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Relationship between Mediterranean diet and depression in South Korea: the Korea National Health and Nutrition Examination Survey

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Background: Several studies have shown that adherence to the Mediterranean diet is associated with a lower risk of depression; however, little is known about the Asian population. This study investigated the relationship between adherence to the Mediterranean diet and depression in a sample of the South Korean population.

Methods: In total, 5,849 adults from the 2014 and 2016 Korea National Health and Nutrition Examination Surveys were included in the study. The Mediterranean diet adherence was measured using a modified alternate Mediterranean diet score (mMED) developed to adjust for Korean dietary patterns. The mMED scores using the Food Frequency Questionnaire were divided into four categories (0–2, 3–4, 5–6, and 7–9 points). Subjects with depression were defined as having moderate-to-severe depressive symptoms using the Patient Health Questionnaire-9, with a cutoff value of 10. Logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs). A subgroup analysis was performed based on sex.

Results: The results of logistic regression analysis indicated that individuals with higher mMED were 42–73% less likely to report depression compared to individuals with the lowest mMED [ORs (95% Cls) = 0.58 (0.37-0.90), 0.50 (0.31-0.80), 0.27 (0.15-0.47)] after adjusting for socio-demographic and health-related variables. In women, individuals with mMED of 7–9 had 71% lower odds of depression [ORs (95% Cls): 0.29 (0.13-0.64)]. In men, individuals with mMED of 5–9 had 55% [ORs (95% Cls): 0.45 (0.23-0.91)] to 79% [ORs (95% Cls): 0.21 (0.08-0.57)] lower odds of depression.

Conclusion: This study suggests that adherence to the Mediterranean diet is inversely associated with depression in both men and women among Korean adults. This study provides evidence that a Mediterranean diet is crucial in preventing depressive symptoms in Asian populations.

KEYWORDS

depressive symptoms, dietary patterns, KNHANES, Mediterranean diet score, sex difference

1. Introduction

It is estimated that approximately 256 million adults (5.02%) worldwide suffer from depression in 2019 (1), and the prevalence of depression has increased more than three times during the COVID-19 pandemic (2, 3). Depression is a leading cause of disability and contributes to the overall burden of disease worldwide (4). A longitudinal study demonstrated that depressive symptoms are associated with an approximately 8-fold increased risk of suicide attempts (5). Furthermore, South Korea has the highest suicide rate among Organization for Economic Cooperation and Development (OECD) countries (6). Effective treatment modalities, including pharmacotherapy for depression, have been established; however, half of the patients with depression show an inadequate response to antidepressants (7). Therefore, developing effective strategies to prevent depression is necessary.

Lifestyle modifications, such as dietary advice or exercise coaching, could be important in preventing depression (8, 9). Particularly, recent systematic reviews and meta-analyses indicated that adhering to a healthy diet can reduce the risk of clinical depression or depressive symptoms (10, 11). Diet quality has been reported to influence several biological processes associated with depression, including the production of monoamine neurotransmitters such as serotonin and dopamine, levels of oxidative stress, brain-derived neurotrophic factor (BDNF), and hypothalamic-pituitary-adrenal (HPA) activity (12).

The Mediterranean diet emerged from a classical study by Keys (13) and has been recognized by the United Nations Educational, Scientific, and Cultural Organization (UNESCO) as an intangible cultural heritage of humanity (14). The Mediterranean diet consists of a daily intake of whole grains, vegetables, legumes, fruits, nuts, dairy products, and olive oil; a weekly intake of fish (often); white meat (moderately); red and processed meat (less often); and moderate amounts of wine (15, 16). Previous evidence has shown that Mediterranean diet adherence is associated with a decreased risk of depression in the Mediterranean and other Western countries, including Greece, Italy, Spain, France, the U.K., the Netherlands, the U.S., and Australia (10, 17–19). Longitudinal studies have shown that the association between diet and depression is not significant in women (20, 21), suggesting sex-based differences.

Among the non-Caucasian population, a cross-sectional study of Iranian adults found an inversely significant association between adherence to a Mediterranean diet and depression (22). The Mediterranean diet index is commonly calculated using the median cutoff from each study sample; therefore, these results may be difficult to apply to other cultures (23). To the best of our knowledge, no evidence exists suggesting that adherence to a Mediterranean diet is associated with depression in Asian populations. Therefore, this study aimed to determine the relationship between adherence to the Mediterranean diet and depression in a nationally representative sample of Korean adults. We also investigated whether the association between depression and Mediterranean diet adherence differed between men and women.

2. Materials and methods

2.1. Data source and study population

Data were obtained from the National Health and Nutrition Examination Survey of South Korea (KNHANES), conducted by the Korea Centers for Disease Control and Prevention (KCDC). This nationwide survey comprised approximately 10,000 individuals over the age of 1 each year. The objectives of the KNHANES include monitoring trends in health-risk factors and their prevalence. The survey consisted of a health examination, health interview, and nutrition survey conducted by trained medical staff and interviewers. The available database and detailed descriptions can be found on the KNHANES website.¹

Our primary sample included 15,700 individuals who completed all three surveys (health examination, health interview, and nutrition survey) in the 2014 and 2016 KNHANES. We excluded individuals with missing valid Patient Health Questionnaire-9 (PHQ-9) scores (n = 4,990), Food Frequency Questionnaire (FFQ) scores (n = 4,614), or covariate scores (n=34) from this analysis. Individuals who were aged ≤ 19 or >69 years (*n*=93), pregnant or breastfeeding (*n*=105) (24), or had extreme energy intake (\leq 500 or > 6,000 kcal/day) (n = 15) (25) were excluded. The final sample included 5,849 individuals (Figure 1). All participants signed an informed consent form. The KNHANES was reviewed and approved by the KCDC Research Ethics Review Committee, which operates under domestic and international regulations, including the Declaration of Helsinki. The Institutional Review Board (IRB) of CHA Bundang Medical Center of CHA University exempted this IRB review because the databases provided publicly available secondary data (no. 2022-12-051).

2.2. Adherence to the Mediterranean diet

Adherence to the Mediterranean diet was measured using the modified alternate Mediterranean diet score (mMED) developed by Kim and Je (25) to adjust for Korean dietary patterns based on the alternate Mediterranean diet score (26). To calculate the mMED, dietary intake was evaluated using semiquantitative FFQ data from the KNHANES from 2012 to 2016. The FFQ consists of 112 items measuring the average frequency of food intake and service size over the past year. Regarding the frequency of food intake, nine categories were general options (from less than once per month to more than three times per day). For the serving size, the three categories were general options (0.5, 1, or 1.5 being the standard serving size), and the amount of alcoholic beverage was measured using open-ended questions. The consumption of each food item was estimated by multiplying the frequency of intake per week by the serving size (25). The reproducibility of the FFQ was acceptable, ranging from 0.54 to 0.61, and the validity was modest, ranging from 0.29 to 0.45 (27).

The mMED classifies 65 foods into nine groups: vegetables, legumes, fruits, whole grains, red or processed meats, white meat, fish/ peanuts, dairy products, and alcohol (25). The mMED was calculated using sex-specific medians for the frequency of intake of each food group as cut-offs. The total mMED ranged from 0 to 9, with each food group scoring either 0 or 1. For vegetables, legumes, fruits, whole grains, white meats, fish/peanuts, and dairy products, the participants were awarded a point if they consumed more than the median intake. For red or processed meat, considering that the intake of red meat is relatively low in Korea (28), a point was awarded if the subjects

¹ https://knhanes.kdca.go.kr



consumed less than the 75th percentile. Ethanol consumption in alcoholic beverages was calculated according to the 8th Revision Korean Food Composition Table provided by the Korean Nutrition Society (29). A point was awarded for ethanol consumed of 10–50 g and 5–25 g per day for men and women, respectively. Otherwise, zero points were awarded. Finally, mMED was divided into four categories (0–2, 3–4, 5–6, and 7–9 points) for statistical analysis (25).

2.3. Depression

The PHQ-9, which has been administered biannually in the KNHANES since 2014, was used to evaluate depression severity (30). The PHQ-9 consists of nine criteria for depressive disorder from the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV), each rated on a scale from *not at all* (0), *several days* (1), *more than half the days* (2), and *nearly every day* (3), resulting in a total score ranging from 0 to 27. The PHQ-9 cut-point of 10 for major depressive disorder had a high sensitivity (88%) and specificity (88%) (30), and a validation study reported that the Cronbach's α of the

Korean version of PHQ-9 was 0.81 (31). In this study, depression was defined as a PHQ-9 score of 10 (moderate or severe depression) (30).

2.4. Covariates

Sociodemographic (sex, age, residential area, household income, marital status, and education) and health-related (sleep, exercise variations, smoking, alcohol use, body mass index, chronic medical diseases, and energy intake) variables were selected as covariates that could affect diet quality or depression.

Household income was classified into quintiles based on the Korean population. Sleep duration was classified as *insufficient* (<6*h*/*day*), *normal*, (<9*h*/*day*), and *excessive* (\geq 9*h*/*day*). Exercise variation was classified as *none*, *one*, *two*, *or more*, depending on whether the three types of exercise (strength, aerobic, and walking) were performed at least once a week. Smoking and alcohol use were classified as *current* or *non-use*. Body Mass Index (BMI; kg/m²) was classified into four categories: *underweight* (*BMI*<18.5), *normal weight* (18.5 \leq BMI < 23), *overweight* (23 \leq BMI < 25), and *obesity*

 $(25 \le BMI)$ by calculating the weight and height measured by trained staff. Chronic medical diseases were classified as *none, one, two, or more*, and diabetes mellitus, hypertension, dyslipidemia, stroke, chronic renal failure, and coronary heart disease, which could directly or indirectly affect depression, were included as comorbidities (32). Energy intake was classified into quartiles according to sex based on the study data.

2.5. Statistical analysis

Descriptive statistics were calculated for the frequencies and percentages of sociodemographic and clinical characteristics. Differences between participants' characteristics were tested using the chi-square test. A False Discovery Rate (FDR) correction was performed to correct for type I error inflation. Using multivariate logistic regression analysis, odds ratios (ORs) and 95% confidence intervals (CIs) for depression were estimated in groups with mMED of 3–4, 5–6, and 7–9 when controlling covariates. Additional analysis was performed to investigate the ORs and 95% CIs for sex differences in the impact on depression using multivariable logistic regression analysis. All data processing and analysis were performed using Python (version 3.9), and a *p*-value < 0.05 was considered significant.

3. Results

3.1. Description of the study sample

The sociodemographic and clinical characteristics of the 5,849 participants based on the presence of moderate or severe depressive symptoms are summarized in Table 1. Among the participants, the prevalence of depression was 5.5% (4.0% for men and 6.4% for women; more details are presented in Table 1). The results of the chi-square test indicated that the higher the mMED, the lower the frequency of depression [9.7% vs. 6.5% vs. 5.5% vs. 3.3% (FDR-corrected p < 0.001)]. The residential area, alcohol consumption, and energy intake were not significantly associated with depression. In contrast, other sociodemographic and health-related variables, including sex, age, household income, marital status, education, sleep, exercise variations, smoking, BMI group, and chronic medical diseases, were significantly associated with depression (FDR-corrected p < 0.05).

3.2. Association between the Mediterranean diet and depression

The results of the multivariate logistic regression analysis of the association between the mMED and depression are presented in Table 2. The mMED significantly decreased the odds of depression [ORs (95% CIs): 0.65 (0.44–0.97), 0.54 (0.36–0.80), 0.32 (0.20–0.50); Model 1]. The association between the mMED and depression remained significant after adjusting socio-demographic variables [ORs (95% CIs): 0.56 (0.37–0.86), 0.50 (0.33–0.77), 0.30 (0.19–0.49); model 2] and all other covariates including sleep, exercise variations, smoking, alcohol use, BMI group, chronic medical disease, and energy intake [ORs (95% CIs): 0.58 (0.37–0.90), 0.50 (0.31–0.80), 0.27

(0.15–0.47); model 3]. This result indicates that individuals with higher mMED were 42 to 73% less likely to report depression compared to those with the lowest mMED.

3.3. Sex differences in the impact of Mediterranean diet adherence on depression

The results of the multivariate logistic regression analysis for sex differences in the impact of mMED on depression are shown in Figure 2. A significant association was found between depression and mMED after adjusting for all covariates in both men and women. In women, compared to the individuals in the lowest mMED group, individuals with mMED of 7–9 had 71% lower odds of depression [ORs (95% CIs): 0.29 (0.13–0.64)]. In men, individuals with a mMED of 5–9 had a 55% [ORs (95% CIs): 0.45 (0.23–0.91)] to 79% [ORs (95% CIs): 0.21 (0.08–0.57)] lower risk of depression.

Regarding the impact of sociodemographic and health-related factors on depression, men and women who were current smokers or reported having insufficient sleep were more likely to report depression. However, men and women who were married or had higher household incomes were less likely to report depression. Being underweight and high energy consumption were associated with depression only in men.

4. Discussion

This study investigated the relationship between adherence to the Mediterranean diet and depression using a representative sample of South Korean adults. We found that individuals with greater adherence to the Mediterranean diet had a lower risk of depression after adjusting for the confounding effects of sociodemographic and health-related variables. Furthermore, a significant association was observed between adherence to Mediterranean diet and depression in both men and women. To the best of our knowledge, this is the first study to examine the relationship between the Mediterranean diet and depression in an Asian population.

Our study found that individuals with greater adherence to the Mediterranean diet had a 42–73% lower risk of depression. This finding was consistent with previous studies suggesting that people with high Mediterranean diet scores were reported to have a 40–45% lower risk of depression (22, 33). Other meta-analysis studies showed adherence to the Mediterranean diet was associated with a 19% lower risk of depression (18, 19). Furthermore, randomized controlled trials have reported that Mediterranean dietary interventions significantly improved depressive symptoms (34, 35). Generally, these consistent results among non-Asian populations suggest the beneficial role of the Mediterranean diet in depression, and our results may confirm the relationship between the Mediterranean diet and depression in Asian cultures.

The mechanism underlying the association between the Mediterranean diet and depression is unclear; however, several potential explanations exist. The Mediterranean diet is rich in vitamin B and omega-3 polyunsaturated fatty acids (PUFA). Vitamin B can be involved in several methylation reactions, including serotonin and other monoamine neurotransmitters, and PUFA can play an important

TABLE 1 Socio-demographics and clinical characteristics of study participants by the presence of depression.

Characteristics	Total (<i>n</i> =5,849)	Depressive (n=319, %)	Non-depressive (n=5,530, %)	<i>p</i> -value			
Mediterranean diet score				<0.001			
0-2	401	36 (8.98)	365 (91.02)				
3-4	1,684	114 (6.77)	1,570 (93.23)				
5–6	2,174	122 (5.61)	2,052 (94.39)				
7–9	1,590	47 (2.96)	1,543 (97.04)				
Sex							
Men	2,265	91 (4.02)	2,174 (95.98)				
Women	3,584	228 (6.36)	3,356 (93.64)				
Age (years)							
20–29	837	61 (7.29)	776 (92.71)				
30–39	1,404	77 (5.48)	1,327 (94.52)				
40-49	1,467	58 (3.95)	1,409 (96.05)				
50–59	1,458	80 (5.49)	1,378 (94.51)				
50–69	683	43 (6.30)	640 (93.70)				
Residential area							
Rural area	947	54 (5.70)	893 (94.30)				
Urban area	4,902	265 (5.41)	4,637 (94.59)				
Household income							
Quintile 1	603	93 (15.42)	510 (84.58)				
Quintile 2	1,098	63 (5.74)	1,035 (94.26)				
Quintile 3	1,302	61 (4.69)	1,241 (95.31)				
Quintile 4	1,362	54 (3.96)	1,308 (96.04)				
Quintile 5	1,484	48 (3.23)	1,436 (96.77)				
Marital status				<0.001			
Married	4,301	168 (3.91)	4,133 (96.09)				
Separated/divorced/widowed	1,138	87 (7.64)	1,051 (92.36)				
Never married	410	64 (15.61)	346 (84.39)				
Education				<0.001			
Primary or below	556	61 (10.97)	495 (89.03)				
Middle school	517	34 (6.58)	483 (93.42)				
High school	2,148	112 (5.21)	2,036 (94.79)				
College or above	2,628	112 (4.26)	2,516 (95.74)				
Sleep				<0.001			
Insufficient (<6 h/day)	4,740	215 (4.54)	4,525 (95.46)				
Normal (<9 h/day)	714	78 (10.92)	636 (89.08)				
Excessive (≥9 h/day)	395	26 (6.58)	369 (93.42)				
Exercise variations	I	1		<0.001			
None	655	45 (6.67)	610 (93.13)				
One	2,822	180 (6.38)	2,642 (93.62)				
Two or more	2,372	94 (3.96)	2,278 (96.04)				
Smoking	I	1		<0.001			
Non-smoker	4,717	216 (4.58)	4,501 (95.42)				
Smoker	1,132	103 (9.10)	1,029 (90.90)				

(Continued)

TABLE 1 (Continued)

Characteristics	Total (<i>n</i> =5,849)	Depressive (n=319, %)	Non-depressive (n=5,530, %)	<i>p</i> -value			
Alcohol use							
No	2,441	138 (5.65)	2,303 (94.35)				
Yes	3,408	181 (5.31)	3,227 (94.69)				
Body Mass Index group							
Underweight	252	24 (9.52)	228 (90.48)				
Normal weight	2,430	130 (5.35)	2,300 (94.65)				
Overweight	1,303	61 (4.68)	1,242 (95.32)				
Obesity	1864	104 (5.58)	1760 (94.42)				
Chronic medical disease							
None	4,589	236 (5.14)	4,353 (94.86)				
One	804	44 (5.47)	760 (94.53)				
Two or more	456	39 (8.55)	417 (91.45)				
Energy intake							
Quartile 1	1,463	98 (6.70)	1,365 (93.30)				
Quartile 2	1,462	65 (4.45)	1,397 (95.55)				
Quartile 3	1,462	74 (5.06)	1,388 (94.94)				
Quartile 4	1,462	82 (5.61)	1,380 (94.39)				

Depression was defined as a patient health questionnaire-9 score of 10. Bold values were defined as significant at *p*-values < 0.05.

TABLE 2 Odds ratios and 95% confidence intervals of the multivariable logistic regression for the association between modified Mediterranean diet score (mMED) and depression (PHQ-9 \geq 10).

	Mediterranean diet score							
	0-2	3–4		5–6		7–9		
	ORs	ORs (95% Cls)	<i>p</i> -value	ORs (95% CIs)	<i>p</i> -value	ORs (95% CIs)	<i>p</i> -value	
Model 1ª	1.0 (ref)	0.65 (0.44-0.97)	0.034	0.54 (0.36-0.80)	0.002	0.32 (0.20-0.50)	< 0.001	
Model 2 ^b	1.0 (ref)	0.56 (0.37-0.86)	0.007	0.50 (0.33-0.77)	0.002	0.30 (0.19-0.49)	<0.001	
Model 3 ^c	1.0 (ref)	0.58 (0.37-0.90)	0.015	0.50 (0.31-0.80)	0.004	0.27 (0.15-0.47)	< 0.001	

^aModel 1 was unadjusted.

^bModel 2 was adjusted for sex, age, residential area, household income, marital status, and educational level.

^cModel 3 was additionally adjusted for sleep, exercise variations, smoking, alcohol use, BMI group, chronic medical disease, and energy intake.

Each modified Mediterranean diet score group was compared with the 0-2 group and p-value < 0.05 was defined as significant. PHQ-9, patient health questionnaire-9; ORs, odds ratios; CIs, confidence intervals; ref, reference group; BMI, body mass index.

role in central nervous system function and membrane fluidity, which could influence serotonin transport (36). Moreover, fruits, vegetables, and rice wine (37) in the Mediterranean diet may be rich sources of polyphenols with antioxidative and anti-inflammatory effects on depression (38, 39). Polyphenols can also induce BDNF expression by inducing cyclic adenosine monophosphate (cAMP) response element binding (CREB) (40). BDNF activation in the hippocampus and prefrontal cortex plays an important role in regulating depressive symptoms (41). The synergistic effects of these nutrients in the Mediterranean diet may contribute to its protective role against depression. Since this study could not identify the mechanism involved in nutritional biology, further research is needed to identify the mechanisms for the antidepressant properties of the Mediterranean diet.

We conducted further analyses to investigate sex differences in the effects of the Mediterranean diet and other demographic and

health-related factors on depression. We found that moderate and high adherence to the Mediterranean diet was associated with a lower risk of depression in men, whereas women showed this relationship only in the high Mediterranean diet group. A previous large prospective cohort study showed that adherence to the Mediterranean diet was associated with incident depression in a male subgroup but not in a female subgroup (20), suggesting that there may be sex differences. Multiple factors, including biological, cultural, and reproductive events, can affect sex differences in the development of depression (42). Particularly, female sex hormones may induce changes in food intake and taste preference (43), as well as affect neuroinflammation and endocrine systems that contribute to depression (44–46). Body image perception by sex can also be considered as another possible explanation (47). Furthermore, longitudinal studies are required to investigate sex differences in the



Odds Ratio and 95% Confidence Interval for depression

causal relationship between Mediterranean diet adherence and

odds ratios; CI, confidence intervals; vs., versus; BMI, body mass index.

depression in Asian populations. Regarding sociodemographic and health-related factors, in both men and women, the risk of depression was associated with household income, marital status, sleep duration, and smoking, showing a pattern similar to that of previous studies (48–50). Interestingly, the risk of depression was significantly associated only with being underweight in the male group. Considering a previous result that men with depression are more likely to report decreased appetite and weight loss than women (51), low body weight may significantly impact depression in men.

Although this study investigated the adherence to the Mediterranean diet using the mMED index reflecting the Korean food culture, there are some points to consider the characteristics of the Korean dietary situation possibly affecting mental health. For example, most Koreans eat fermented vegetables, including Kimchi and soybean paste. Some studies suggested that fermented food modulates the composition of microbiota, especially via *Lactobacillus* (52, 53). As several studies examined the effect of the microbiome on mental health, such as mood disorders, anxiety disorder, and autism spectrum disorder (54, 55), adherence to fermented food might be linked with mental disorders. Future research investigating the effect of Korean food on depression would elucidate the association between diet and depression in Korean culture.

This study's key advantage is that it used large and homogeneous national data to analyze the relationship between adherence to the Mediterranean diet and depression among Asians. We used a validated measure of food intake frequency calculated from the Mediterranean diet scoring index based on Korean foods to assess diet adherence (25). Additionally, unlike previous studies on the Mediterranean diet and depression, our findings were adjusted for the effects of various sociodemographic and health-related variables to control for possible confounding effects. However, this study has several limitations. First, this was a cross-sectional study that could not clarify whether adherence to the Mediterranean diet could cause depression. Future prospective studies are required to confirm this causal direction. Second, the FFQ is a self-reported dietary assessment that may be biased toward dietary changes or recall errors. However, the FFQ has been commonly used to measure dietary patterns in epidemiological studies of diet and health and maybe more suitable than other dietary assessment methods for estimating usual intake (56). Third, this study investigated the Mediterranean diet according only to the frequency and amount of food. Therefore, we could not determine the effect of micronutrients. Furthermore, we could not control the impact of behavioral patterns related to food or alcohol consumption including solitary alcohol consumption. Previous studies reported that drinking alone was associated with depression (57, 58). Finally, this study was unable to explain the exact physiological mechanisms underlying the impact of the Mediterranean diet because biomarkers were not used. Future studies should include an assessment of biological mediators to identify the mechanisms by which the Mediterranean diet affects depression.

In summary, our study revealed that adherence to the Mediterranean diet was inversely associated with depression in both women and men in a nationally representative sample of Koreans. This study provides evidence that a Mediterranean diet is crucial in preventing symptoms and supporting positive mental health, even among non-Caucasians.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding authors.

Ethics statement

The studies involving human participants were reviewed and approved by Institutional Review Board of CHA Bundang Medical Center. The ethics committee waived the requirement of written informed consent for participation.

Author contributions

Y-GH: conceptualization, formal analysis, data curation, and writing of the original draft. CP: methodology and validation. S-HL: supervision, conceptualization, project administration, and funding acquisition. K-HY supervised, validated, wrote, reviewed, and edited the manuscript. CIP: supervision, validation, study design, project administration, funding acquisition, and writing—review and editing. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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