39] further supports the protective effect of omega-3 fatty acids on depression, as evidenced through an established cohort study. Additionally, a recent meta-analysis [40] explored the dose-response association between omega-3 fatty acids and depression, revealing a reverse J-shaped effect.

Omega-6 fatty acids have traditionally been associated with pro-inflammatory effects, and diets high in omega-6 have been thought to counteract the anti-inflammatory benefits of omega-3 fatty acids [41]. However, recent evidence suggests that increased omega-6 fatty acids intake, such as LA, does not necessarily elevate inflammatory markers and may even contribute to reduced inflammation [41, 42]. Given that inflammation is implicated in the pathogenesis of depression [43], these findings are particularly relevant. Thesing et al. found an inverse association between omega-6 fatty acids intake and the prevalence of depression [44]. Similarly, Shi et al. found that infertile female consuming moderate amounts of omega-6 fatty acids exhibited a reduced prevalence of depressive symptoms [45]. These studies align with the findings of

Table 2 Associations between dietary Omega fatty acids intake and the prevalence of suicidal ideation

subgroups	Model1		Model2		Model3	
	OR (95%CI)	*P*-value	OR (95%CI)	*P*-value	OR (95%CI)	*P*-value
Omega-3 fatty acids intake						
Q1(< 0.90 g/d)	1(Ref)		1(Ref)		1(Ref)	
Q2 (0.90–1.45 g/d)	0.71 (0.6 ~ 0.84)	< 0.001	0.72 (0.61 ~ 0.85)	< 0.001	0.75 (0.63 ~ 0.90)	0.002
Q3 (1.45–2.27 g/d)	0.65 (0.55 ~ 0.77)	< 0.001	0.67 (0.56 ~ 0.79)	< 0.001	0.68 (0.56 ~ 0.82)	< 0.001
Q4 (> 2.27 g/day)	0.61 (0.51 ~ 0.72)	< 0.001	0.63 (0.53 ~ 0.75)	< 0.001	0.60 (0.47 ~ 0.75)	< 0.001
P for trend	0.85 (0.80 ~ 0.89)	< 0.001	0.86 (0.81 ~ 0.91)	< 0.001	0.84 (0.78 ~ 0.91)	< 0.001
Omega-6 fatty acids intake						
Q1 (< 8.61 g/d)	1(Ref)		1(Ref)		1(Ref)	
Q2 (8.61–13.79 g/d)	0.72 (0.61 ~ 0.85)	< 0.001	0.72 (0.61 ~ 0.86)	< 0.001	0.75 (0.62 ~ 0.89)	0.002
Q3 (13.79–20.95 g/d)	0.69 (0.58 ~ 0.82)	< 0.001	0.71 (0.59 ~ 0.84)	< 0.001	0.75 (0.62 ~ 0.91)	0.004
Q4 (> 20.95 g/day)	0.67 (0.56 ~ 0.79)	< 0.001	0.69 (0.58 ~ 0.83)	< 0.001	0.70 (0.55 ~ 0.89)	0.003
P for trend	0.87 (0.83 ~ 0.92)	< 0.001	0.89 (0.84 ~ 0.94)	< 0.001	0.89 (0.83 ~ 0.96)	0.003
Omega-6/3 fatty acids ratio						
Q1 (< 7.53)	1(Ref)		1(Ref)		1(Ref)	
Q2 (7.53–9.10)	0.98 (0.82 ~ 1.18)	0.854	0.99 (0.83 ~ 1.19)	0.912	0.99 (0.82 ~ 1.20)	0.918
Q3 (9.10-11.41)	1.00 (0.83 ~ 1.19)	0.963	1.00 (0.84 ~ 1.20)	0.972	1.01 (0.84 ~ 1.22)	0.884
Q4 (> 11.41)	1.21 (1.02 ~ 1.44)	0.029	1.22 (1.03 ~ 1.46)	0.021	1.25 (1.04 ~ 1.50)	0.017
P for trend	1.06 (1.01 ~ 1.12)	0.03	1.07 (1.01 ~ 1.13)	0.022	1.07 (1.01 ~ 1.14)	0.017

Model 1: None covariable were adjusted

Model 2: gender and age were adjusted

Model 3, gender, age, race, drinking, BMI, total energy intake, smoking, hypertension, physical activities, CHD, hyperlipidemia, stroke, PIR, education level, marital status, albumin, creatinine and cancer were adjusted

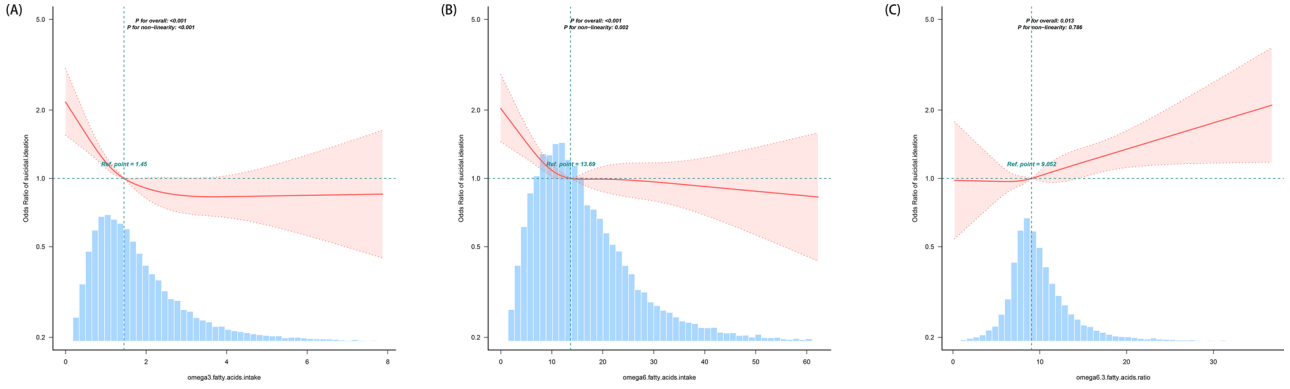

Fig. 4 Restricted cubic spline fitting for the association between suicidal ideation and (**A**)dietary omega-3 intake, (**B**) dietary omega-6 intake, (**C**) dietary omega-6/3 ratio

this study, which, for the first time, suggest that a moderate intake of omega-6 fatty acids (less than 13.69 g/d) may be advantageous in mitigating the prevalence of suicidal ideation.

These findings indicate a positive association between omega-6/3 ratio and the prevalence of suicidal ideation, aligning with several studies suggesting that a lower omega-6/3 intake ratio may enhance health outcomes and mitigate the prevalence of various chronic diseases [46, 47]. Although the mechanisms between omega-6/3 ratio and the increased the prevalence of suicidal ideation are not fully understood, several possibilities have been proposed. Primarily, a high omega-6/3 ratio promotes the production of arachidonic acid (AA) derived from omega-6 eicosanoids, and AA has been shown to increase the production of proinflammatory factors, which may increase the incidence of suicidal ideation [48]. Another possible mechanism is that a high omega-6/3 ratio is related to catecholaminergic or serotonergic neurotransmission [49], which may also contribute to an

Table 3 Threshold effect analysis of dietary Omega fatty acids intake and suicidal ideation using the two-piecewise linear regression model

dietary omega intake	Adjusted OR (95% CI)	*P* value
Omega-3 fatty acids intake		
Inflection point	1.36 g/d	
Omega-3 intake < 1.36 g/d	0.54 (0.39, 0.74)	< 0.001
Omega-3 intake > 1.36 g/d	0.98 (0.89, 1.08)	0.630
Log likelihood ratio		0.001
Omega-6 fatty acids intake		
Inflection point	13.69 g/d	
Omega-6 intake < 13.69 g/d	0.94 (0.91, 0.97)	< 0.001
Omega-6 intake > 13.69 g/d	1.00 (0.99, 1.01)	0.986
Log likelihood ratio		< 0.001

Gender, age, race, drinking, BMI, total energy intake, smoking, hypertension, physical activities, CHD, hyperlipidemia, stroke, PIR, education level, marital status, albumin, creatinine and cancer were adjusted

increased risk of suicidal ideation. Serotonin primarily influences mood, while catecholamines are involved in motivational aspects; deficiencies in catecholamines can lead to symptoms such as apathy, asthenia, abulia, and anhedonia [36].

The findings of this study provide further clarification on the L-shaped association between dietary omega fatty acids intake and the prevalence of suicidal ideation in American adults, indicating that the consumption of increased omega fatty acids may function as a non-pharmacological preventive measure. Additionally, combined with our findings, it appears that the potential therapeutic value of exceeding the threshold of omega-3, and omega-6 fatty acids intake may be limited. For individuals at risk, it is advisable to meet the recommended daily omega-3 or omega-6 fatty acids intake of 1.36 g/d and 13.69 g/d, respectively. Considering individual differences and dietary patterns, it is necessary to conduct additional research to explore the optimal level of omega fatty acids intake.

The results of this study suggest that CRP may partially mediate the association between dietary omega fatty acids intake and suicidal ideation, highlighting the importance of monitoring inflammation levels in individuals

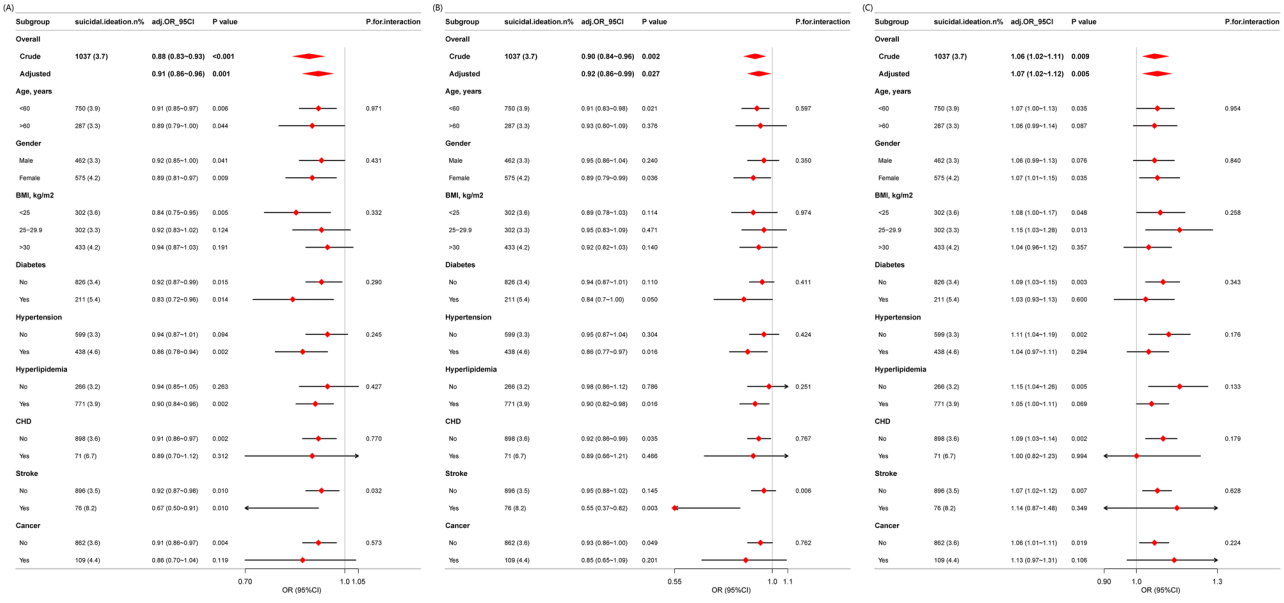

Fig. 5 Association between suicidal ideation and (**A**)dietary omega-3 intake, (**B**) dietary omega-6 intake, (**C**) dietary omega-6/3 ratio in various subgroups

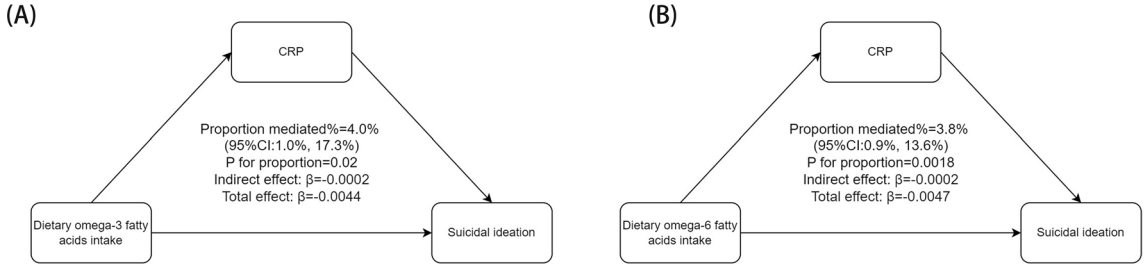

Fig. 6 Mediated analysis model path diagram. Notes: dietary omega-3, omega-6 intake was defined as the independent variable; suicidal ideation as the dependent variable; and CRP as the mediating variable

with lower omega consumption. Omega-3 and omega-6 fatty acids is known for its potent anti-inflammatory properties, and its higher intake has been associated with declined levels of inflammatory markers [42]. Consequently, increasing dietary omega fatty acids intake may attenuate the inflammatory response by reducing CRP levels, thereby potentially reducing the prevalence of suicidal ideation. Hence, it is plausible to hypothesize that in patients experiencing suicidal ideation, the concurrent use of anti-inflammatory medications and omega fatty acids derived from natural food sources could synergistically enhance the therapeutic outcomes.

The inverse association between omega fatty acids intake and suicidal ideation may be attributed to several mechanisms potentially influencing the pathology of suicidal ideation. Omega fatty acids, especially DHA and EPA, significantly influence the fluidity and signaling functions of cell membranes [50, 51]. The presence of these fatty acids improves the structure and function of neuronal membranes, thereby affecting neurotransmitter release and neural signaling. Omega fatty acids deficiency has been documented to be linked with impairments in dopamine, serotonin, and norepinephrine neurotransmission, which are associated with emotional disorders, including suicidal ideation [52]. Moreover, a substantial body of research indicates that individuals with psychiatric disorders tend to exhibit elevated levels of oxidative stress and inflammation, coupled with a comparatively low intake of dietary antioxidants [53, 54]. A cross-sectional study involving 364 patients undergoing secondary prevention for CVD demonstrates an inverse association between increased dietary intake of omega-3 and omega-6 fatty acids and the levels of IL-1β, CRP, IL-12, and IL-10 [55]. Omega-3 and omega-6 fatty acids, acting as signaling molecules, can activate peroxisome proliferator-activated receptors, which in turn regulate various processes including inflammatory responses, oxidative stress, lipogenesis, and glucose and lipid metabolism [56]. This comprehensive effect may potentially contribute to a declined risk of suicidal ideation.

Study strengths and limitations

This study exhibits several notable strengths. Firstly, a nationally representative and substantial sample of American adults was employed. Secondly, the study concurrently examined the association between omega-3 and omega-6 fatty acids intake, as well as omega-6/3 ratio, with the prevalence of suicidal ideation, while also exploring the dose–response association. However, the study has its limitations: (1) The cross-sectional design limits the ability to establish causality, as it captures associations at a single point in time. This limitation renders the causal relationship between dietary omega fatty acid intake and suicidal ideation indeterminate. (2) The assessment on suicidal ideation predominantly relied on questionnaires, which may introduce measurement errors. (3) It is crucial to recognize that variables such as treatment modalities for individuals experiencing suicidal ideation, as well as the presence of food allergies or gastrointestinal disorders, may significantly influence the findings of this study. Future studies should systematically integrate these factors and their potential confounding effects to enhance the understanding of the association between suicidal ideation and dietary omega fatty acids intake.

Conclusion

This study demonstrates an inverse association between the intake of omega-3 and omega-6 fatty acids and the prevalence of suicidal ideation, while a positive association was observed with omega-6/3 ratio and the prevalence of suicidal ideation. These findings imply that adequate omega fatty acid intake, particularly omega-3, may contribute to the prevention of suicidal ideation. However, further research is necessary to validate these results and to explore the underlying mechanisms linking dietary omega fatty acid consumption with suicidal ideation.

Acknowledgements

We would like to thank the NHANES database for providing the data source for this study.

Author contributions

SSQ designed the study; ZBB, DKW and QY collected biochemical data; HL drafted the manuscript. All authors read and approved the final manuscript.

Funding

Not applicable.

Data availability

The datasets generated and analysis during the current study are available in the NHANES, http://www.cdc.gov/nchs/NHANEs/.

Declarations

Ethics approval and consent to participate

The study was approved by the National Centre for Health Statistics Research Ethics Review Board, and every participant signed informed consent.
The written informed consent of all subjects was obtained following the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 19 March 2025 / Accepted: 29 April 2025
Published online: 15 May 2025

References

1. Mudiyanselage SPK, Tsai YT, Tsai YJ, Yang YH, Lu ZT, Ko NY. Global overview of suicidal behavior and risk factors among the general population during the COVID-19 pandemic: a scoping review. BMC Psychol. 2024;12:727.

2. Singh OP. Comprehensive mental health action plan 2013–2030: we must rise to the challenge. Indian J Psychiatry. 2021;63:415–7.
3. Klonsky ED, Saffer BY, Bryan CJ. Ideation-to-action theories of suicide: a conceptual and empirical update. Curr Opin Psychol. 2018;22:38–43.
4. Hubers AAM, Moaddine S, Peersmann SHM, Stijnen T, van Duijn E, van der Mast RC, Dekkers OM, Giltay EJ. Suicidal ideation and subsequent completed suicide in both psychiatric and non-psychiatric populations: a meta-analysis. Epidemiol Psychiatr Sci. 2018;27:186–98.
5. Lee JI, Lee MB, Liao SC, Chang CM, Sung SC, Chiang HC, Tai CW. Prevalence of suicidal ideation and associated risk factors in the general population. J Formos Med Assoc. 2010;109:138–47.
6. Nock MK, Borges G, Bromet EJ, Alonso J, Angermeyer M, Beautrais A, Bruffaerts R, Chiu WT, de Girolamo G, Gluzman S, et al. Cross-national prevalence and risk factors for suicidal ideation, plans and attempts. Br J Psychiatry. 2008;192:98–105.
7. D'Souza S, Thompson JM, Slykerman R, Marlow G, Wall C, Murphy R, Ferguson LR, Mitchell EA, Waldie KE. Environmental and genetic determinants of childhood depression: the roles of DAT1 and the antenatal environment. J Affect Disord. 2016;197:151–8.
8. Wang Q, Shelton RC, Dwivedi Y. Interaction between early-life stress and FKBP5 gene variants in major depressive disorder and post-traumatic stress disorder: A systematic review and meta-analysis. J Affect Disord. 2018;225:422–8.
9. Xia Y, Wang N, Yu B, Zhang Q, Liu L, Meng G, Wu H, Du H, Shi H, Guo X, et al. Dietary patterns are associated with depressive symptoms among Chinese adults: a case-control study with propensity score matching. Eur J Nutr. 2017;56:2577–87.
10. Lassale C, Batty GD, Baghdadli A, Jacka F, Sanchez-Villegas A, Kivimaki M, Akbaraly T. Healthy dietary indices and risk of depressive outcomes: a systematic review and meta-analysis of observational studies. Mol Psychiatry. 2019;24:965–86.
11. Romero-Blanco C, Hernandez-Martinez A, Parra-Fernandez ML, Onieva-Zafra MD, Prado-Laguna MDC, Rodriguez-Almagro J. Food addiction and lifestyle habits among university students. Nutrients. 2021;13.
12. Firth J, Teasdale SB, Allott K, Siskind D, Marx W, Cotter J, Veronese N, Schuch F, Smith L, Solmi M, et al. The efficacy and safety of nutrient supplements in the treatment of mental disorders: a meta-review of meta-analyses of randomized controlled trials. World Psychiatry. 2019;18:308–24.
13. Gianfredi V, Koster A, Odone A, Amerio A, Signorelli C, Schaper NC, Bosma H, Kohler S, Dagnelie PC, Stehouwer CDA et al. Associations of dietary patterns with incident depression: the Maastricht study. Nutrients. 2021;13.
14. Zhang R, Sun J, Li Y, Zhang D. Associations of n-3, n-6 fatty acids intakes and n-6:n-3 ratio with the risk of depressive symptoms: NHANES 2009–2016. Nutrients. 2020;12.
15. Kapoor B, Kapoor D, Gautam S, Singh R, Bhardwaj S. Dietary polyunsaturated fatty acids (PUFAs): uses and potential health benefits. Curr Nutr Rep. 2021;10:232–42.
16. Djuricic I, Calder PC. Beneficial outcomes of Omega-6 and Omega-3 polyunsaturated fatty acids on human health: an update for 2021. Nutrients. 2021;13.
17. D'Angelo S, Motti ML, Meccariello R. omega-3 and omega-6 polyunsaturated fatty acids, obesity and Cancer. Nutrients. 2020;12.
18. Hallahan B, Hibbeln JR, Davis JM, Garland MR. Omega-3 fatty acid supplementation in patients with recurrent self-harm. Single-centre double-blind randomised controlled trial. Br J Psychiatry. 2007;190:118–22.
19. Bellino S, Bozzatello P, Rocca G, Bogetto F. Efficacy of omega-3 fatty acids in the treatment of borderline personality disorder: a study of the association with valproic acid. J Psychopharmacol. 2014;28:125–32.
20. Bozzatello P, Rocca P, Bellino S. Combination of Omega-3 fatty acids and valproic acid in treatment of borderline personality disorder: A Follow-Up study. Clin Drug Investig. 2018;38:367–72.
21. Xiao Y, Huang W. Association of dietary inflammatory index with depression and suicidal ideation in older adult: results from the National health and nutrition examination surveys 2005–2018. Front Psychiatry. 2022;13:944154.
22. Hu YQ, Niu TT, Xu JM, Peng L, Sun QH, Huang Y, Zhou J, Ding YQ. Negative air ion exposure ameliorates depression-like behaviors induced by chronic mild stress in mice. Environ Sci Pollut Res Int. 2022;29:62626–36.
23. Benatti C, Blom JM, Rigillo G, Alboni S, Zizzi F, Torta R, Brunello N, Tascedda F. Disease-Induced neuroinflammation and depression. CNS Neurol Disord Drug Targets. 2016;15:414–33.
24. Turiaco F, Iannuzzo F, Bruno A, Drago A. Genetics of suicide ideation. A role for inflammation and neuroplasticity? Eur Arch Psychiatry Clin Neurosci. 2024;274:1527–41.
25. Kavyani Z, Musazadeh V, Fathi S, Hossein Faghfouri A, Dehghan P, Sarmadi B. Efficacy of the omega-3 fatty acids supplementation on inflammatory biomarkers: an umbrella meta-analysis. Int Immunopharmacol. 2022;111:109104.
26. Singh JE. Dietary sources of Omega-3 fatty acids versus Omega-3 fatty acid supplementation effects on cognition and inflammation. Curr Nutr Rep. 2020;9:264–77.
27. Zipf G, Chiappa M, Porter KS, Ostchega Y, Lewis BG, Dostal J. National health and nutrition examination survey: plan and operations, 1999–2010. Vital Health Stat *1* 2013:1–37.
28. Wu Z, Ruan Z, Liang G, Wang X, Wu J, Wang B. Association between dietary magnesium intake and peripheral arterial disease: results from NHANES 1999–2004. PLoS ONE. 2023;18:e0289973.
29. Chen J, Sun B, Zhang D. Association of dietary n3 and n6 fatty acids intake with hypertension: NHANES 2007–2014. Nutrients. 2019;11.
30. Chen Y, Lin H, Xu J, Zhou X. Estimated glucose disposal rate is correlated with increased depression: a population-based study. BMC Psychiatry. 2024;24:786.
31. Zhou X, Weng X, Xu J, Wang W. Correlation between remnant cholesterol and hyperuricemia in American adults. Lipids Health Dis. 2024;23:176.
32. Piercy KL, Troiano RP, Ballard RM, Carlson SA, Fulton JE, Galuska DA, George SM, Olson RD. The physical activity guidelines for Americans. JAMA. 2018;320:2020–8.
33. Wei L, Wu Z, Chen YQ. Multi-targeted therapy of cancer by omega-3 fatty acids-an update. Cancer Lett. 2022;526:193–204.
34. Simopoulos AP. The importance of the omega-6/omega-3 fatty acid ratio in cardiovascular disease and other chronic diseases. Exp Biol Med (Maywood). 2008;233:674–88.
35. Bozzatello P, De Rosa ML, Rocca P, Bellino S. Effects of Omega 3 fatty acids on main dimensions of psychopathology. Int J Mol Sci. 2020;21.
36. Pruneti C, Guidotti S. Need for multidimensional and multidisciplinary management of depressed preadolescents and adolescents: A review of randomized controlled trials on oral supplementations (Omega-3, fish oil, vitamin D(3)). Nutrients. 2023;15.
37. DiNicolantonio JJ, O'Keefe JH. The importance of marine Omega-3s for brain development and the prevention and treatment of behavior, mood, and other brain disorders. Nutrients. 2020;12.
38. Farioli Vecchioli S, Sacchetti S, Nicolis di Robilant V, Cutuli D. The role of physical exercise and Omega-3 fatty acids in depressive illness in the elderly. Curr Neuropharmacol. 2018;16:308–26.
39. Horikawa C, Otsuka R, Kato Y, Nishita Y, Tange C, Rogi T, Kawashima H, Shibata H, Ando F, Shimokata H. Longitudinal Association between n-3 Long-Chain Polyunsaturated Fatty Acid Intake and Depressive Symptoms: A Population-Based Cohort Study in Japan. Nutrients 2018;10.
40. Grosso G, Micek A, Marventano S, Castellano S, Mistretta A, Pajak A, Galvano F. Dietary n-3 PUFA, fish consumption and depression: A systematic review and meta-analysis of observational studies. J Affect Disord. 2016;205:269–81.
41. Innes JK, Calder PC. Omega-6 fatty acids and inflammation. Prostaglandins Leukot Essent Fat Acids. 2018;132:41–8.
42. Li Y, Tang H, Yang X, Ma L, Zhou H, Zhang G, Chen X, Ma L, Gao J, Ji W. Associations of omega-3, omega-6 polyunsaturated fatty acids intake and omega-6: omega-3 ratio with systemic immune and inflammatory biomarkers: NHANES 1999–2020. Front Nutr. 2024;11:1410154.
43. Grosso G, Galvano F, Marventano S, Malaguarnera M, Bucolo C, Drago F, Caraci F. Omega-3 fatty acids and depression: scientific evidence and biological mechanisms. Oxid Med Cell Longev. 2014;2014:313570.
44. Thesing CS, Bot M, Milaneschi Y, Giltay EJ, Penninx B. Omega-3 and omega-6 fatty acid levels in depressive and anxiety disorders. Psychoneuroendocrinology. 2018;87:53–62.
45. Hong Y, Jin X, Shi L. Association between polyunsaturated fatty acids and depression in women with infertility: a cross-sectional study based on the National health and nutrition examination survey. Front Psychiatry. 2024;15:1345815.
46. Simopoulos AP. An increase in the Omega-6/Omega-3 fatty acid ratio increases the risk for obesity. Nutrients. 2016;8:128.
47. Kew S, Banerjee T, Minihane AM, Finnegan YE, Williams CM, Calder PC. Relation between the fatty acid composition of peripheral blood mononuclear cells and measures of immune cell function in healthy, free-living subjects aged 25–72 y. Am J Clin Nutr. 2003;77:1278–86.
48. Bagga D, Wang L, Farias-Eisner R, Glaspy JA, Reddy ST. Differential effects of prostaglandin derived from omega-6 and omega-3 polyunsaturated fatty

acids on COX-2 expression and IL-6 secretion. Proc Natl Acad Sci U S A. 2003;100:1751–6.
49. Haag M. Essential fatty acids and the brain. Can J Psychiatry. 2003;48:195–203.
50. Dyall SC. Long-chain omega-3 fatty acids and the brain: a review of the independent and shared effects of EPA, DPA and DHA. Front Aging Neurosci. 2015;7:52.
51. Sherratt SCR, Mason RP, Libby P, Steg PG, Bhatt DL. Do patients benefit from omega-3 fatty acids? Cardiovasc Res. 2024;119:2884–901.
52. Su KP. Biological mechanism of antidepressant effect of omega-3 fatty acids: how does fish oil act as a 'mind-body interface'? Neurosignals. 2009;17:144–52.
53. Bhatt S, Nagappa AN, Patil CR. Role of oxidative stress in depression. Drug Discov Today. 2020;25:1270–6.
54. Huang Q, Liu H, Suzuki K, Ma S, Liu C. Linking what we eat to our mood: A review of diet, dietary antioxidants, and depression. Antioxid (Basel) 2019, 8.
55. Bersch-Ferreira AC, Sampaio GR, Gehringer MO, Ross-Fernandes MB, Kovacs C, Alves R, Pereira JL, Magnoni CD, Weber B, Rogero MM. Association between polyunsaturated fatty acids and inflammatory markers in patients in secondary prevention of cardiovascular disease. Nutrition. 2017;37:30–6.
56. Echeverria F, Ortiz M, Valenzuela R, Videla LA. Long-chain polyunsaturated fatty acids regulation of PPARs, signaling: relationship to tissue development and aging. Prostaglandins Leukot Essent Fat Acids. 2016;114:28–34.

Publisher's note