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Research paper

Independent and joint associations of dietary antioxidant intake with risk of post-stroke depression and all-cause mortality

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ABSTRACT

Background: Few observational studies have investigated the association of dietary antioxidant intake with post-stroke depression (PSD) risk. We used the cross-sectional and longitudinal design to investigate the independent and joint associations between dietary antioxidant intake and PSD risk and all-cause mortality.

Methods: Participants from the 2005–2014 National Health and Nutrition Examination Survey (NHANES) aged 20 years and older with stroke were included. Logistic and Cox regression analyses were used to assess the associations of dietary antioxidant intake, including vitamin A, vitamin C, vitamin E, zinc, selenium, and carotenoids, and composite dietary antioxidant index (CDAI) with PSD risk and all-cause mortality.

Results: The highest quartile of dietary vitamin A (OR: 0.54, 95%CI: 0.32, 0.92), total carotenoids (OR: 0.56, 95% CI: 0.34, 0.94), and selenium intake (OR: 0.53, 95%CI: 0.31, 0.90) were associated with decreased PSD risk compared with those in the lowest quartile. The results showed a negative association between CDAI and PSD risk, with the lowest OR in the third quartiles (OR: 0.49, 95%CI: 0.30, 0.83). Furthermore, the highest quartile of dietary vitamin A (HR: 0.63, 95%CI: 0.45, 0.89), vitamin E (HR: 0.69, 95%CI: 0.48, 0.99), zinc (HR: 0.57, 95%CI: 0.40, 0.81), selenium (HR: 0.64, 95%CI: 0.46, 0.90), and total carotenoids (HR: 0.66, 95%CI: 0.47, 0.92) intake and CDAI (HR: 0.56, 95%CI: 0.39, 0.81) were associated with decreased all-cause mortality compared with those in the lowest quartile.

Conclusion: Increased intake of dietary antioxidant may protect from depressive symptoms and improve the prognosis of stroke patients.

1. Introduction

Stroke is the leading cause of long-term disability in adults and the fourth most common cause of death (Cai et al., 2019). Depression is the most common mental disease after stroke (Jorgensen et al., 2016), and the prevalence of depression is high in patients with stroke (18 %–33 %) (Ayerbe et al., 2013; Hackett and Pickles, 2014; Mitchell et al., 2017). Post-stroke depression (PSD) has a negative impact on long-term rehabilitation (Gillen et al., 2001) and quality of life of survivors (Villa et al., 2018), and patients with PSD have more functional disability (Cully et al., 2005), cognitive disorders (Chemerinski et al., 2001), and mortality (Bartoli et al., 2018; Cai et al., 2019).

Studies have been investigating the potential role of diet in reducing the risk of depression. For example, a diet rich in vegetables, fruits, fish, and olive oil may protect against depression (Canheta et al., 2021; Dharmayani et al., 2021; Glabska et al., 2020; Li et al., 2016). It is well known that stroke can lead to increased levels of reactive oxygen, nitrogen species and inflammation (Bolanos et al., 2009), which is closely associated with the development of depressive symptoms (Berk et al., 2013; Vavakova et al., 2015). Given that several dietary compounds can affect susceptibility to oxidative stress, we hypothesized that the intake of antioxidant nutrients could protect against the onset of depression among stroke patients.

To date, few observational studies have investigated the independent and joint associations of dietary antioxidant intake with depression risk among patients with stroke. By contrast, there is evidence supporting that intakes of antioxidant vitamin A, C, and E were negatively associated with depression risk in the general population (Ding and Zhang, 2022; Zhang et al., 2022), whereas whether dietary carotene also lowers the risk of depression is controversial (Lai et al., 2016; Lin and Shen, 2021). Furthermore, previous studies have suggested that dietary antioxidants, including zinc and selenium, were associated with a decreased risk of depression (Wang et al., 2018). For the joint association of dietary antioxidant intake with depression risk, a recent systematic review of

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Table 1
Characteristics of the study population.

	Study participants (n = 962)
Age, years	66.51 ± 13.22
Sex, %	
Male	468 (48.65)
Female	494 (51.35)
Race, %	
Non-Hispanic White	515 (53.53)
Black	261 (27.13)
Mexican American	85 (8.84)
Other Hispanic	51 (5.30)
Other race	50 (5.20)
Marital status, %	
Married/living with partner	486 (50.52)
Widowed/divorced/separated	402 (41.79)
Never married	74 (7.69)
Education level, %	
Less than high school	355 (36.94)
High school	249 (25.91)
More than high school	357 (37.15)
Body mass index, kg/m^2	
<18.5	15 (1.66)
18.5 to <25	210 (23.28)
25 to <30	289 (32.04)
≥30	388 (43.02)
Currently smoking, %	
Never	368 (38.25)
Past or current	594 (61.75)
Alcohol use, %	
No	813 (84.51)
Yes	149 (15.49)
Diabetes, %	
No	595 (64.46)
Yes	328 (35.54)
Hypertension, %	
No	216 (22.52)
Yes	743 (77.48)
Hypercholesterolemia, %	
No	370 (42.09)
Yes	509 (57.91)

observational studies indicated that the consumption of a diet rich in antioxidants, characterized by high dietary total antioxidant capacity (DTAC) scores, seems to be inversely associated with depression (Pereira et al., 2021).

In this study of nationally representative sample in the United States, we first used a cross-sectional design to assess the independent and joint associations of dietary antioxidant intake, including vitamin A, vitamin C, vitamin E, total carotenoids, zinc, and selenium, with the PSD risk, and then used a longitudinal design to assess the association between dietary antioxidant intake and all-cause mortality.

2. Methods

2.1. Data source and population

We used data from five 2-year cycles (2005–2014) of National Health and Nutrition Examination Survey (NHANES). NHANES is a population-based survey designed to assess the health and nutritional status of adults and children in the United States. In these surveys, a stratified multistage probability design was used to derive a representative sample. Details methodology of NHANES has been published previously (Kase et al., 2021). Surveys protocols are approved by Institutional Review Board of the National Center for Health Statistics of the Center for Disease Control and Prevention (CDC). Informed consent is obtained from each participant.

For the period 2005–2014, there were a total of 50,965 individuals and our current study limited the participants aged 20 years and older with stroke (n = 1109). NHANES provided self-reported personal interview data on medical conditions. The stroke status in all participants defined as an affirmative response to the questions, "Has a doctor or other health professional ever told you had a stroke?" Furthermore, to be included in the present study, participants had to provide dietary intake data and information on depression. Finally, 962 subjects were included in the analyses.

Table 2
The crude and adjusted odds ratios (ORs) with 95 % confidence intervals (CIs) for risk of post-stroke depression across quartiles of dietary intakes of vitamin A, vitamin C, vitamin E, total carotenoids, zinc, and selenium.

	Crude		Adjusted[a]	
	OR (95%CI)	P value	OR (95%CI)	P value
Vitamin A				
Q1	1.00 (ref.)		1.00 (ref.)	
Q2	0.66 (0.42, 1.03)	0.064	0.80 (0.49, 1.30)	0.370
Q3	0.51 (0.32, 0.82)	0.005	0.59 (0.35, 0.97)	0.039
Q4	0.42 (0.26, 0.68)	<0.001	0.54 (0.32, 0.92)	0.024
P for trend	<0.001		0.011	
Vitamin C				
Q1	1.00 (ref.)		1.00 (ref.)	
Q2	0.57 (0.36, 0.90)	0.016	0.63 (0.38, 1.03)	0.066
Q3	0.52 (0.32, 0.82)	0.006	0.65 (0.39, 1.09)	0.103
Q4	0.54 (0.34, 0.85)	0.008	0.70 (0.42, 1.16)	0.166
P for trend	0.006		0.173	
Vitamin E				
Q1	1.00 (ref.)		1.00 (ref.)	
Q2	0.64 (0.40, 1.01)	0.053	0.67 (0.41, 1.10)	0.117
Q3	0.61 (0.39, 0.97)	0.038	0.73 (0.44, 1.20)	0.217
Q4	0.56 (0.35, 0.89)	0.015	0.70 (0.42, 1.18)	0.184
P for trend	0.014		0.206	
Total carotenoids				
Q1	1.00 (ref.)		1.00 (ref.)	
Q2	0.56 (0.35, 0.88)	0.013	0.55 (0.33, 0.90)	0.047
Q3	0.55 (0.35, 0.88)	0.012	0.55 (0.33, 0.92)	0.008
Q4	0.52 (0.32, 0.83)	0.006	0.56 (0.34, 0.94)	0.031
P for trend	0.006		0.027	
Zinc				
Q1	1.00 (ref.)		1.00 (ref.)	
Q2	0.69 (0.43, 1.08)	0.104	0.72 (0.44, 1.19)	0.201
Q3	0.53 (0.33, 0.85)	0.009	0.58 (0.34, 0.98)	0.042
Q4	0.65 (0.41, 1.03)	0.065	0.62 (0.37, 1.05)	0.074
P for trend	0.032		0.049	
Selenium				
Q1	1.00 (ref.)		1.00 (ref.)	
Q2	0.68 (0.44, 1.07)	0.098	0.72 (0.43, 1.19)	0.194
Q3	0.51 (0.31, 0.82)	0.005	0.45 (0.27, 0.77)	0.003
Q4	0.56 (0.35, 0.89)	0.014	0.53 (0.31, 0.90)	0.020
P for trend	0.006		0.005	

[a] Adjusted for age (continuous), sex (male or female), race (non-Hispanic white, black, Mexican American, other Hispanic, or other race), education level (less than high school, high school, or more than high school), marital status (married/living with partner, widowed/divorced/separated, or never married), body mass index (<18.5, 18.5 to <25, 25 to <30, or ≥30 kg/m^2), currently smoking (yes or no), alcohol use (yes or no), diabetes (yes or no), hypertension (yes or no), and hypercholesterolemia (yes or no).

2.2. Dietary assessment

Information on dietary antioxidant intake and other food components were obtained from 24-hour dietary recall interviews. Participants were asked to recall the details of food and beverages consumed in the 24-hour period before the interview. Six dietary antioxidant exposures of interest were investigated: vitamin A, vitamin C, vitamin E, zinc, selenium, and total carotenoids. The dietary antioxidant estimates did not include those obtained from dietary supplements, medications, or plain drinking water. To assess the combined exposure of dietary antioxidant intake, we used a modified version of the composite dietary antioxidant index (CDAI), developed by Wright et al. (Maugeri et al., 2019; Wright et al., 2004). Intake of each antioxidant nutrient was standardized by subtracting the mean and dividing by the standard deviation. The CDAI was calculated by summing the standardized dietary antioxidant

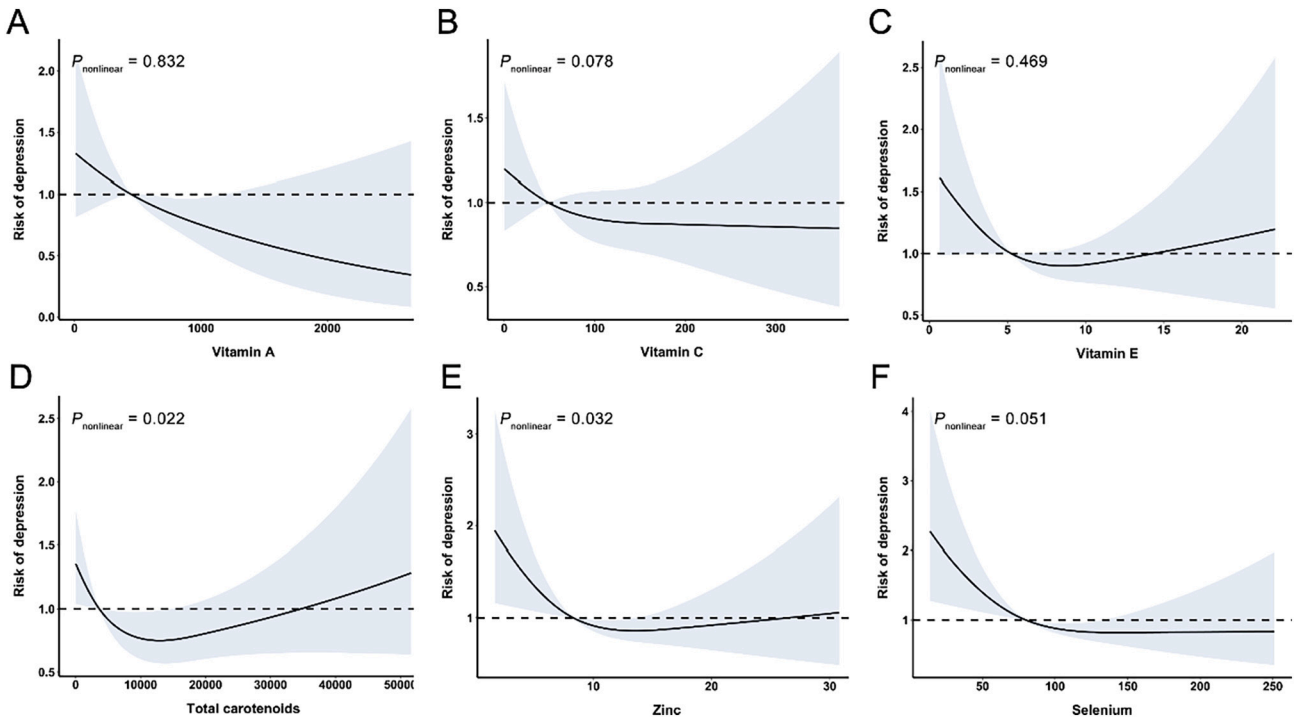

Fig. 1. Restricted cubic splines for the relationships between dietary vitamin A, vitamin C, vitamin E, total carotenoids, zinc, and selenium intake and risk of post-stroke depression. A, vitamin A; B, vitamin C; C, vitamin E; D, total carotenoids; E; zinc; F, selenium.

intakes.

2.3. Depressive symptom assessment

A validated 9-item Patient Health Questionnaire (PHQ-9) was used to assess depressive symptoms. For each item, 4 response categories were included: "not at all", "several days", "more than half the day", and "nearly every day". Responses were scored between 0 and 3. Final composite scores were calculated as the sum of the points in each item ranging from 0 to 27. A cutoff score of 10 is commonly used to identify depression (Kroenke et al., 2001).

2.4. Mortality

Data on all-cause mortality status were determined by using a probabilistic match between NHANES and the National Death Index (NDI) death certificate records. Additional sources of follow-up for mortality included the US Social Security Administration, the Centers for Medicare and Medicaid Services, and death certificates. The follow-up time was defined as the time period from the interview date to the date of death or to the end of follow-up (December 31, 2015).

2.5. Statistical analysis

The characteristics of the participants were described using percentage (%) or mean and their standard deviation (SD). Univariate and multivariate logistic regression analyses were used to assess the odds ratios (ORs) and 95 % confidence intervals (CIs) for the association of dietary antioxidant intake with PSD risk. Moreover, univariate and multivariable Cox regression analyses were used to assess the hazard ratios (HRs) and 95 % CIs for the association of dietary antioxidant intake with all-cause mortality among patients with stroke. The multivariate logistic and Cox regression models were adjusted for age (continuous), sex (male or female), race (non-Hispanic white, black, Mexican American, other Hispanic, or other race), education level (less than high school, high school, or more than high school), marital status (married/living with partner, widowed/divorced/separated, or never married), body mass index (<18.5, 18.5 to <25, 25 to <30, or ≥30 kg/m^2), currently smoking (yes or no), alcohol use (yes or no), diabetes (yes or no), hypertension (yes or no), and hypercholesterolemia (yes or no). Furthermore, we used restricted cubic splines fitting to assess the possibility of the non-linear associations between dietary intakes of vitamin A, vitamin C, vitamin E, total carotenoids, zinc, and selenium and PSD risk and all-cause mortality. Tests for non-linearity used the likelihood ratio test, comparing the model with only the linear term to the model with both linear and cubic spline terms (McMullan et al., 2013). We also used CDAI to assess the joint associations of multiple antioxidant nutrients with PSD risk and all-cause mortality. All data analyses were performed using the R 3.6.2 (http://www.R-project.org). A two-sided *P* value <0.05 was considered significant.

3. Results

Table 1 shows the characteristics of the study population. The study sample consisted of 962 participants with a self-reported history of stroke. The mean age of stroke patients was 66.52 ± 13.22 years old, and 48.65 % were male. In addition, most subjects were white, had high school degree or above, and were married or living with a partner.

The crude and adjusted ORs with 95 % CIs for PSD risk across quartiles of six dietary antioxidant exposures are shown in Table 2. In crude logistic regression model, the negative associations between dietary vitamin A, vitamin C, vitamin E, total carotenoids, zinc, and selenium intake and PSD risk were observed (all *P* for trend <0.05). After adjustments for potential confounders, higher dietary vitamin A, total carotenoids, and selenium intake were associated with decreased risk of PSD (all *P* for trend <0.05). The corresponding ORs were 0.54 (95 % CI: 0.32, 0.92), 0.56 (95 % CI: 0.34, 0.94), and 0.53 (95 % CI: 0.31, 0.90), respectively, for dietary intake in the highest quartile (Q4) compared with those in the lowest quartile (Q1). Furthermore, compared with participants in the first quartile (Q1), those in the third quartile (Q3) of dietary zinc intake was associated with decreased PSD risk (OR: 0.58, 95 % CI: 0.34, 0.98). The restricted cubic splines results showed the U-

Table 3
The crude and adjusted hazard ratios (HRs) with 95 % confidence intervals (CIs) for all-cause mortality according to quartile of dietary intakes of vitamin A, vitamin C, vitamin E, total carotenoids, zinc, and selenium among patients with stroke.

	Crude		Adjusted[a]	
	HR (95%CI)	P value	HR (95%CI)	P value
Vitamin A				
Q1	1.00 (ref.)		1.00 (ref.)	
Q2	1.03 (0.75, 1.43)	0.851	0.77 (0.54, 1.08)	0.126
Q3	1.07 (0.77, 1.48)	0.685	0.73 (0.52, 1.02)	0.067
Q4	0.99 (0.72, 1.38)	0.964	0.63 (0.45, 0.89)	0.009
P for trend	0.987		0.012	
Vitamin C				
Q1	1.00 (ref.)		1.00 (ref.)	
Q2	1.17 (0.83, 1.63)	0.366	1.10 (0.78, 1.56)	0.570
Q3	1.27 (0.91, 1.76)	0.161	0.99 (0.71, 1.39)	0.972
Q4	1.21 (0.86, 1.68)	0.270	1.01 (0.72, 1.42)	0.950
P for trend	0.2370		0.881	
Vitamin E				
Q1	1.00 (ref.)		1.00 (ref.)	
Q2	1.18 (0.87, 1.61)	0.285	1.10 (0.79, 1.51)	0.580
Q3	0.98 (0.71, 1.34)	0.897	0.84 (0.60, 1.17)	0.301
Q4	0.82 (0.59, 1.15)	0.257	0.69 (0.48, 0.99)	0.042
P for trend	0.1789		0.018	
Total carotenoids				
Q1	1.00 (ref.)		1.00 (ref.)	
Q2	0.80 (0.59, 1.10)	0.172	0.86 (0.62, 1.19)	0.359
Q3	0.81 (0.60, 1.10)	0.181	0.83 (0.61, 1.14)	0.259
Q4	0.65 (0.47, 0.90)	0.011	0.66 (0.47, 0.92)	0.015
P for trend	0.0150		0.019	
Zinc				
Q1	1.00 (ref.)		1.00 (ref.)	
Q2	0.83 (0.60, 1.13)	0.226	0.64 (0.46, 0.89)	0.008
Q3	0.80 (0.59, 1.09)	0.158	0.61 (0.44, 0.86)	0.004
Q4	0.67 (0.49, 0.94)	0.017	0.57 (0.40, 0.81)	0.002
P for trend	0.021		0.002	
Selenium				
Q1	1.00 (ref.)		1.00 (ref.)	
Q2	0.90 (0.67, 1.21)	0.473	0.72 (0.52, 0.98)	0.039
Q3	0.63 (0.45, 0.87)	0.006	0.50 (0.36, 0.71)	<0.001
Q4	0.71 (0.52, 0.98)	0.037	0.64 (0.46, 0.90)	0.011
P for trend	0.007		0.001	

[a] Adjusted for age (continuous), sex (male or female), race (non-Hispanic white, black, Mexican American, other Hispanic, or other race), education level (less than high school, high school, or more than high school), marital status (married/living with partner, widowed/divorced/separated, or never married), body mass index (<18.5, 18.5 to <25, 25 to <30, or ≥30 kg/m^2), currently smoking (yes or no), alcohol use (yes or no), diabetes (yes or no), hypertension (yes or no), and hypercholesterolemia (yes or no).

shape associations between dietary total carotenoids, zinc and selenium intake and PSD risk (all $P_{nonlinear}$ <0.05) (Fig. 1).

Table 3 shows the crude and adjusted associations of dietary antioxidant intake with all-cause mortality among stroke patients. In multivariate Cox regression model, the highest quartile (Q4) of dietary vitamin A (HR: 0.63, 95 % CI: 0.45, 0.89), vitamin E (HR: 0.69, 95 % CI: 0.48, 0.99), total carotenoids (HR: 0.66, 95 % CI: 0.47, 0.92), zinc (HR: 0.57, 95 % CI: 0.40, 0.81), and selenium (HR: 0.64, 95 % CI: 0.46, 0.90) intakes were significantly associated with decreased all-cause mortality compared with those in the lowest quartile (Q1). By contrast, there was no significant association between dietary vitamin C intake and all-cause mortality. The restricted cubic splines results showed the negative linear dose-response associations between dietary vitamin A, vitamin E, total carotenoids, and zinc intake and all-cause mortality (all $P_{nonlinear}$ >0.05) (Fig. 2). Furthermore, the association between dietary selenium intake and all-cause mortality presents a nonlinear U-shaped dose-response relationship ($P_{nonlinear}$ = 0.010), indicating a positive association with all-cause mortality at the higher dietary selenium exposure range.

We also used the CDAI to assess the joint associations of six dietary antioxidants with PSD risk and all-cause mortality (Fig. 3). The results showed a negative association between CDAI and PSD risk, with the lowest OR in the third quartiles (Q3) (OR: 0.49, 95 % CI: 0.30, 0.83). Furthermore, the highest quartile (Q4) of CDAI was associated with decreased all-cause mortality compared with those in the lowest quartile (Q1) (HR: 0.56, 95 % CI: 0.39, 0.81).

4. Discussion

The cross-sectional and longitudinal analysis of a representative sample of patients with stroke from the United States indicated that intakes of dietary antioxidant nutrients, including dietary vitamin A, total carotenoids, zinc, and selenium, were negatively associated with PSD risk. In addition, stroke patients with the highest quartiles of dietary vitamin A, vitamin E, zinc, selenium, and total carotenoid intakes were associated with decreased all-cause mortality compared to those with the lowest quartiles. The CDAI was used to assess the joint associations of multiple antioxidant nutrients with the PSD risk, and the results indicated that the PSD risk decreased with an increase in CDAI. A similar finding was also observed between CDAI and all-cause mortality.

To date, few studies have reported the association between dietary antioxidant intake and PSD risk. Similar with our findings, several cross-sectional studies have revealed a significant inverse relationship between essential microelement intake, including zinc, iron, copper, and selenium intake and depression risk (Li et al., 2018; Wang et al., 2018). By contrast, a prospective population-based study including 2317 men has demonstrated that dietary zinc intake may not help in preventing depression (Lehto et al., 2013). Several observational and interventional studies revealed no significant association between selenium intake and depression risk (Ekramzadeh et al., 2015; Shor-Posner et al., 2003). In addition, data on the effects of dietary total carotenoids on depression also remain limited and controversial. In a cross-sectional study in the United States, a higher dietary carotenoid intake was associated with a lower prevalence of depressive symptoms (Beydoun et al., 2015). However, Lin et al. have reported that the prevalence of depressive symptoms decreased with increased dietary intake of beta-cryptoxanthin but not alpha-carotene, beta-carotene, lycopene, or lutein/zeaxanthin (Lin and Shen, 2021). In a longitudinal cohort of adults in Australia, no significant associations were observed between dietary carotenoid intake and depressive symptoms for either sex (Lai et al., 2016). For dietary antioxidant vitamins, sufficient intakes of vitamins A, C, and E have been shown to be associated with a decreased risk of depression (Das et al., 2021; LaChance and Ramsey, 2018; Wang et al., 2021). However, these associations were not significant for vitamins C and E in our study, which may be attributed to the limited sample size.

Interestingly, our study also found the nonlinear U-shape relationships between dietary total carotenoid, zinc, and selenium intakes and PSD risk, indicating the inverse associations may change with increasing dietary total carotenoid, zinc, and selenium intakes. One possible explanation for this observation is that dietary zinc, total carotenoid, and selenium may have both antioxidant and pro-oxidative properties, which can elicit oxidative stress when they are beyond the physiological range (Lee and Jeong, 2012; Young and Lowe, 2018; Yuan et al., 2014).

Although single antioxidant nutrients may play a role in the etiology of PSD, the biological interaction between dietary antioxidants should also be considered. In the present study, we used CDAI to estimate the joint exposure of six dietary antioxidants and found that there may be a dose–response association between combined antioxidant intake and PSD risk. The risk of PSD gradually decreased with the increase of CDAI. Similar to our findings, a recent cross-sectional study including 265 women with type 2 diabetes demonstrated a significant negative association between DTAC and psychological disorders (Daneshzad et al., 2020). Another study reported that a higher total antioxidant intake was significantly associated with lower odds of depression, and a significant negative dose–response association was observed in women (Ferriani

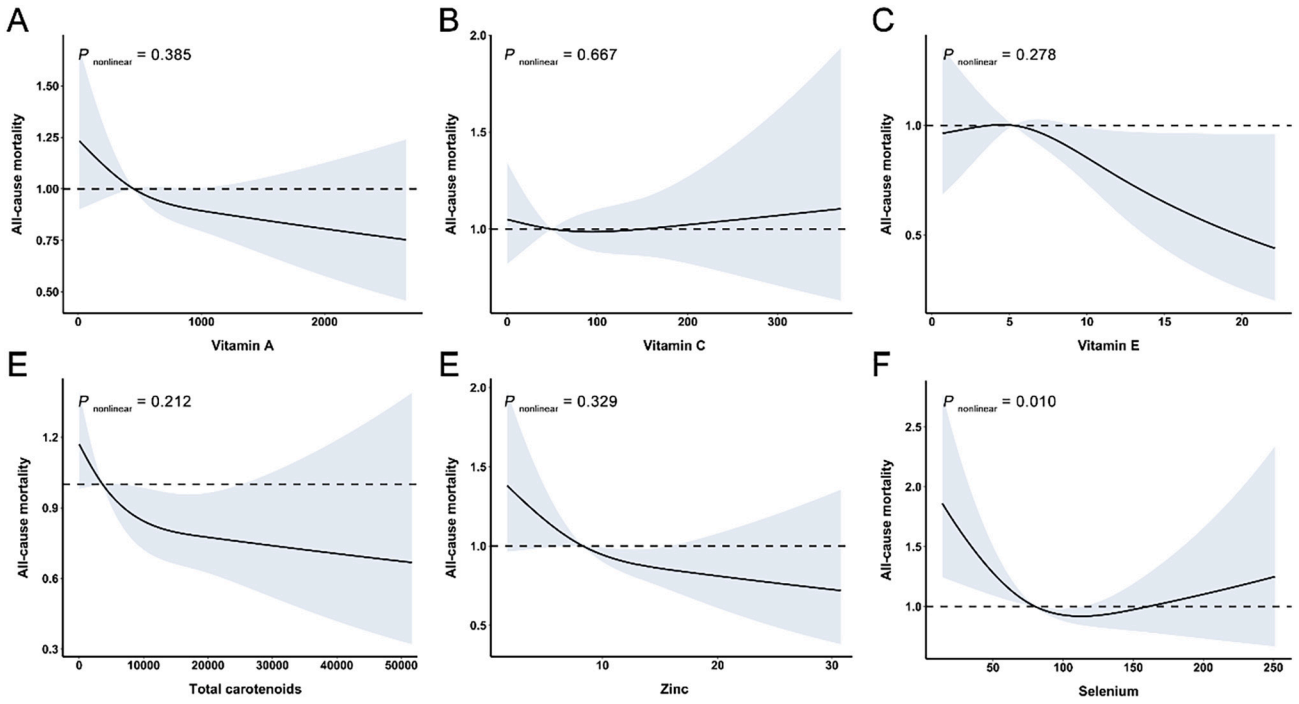

Fig. 2. Restricted cubic splines for the relationships between dietary vitamin A, vitamin C, vitamin E, total carotenoids, zinc, and selenium intake and all-cause mortality. A, vitamin A; B, vitamin C; C, vitamin E; D, total carotenoids; E; zinc; F, selenium.

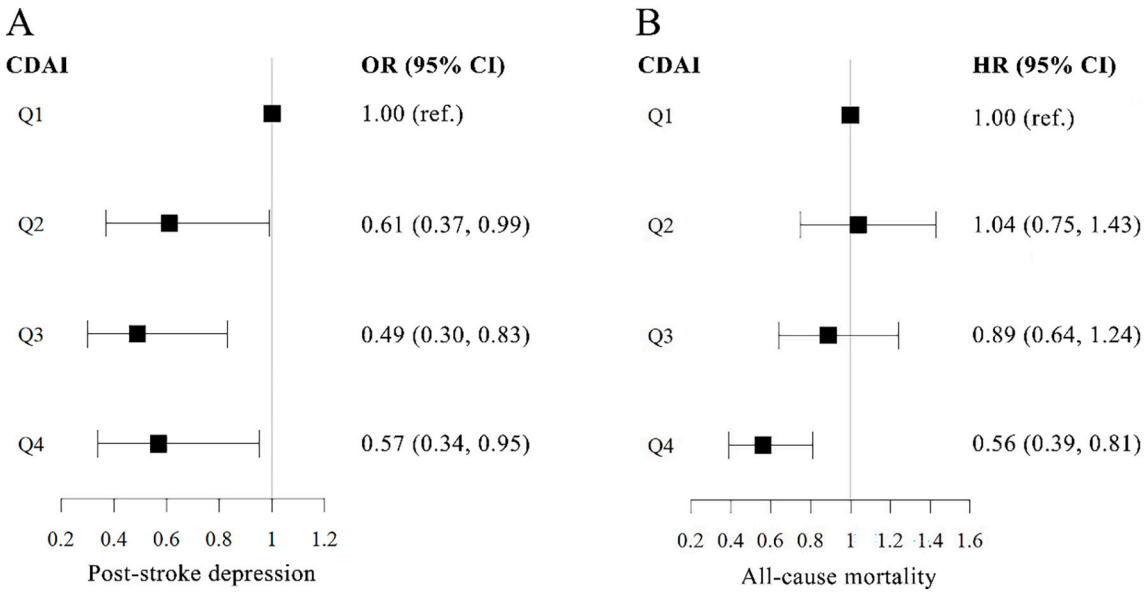

Fig. 3. Association of composite dietary antioxidant index with risk of post-stroke depression and all-cause mortality. A, post-stroke depression; B, all-cause mortality. Models were adjusted for age (continuous), sex (male or female), race (non-Hispanic white, black, Mexican American, other Hispanic, or other race), education level (less than high school, high school, or more than high school), marital status (married/living with partner, widowed/divorced/separated, or never married), body mass index (<18.5, 18.5-<25, 25- <30, or ≥30 kg/m^2), currently smoking (yes or no), alcohol use (yes or no), diabetes (yes or no), hypertension (yes or no), and hypercholesterolemia (yes or no).

et al., 2022). Overall, our findings support a public health recommendation for increasing dietary antioxidant intake in stroke patients to reduce PSD risk.

The etiology and pathophysiology of PSD remain unclear. Potential pathophysiological mechanisms of PSD include lower levels of monoamines, increased inflammation with dysregulation of the hypothalamic–pituitary–adrenal axis, abnormal neurotrophic response, and glutamate toxicity (Medeiros et al., 2020). In addition, oxidative stress plays a key role in PSD pathogenesis, which may explain the protective effect of dietary antioxidant intake on PSD. ROS produced during stroke can cause oxidative stress, lipid and protein peroxidation, and DNA damage in nerve tissue, which is an essential mechanism that induces PSD (Nabavi et al., 2015). Previous studies have suggested that oxidative stress biomarkers, including malondialdehyde DHA, palmitic acid, and trimethylglycine, were positively associated with risk of depression (Liu et al., 2017; Wang et al., 2020). However, antioxidant nutrients

from dietary sources enhance the body's antioxidant defense mechanisms, support the body in eliminating excessive free radicals, and then reduce oxidative stress in the body (Besagil et al., 2020; Hegazy et al., 2019).

Depression often complicates the course of the post-stroke period and PSD is closely related to an increased all-cause mortality. In the present study, we first found that higher dietary vitamin A, vitamin E, total carotenoid, zinc, and selenium intake and CDAI were associated with decreased all-cause mortality among patients with stroke. Our findings are consistent with those of previous prospective studies demonstrating the negative associations between dietary antioxidant nutrients and DTAC and mortality (Ma et al., 2018; Sheng et al., 2022). In adults with diabetes patients, higher intake of overall dietary antioxidants was associated with lower risk of all-cause and cardiovascular disease (CVD) related mortality (Wang et al., 2022). A large prospective study conducted in a middle-aged or elderly Chinese population has demonstrated that dietary antioxidant vitamin intakes, including total carotene and vitamin C, were inversely associated with deaths from all causes and CVD (Zhao et al., 2017). Notably, similar to the results of previous studies, we also observed the nonlinear U-shape relationship between dietary selenium intake and all-cause mortality (Xie et al., 2020), indicating the stroke patients should be cautious about the potential harmful effects of excessive selenium intake.

Stroke is the leading cause of disability, cognitive impairment, and death. In the United States, 3.88 % of the population over the age of 18 is projected to have a stroke by 2030 (Ovbiagele et al., 2013). PSD is a common and serious sequela of stroke. Given that PSD is persistent and has a high risk of recurrence even after long-term remission (Ayerbe et al., 2011), the development of depression must be prevented in patients with stroke. Therefore, the findings of present study may have potential public health implications for developing strategies to reduce the PSD risk and improve the prognosis of stroke patients.

Our study also has several strengths. First, we used a nationally representative sample of the population in the United States. NHANES used rigorous data collection procedures that can be extrapolated to the general U.S. population. Second, we used the restricted cubic spline analyses to assess the nonlinear dose–response relationships between dietary antioxidant intake and PSD risk and all-cause mortality. Third, we used a modified version of CDAI to evaluate the joint exposure of six dietary antioxidants, which may be more informative for exploring the associations between dietary antioxidants and PSD risk and all-cause mortality.

This study has some limitations. First, the cross-sectional design precluded the determination of causality in the associations of dietary antioxidant intake with the risk of PSD. Second, because of the nature of the NHANES database, the stroke status and dietary questionnaire information were both self-reported, which might introduce recall bias. Third, our sample size was relatively small, and results will need to be verified in ongoing larger prospective studies.

5. Conclusion

Data from this cross-sectional and longitudinal study suggest that increased intakes of dietary antioxidants were negatively associated with PSD risk and all-cause mortality. Our findings support a public health recommendation for increasing dietary antioxidant intake in patients with stroke to reduce PSD risk and improve the prognosis. Future prospective large-scale studies are required to confirm these results.

Submission declaration

This article has not been published previously, it is not under consideration for publication elsewhere and the publication is approved by all authors.

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CRediT authorship contribution statement

Qianqian Xu: Conceptualization, Data curation, Formal analysis, Writing – original draft. **Xudong Qian:** Conceptualization, Methodology, Validation. **Fan Sun:** Validation, Conceptualization. **Heng Liu:** Methodology. **Zhijie Dou:** Supervision. **Jian Zhang:** Project administration, Writing – review & editing.

Conflict of interest

We declare that they have no conflict of interest.

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References

Ayerbe, L., Ayis, S., Rudd, A.G., Heuschmann, P.U., Wolfe, C.D., 2011. Natural history, predictors, and associations of depression 5 years after stroke: the South London stroke register. Stroke 42, 1907–1911.

Ayerbe, L., Ayis, S., Wolfe, C.D., Rudd, A.G., 2013. Natural history, predictors and outcomes of depression after stroke: systematic review and meta-analysis. Br. J. Psychiatry 202, 14–21.

Bartoli, F., Di Brita, C., Crocamo, C., Clerici, M., Carra, G., 2018. Early post-stroke depression and mortality: meta-analysis and meta-regression. Front Psychiatry 9, 530.

Berk, M., Williams, L.J., Jacka, F.N., O'Neil, A., Pasco, J.A., Moylan, S., Allen, N.B., Stuart, A.L., Hayley, A.C., Byrne, M.L., Maes, M., 2013. So depression is an inflammatory disease, but where does the inflammation come from? BMC Med. 11, 200.

Besagil, P.S., Calapkorur, S., Sahin, H., 2020. Determination of the relationship between total antioxidant capacity and dietary antioxidant intake in obese patients. Niger. J. Clin. Pract. 23, 481–488.

Beydoun, M.A., Fanelli-Kuczmarski, M.T., Kitner-Triolo, M.H., Beydoun, H.A., Kaufman, J.S., Mason, M.A., Evans, M.K., Zonderman, A.B., 2015. Dietary antioxidant intake and its association with cognitive function in an ethnically diverse sample of US adults. Psychosom. Med. 77, 68–82.

Bolanos, J.P., Moro, M.A., Lizasoain, I., Almeida, A., 2009. Mitochondria and reactive oxygen and nitrogen species in neurological disorders and stroke: therapeutic implications. Adv. Drug Deliv. Rev. 61, 1299–1315.

Cai, W., Mueller, C., Li, Y.J., Shen, W.D., Stewart, R., 2019. Post stroke depression and risk of stroke recurrence and mortality: a systematic review and meta-analysis. Ageing Res. Rev. 50, 102–109.

Canheta, A.B.S., Santos, A., Souza, J.D., Silveira, E.A., 2021. Traditional brazilian diet and extra virgin olive oil reduce symptoms of anxiety and depression in individuals with severe obesity: randomized clinical trial. Clin. Nutr. 40, 404–411.

Chemerinski, E., Robinson, R.G., Kosier, J.T., 2001. Improved recovery in activities of daily living associated with remission of poststroke depression. Stroke 32, 113–117.

Cully, J.A., Gfeller, J.D., Heise, R.A., Ross, M.J., Teal, C.R., Kunik, M.E., 2005. Geriatric depression, medical diagnosis, and functional recovery during acute rehabilitation. Arch. Phys. Med. Rehabil. 86, 2256–2260.

Daneshzad, E., Keshavarz, S.A., Qorbani, M., Larijani, B., Azadbakht, L., 2020. Dietary total antioxidant capacity and its association with sleep, stress, anxiety, and depression score: a cross-sectional study among diabetic women. Clin. Nutr. ESPEN 37, 187–194.

Das, A., Cumming, R.G., Naganathan, V., Ribeiro, R.V., Le Couteur, D.G., Handelsman, D. J., Waite, L.M., Hirani, V., 2021. The association between antioxidant intake, dietary pattern and depressive symptoms in older australian men: the Concord health and ageing in men project. Eur. J. Nutr. 60, 443–454.

Dharmayani, P.N.A., Juergens, M., Allman-Farinelli, M., Mihrshahi, S., 2021. Association between fruit and vegetable consumption and depression symptoms in young people and adults aged 15–45: a systematic review of cohort studies. Int. J. Environ. Res. Public Health 18.

Ding, J., Zhang, Y., 2022. Associations of dietary vitamin C and E intake with depression. A meta-analysis of observational studies. Front Nutr 9, 857823.

Ekramzadeh, M., Mazloom, Z., Sagheb, M., 2015. Association of Depression with Selenium Deficiency and Nutritional Markers in the patients with end-stage renal disease on hemodialysis. J. Ren. Nutr. 25, 381–387.

Ferriani, L.O., Silva, D.A., Molina, M., Mill, J.G., Brunoni, A.R., da Fonseca, M.J.M., Moreno, A.B., Bensenor, I.M., de Aguiar, O.B., Barreto, S.M., Viana, M.C., 2022. Associations of depression and intake of antioxidants and vitamin B complex: results

of the brazilian longitudinal study of adult health (ELSA-Brasil). J. Affect. Disord. 297, 259–268.
Gillen, R., Tennen, H., McKee, T.E., Gernert-Dott, P., Affleck, G., 2001. Depressive symptoms and history of depression predict rehabilitation efficiency in stroke patients. Arch. Phys. Med. Rehabil. 82, 1645–1649.
Glabska, D., Guzek, D., Groele, B., Gutkowska, K., 2020. Fruit and vegetable intake and mental health in adults: a systematic review. Nutrients 12.
Hackett, M.L., Pickles, K., 2014. Part I: frequency of depression after stroke: an updated systematic review and meta-analysis of observational studies. Int. J. Stroke 9, 1017–1025.
Hegazy, A.M., El-Sayed, E.M., Ibrahim, K.S., Abdel-Azeem, A.S., 2019. Dietary antioxidant for disease prevention corroborated by the Nrf2 pathway. J. Complement. Integr. Med. 16.
Jorgensen, T.S., Wium-Andersen, I.K., Wium-Andersen, M.K., Jorgensen, M.B., Prescott, E., Maartensson, S., Kragh-Andersen, P., Osler, M., 2016. Incidence of depression after stroke, and associated risk factors and mortality outcomes, in a large cohort of danish patients. JAMA Psychiatry 73, 1032–1040.
Kase, B.E., Liu, J., Wirth, M.D., Shivappa, N., Hebert, J.R., 2021. Associations between dietary inflammatory index and sleep problems among adults in the United States, NHANES 2005–2016. Sleep Health 7, 273–280.
Kroenke, K., Spitzer, R.L., Williams, J.B., 2001. The PHQ-9: validity of a brief depression severity measure. J. Gen. Intern. Med. 16, 606–613.
LaChance, L.R., Ramsey, D., 2018. Antidepressant foods: an evidence-based nutrient profiling system for depression. World J. Psychiatry 8, 97–104.
Lai, J.S., Oldmeadow, C., Hure, A.J., McEvoy, M., Hiles, S.A., Boyle, M., Attia, J., 2016. Inflammation mediates the association between fatty acid intake and depression in older men and women. Nutr. Res. 36, 234–245.
Lee, K.H., Jeong, D., 2012. Bimodal actions of selenium essential for antioxidant and toxic pro-oxidant activities: the selenium paradox (Review). Mol. Med. Rep. 5, 299–304.
Lehto, S.M., Ruusunen, A., Tolmunen, T., Voutilainen, S., Tuomainen, T.P., Kauhanen, J., 2013. Dietary zinc intake and the risk of depression in middle-aged men: a 20-year prospective follow-up study. J. Affect. Disord. 150, 682–685.
Li, F., Liu, X., Zhang, D., 2016. Fish consumption and risk of depression: a meta-analysis. J. Epidemiol. Community Health 70, 299–304.
Li, Z., Wang, W., Xin, X., Song, X., Zhang, D., 2018. Association of total zinc, iron, copper and selenium intakes with depression in the US adults. J. Affect. Disord. 228, 68–74.
Lin, S., Shen, Y., 2021. Dietary carotenoids intake and depressive symptoms in US adults, NHANES 2015–2016. J. Affect. Disord. 282, 41–45.
Liu, Z., Zhu, Z., Zhao, J., Ren, W., Cai, Y., Wang, Q., Luan, X., Zhao, K., He, J., 2017. Malondialdehyde: a novel predictive biomarker for post-stroke depression. J. Affect. Disord. 220, 95–101.
Ma, E., Iso, H., Yamagishi, K., Ando, M., Wakai, K., Tamakoshi, A., 2018. Dietary antioxidant micronutrients and all-cause mortality: the Japan collaborative cohort study for evaluation of cancer risk. J Epidemiol 28, 388–396.
Maugeri, A., Hruskova, J., Jakubik, J., Kunzova, S., Sochor, O., Barchitta, M., Agodi, A., Bauerova, H., Medina-Inojosa, J.R., Vinciguerra, M., 2019. Dietary antioxidant intake decreases carotid intima media thickness in women but not in men: a cross-sectional assessment in the kardiovize study. Free Radic. Biol. Med. 131, 274–281.
McMullan, C.J., Schernhammer, E.S., Rimm, E.B., Hu, F.B., Forman, J.P., 2013. Melatonin secretion and the incidence of type 2 diabetes. JAMA 309, 1388–1396.
Medeiros, G.C., Roy, D., Kontos, N., Beach, S.R., 2020. Post-stroke depression: a 2020 updated review. Gen. Hosp. Psychiatry 66, 70–80.
Mitchell, A.J., Sheth, B., Gill, J., Yadegarfar, M., Stubbs, B., Yadegarfar, M., Meader, N., 2017. Prevalence and predictors of post-stroke mood disorders: a meta-analysis and meta-regression of depression, anxiety and adjustment disorder. Gen. Hosp. Psychiatry 47, 48–60.
Nabavi, S.F., Dean, O.M., Turner, A., Sureda, A., Daglia, M., Nabavi, S.M., 2015. Oxidative stress and post-stroke depression: possible therapeutic role of polyphenols? Curr. Med. Chem. 22, 343–351.
Ovbiagele, B., Goldstein, L.B., Higashida, R.T., Howard, V.J., Johnston, S.C., Khavjou, O. A., Lackland, D.T., Lichtman, J.H., Mohl, S., Sacco, R.L., Saver, J.L., Trogdon, J.G., , American Heart Association Advocacy Coordinating C., Stroke, C., 2013. Forecasting the future of stroke in the United States: a policy statement from the American Heart Association and American Stroke Association. Stroke 44, 2361–2375.
Pereira, G.A., da Silva, A., Hermsdorff, H.H.M., Moreira, A.P.B., de Aguiar, A.S., 2021. Association of dietary total antioxidant capacity with depression, anxiety, and sleep disorders: a systematic review of observational studies. J. Clin. Transl. Res. 7, 631–640.
Sheng, L.T., Jiang, Y.W., Pan, A., Koh, W.P., 2022. Dietary total antioxidant capacity and mortality outcomes: the Singapore Chinese Health Study. Eur. J. Nutr. 61, 2375–2382.
Shor-Posner, G., Lecusay, R., Miguez, M.J., Moreno-Black, G., Zhang, G., Rodriguez, N., Burbano, X., Baum, M., Wilkie, F., 2003. Psychological burden in the era of HAART: impact of selenium therapy. Int. J. Psychiatry Med. 33, 55–69.
Vavakova, M., Durackova, Z., Trebaticka, J., 2015. Markers of oxidative stress and neuroprogression in depression disorder. Oxidative Med. Cell. Longev. 2015, 898393.
Villa, R.F., Ferrari, F., Moretti, A., 2018. Post-stroke depression: mechanisms and pharmacological treatment. Pharmacol. Ther. 184, 131–144.
Wang, J., Um, P., Dickerman, B.A., Liu, J., 2018. Zinc, magnesium, selenium and depression: a review of the evidence, potential mechanisms and implications. Nutrients 10.
Wang, M., Gui, X., Wu, L., Tian, S., Wang, H., Xie, L., Wu, W., 2020. Amino acid metabolism, lipid metabolism, and oxidative stress are associated with post-stroke depression: a metabonomics study. BMC Neurol. 20, 250.
Wang, A., Luo, J., Zhang, T., Zhang, D., 2021. Dietary vitamin C and vitamin C derived from vegetables are inversely associated with the risk of depressive symptoms among the general population. Antioxidants (Basel) 10.
Wang, W., Wang, X., Cao, S., Duan, Y., Xu, C., Gan, D., He, W., 2022. Dietary antioxidant indices in relation to all-cause and cause-specific mortality among adults with diabetes: a prospective cohort study. Front. Nutr. 9, 849727.
Wright, M.E., Mayne, S.T., Stolzenberg-Solomon, R.Z., Li, Z., Pietinen, P., Taylor, P.R., Virtamo, J., Albanes, D., 2004. Development of a comprehensive dietary antioxidant index and application to lung cancer risk in a cohort of male smokers. Am. J. Epidemiol. 160, 68–76.
Xie, B., Wang, J., Zhang, J., Chen, M., 2020. Dietary and serum selenium in coronary heart disease and all-cause mortality: an international perspective. Asia Pac. J. Clin. Nutr. 29, 827–838.
Young, A.J., Lowe, G.L., 2018. Carotenoids-antioxidant properties. Antioxidants (Basel) 7.
Yuan, Y., Niu, F., Liu, Y., Lu, N., 2014. Zinc and its effects on oxidative stress in Alzheimer's disease. Neurol. Sci. 35, 923–928.
Zhang, Y., Ding, J., Liang, J., 2022. Associations of dietary vitamin a and Beta-carotene intake with depression. A meta-analysis of observational studies. Front Nutr 9, 881139.
Zhao, L.G., Shu, X.O., Li, H.L., Zhang, W., Gao, J., Sun, J.W., Zheng, W., Xiang, Y.B., 2017. Dietary antioxidant vitamins intake and mortality: a report from two cohort studies of Chinese adults in Shanghai. J Epidemiol 27, 89–97.