Clinical, Cosmetic and Investigational Dermatology

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ORIGINAL RESEARCH

The Association Between Psoriasis and Trace Element Serum Levels and Dietary Intake: Results from USA National Health and Nutrition Examination Survey 2011–2014

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Objective: Psoriasis is a common chronic inflammatory disease. However, trace elements are essential to biochemical processes of the skin, it is suspected that the trace elements are vital in the pathogenesis of psoriasis. Our research is aimed to investigate the association between serum levels and dietary intake levels of selenium, zinc, and copper with psoriasis.

Methods: In this cross-sectional study, we utilized the National Health and Nutrition Examination Survey data from 2011 to 2014 to examine the association between psoriasis and serum concentration and dietary intake of trace elements including copper, zinc, and selenium in the US individuals. Our research combined two cycles and weighted the data. Student's t-tests and $\chi 2$ test were used. Subgroup analyses and interaction tests were conducted by IBM SPSS Statistics 22 and EmpowerStats.

Results: This study indicates that the population with psoriasis has a lower dose of dietary intake selenium than the controls, and risk analysis showed that the men with selenium daily intake >150 mcg/day have a decreasing risk for psoriasis compared to those with daily intaking selenium <75 mcg/day. However, there are no differences on daily intake of selenium, zinc, and copper and serum levels of Zinc and Copper between psoriasis and healthy controls. The current study showed that the psoriasis group was significantly older with a bigger waist circumference, a higher education level, a higher ratio of people with smoke every day, and a higher ratio of people in USA and being non-Hispanic White.

Conclusion: This cross-section study showed that a high selenium intake may benefit USA adults from psoriasis, especially for males. The social and cultural background and ethnic differences between the two groups influence the eating and living models, including the trace element intake. The national recommended dietary allowances (RDAs) might be considered to be modified with more reliable investigative clinical data and certain considering the social and cultural models.

Keywords: trace elements, selenium, zinc, copper, serum level, dietary intake

Introduction

Psoriasis is a common chronic inflammatory disease caused mainly by immune responses mediated by T lymphocytes and various other immune cells,[1] and its prevalence ranges from 0.33% to 0.6% in different races.[2]

Trace elements are vital to biochemical processes of the skin, such as keratinization and melanin formation, and participate in immunological and inflammatory reactions.[3] For instance, Selenium (Se), zinc (Zn), and copper (Cu) are involved in the destruction of free radicals through cascading enzyme systems.[4] Selenoprotein has an extensive range of pleiotropic effects such as antioxidant and anti-inflammatory effects, and Se is essential in the synthesis of selenoprotein.[5] Zn and Cu are components of metalloenzymes, including Cu/Zn superoxide dismutase with antioxidant and anti-inflammatory activity.[6]

Received: 17 November 2023
Accepted: 17 May 2024
Published: 18 June 2024

It is speculated that trace elements are essential in the pathogenesis of psoriasis, but recent research on the role of trace elements in the pathogenesis and treatment of psoriasis was limited and in dispute,[7] so this cross-section study to invest the relationship between serum levels and dietary intake levels of Cu, Zn and Se and psoriasis in the US Population by data from National Health and Nutrition Examination Survey (NHANES) 2011–2014.

Materials and Methods

Study Design and Subjects

In this cross-sectional study utilizing the NHANES (https://www.cdc.gov/nchs/nhanes/index.htm) data from 2011 to 2014, An epidemiologic analysis was used to examine the association between psoriasis and serum concentration and dietary intake of trace element including Cu, Zn, and Se in the U.S individuals.

NHANES is a research project geared to estimating the health and nutritional status of people in the United States since the early 1960s. The survey investigates a nationally representative sample of about 5000 persons each year, and every 2 years survey is defined as a cycle. NHANES obtains health information through physical examination data and interviews. In a proportion of subjects, they also carry out laboratory tests.[8,9]

The research used NHANES data from two cycles, 2011–2012 and 2013–2014, and individuals with responses to the psoriasis status confirmed by self-reporting, providing the laboratory data of Se, Cu, and Zn serum levels, and complete dietary data of the first-day and the second-day total nutrients, aged 16–60 years was selected.

Our research collected the following data of participants from NHANES as our variables: demographics, physical examination, laboratory results and questionnaire, demographics information included age, gender, race, income, education level and marital status. From the examination, the body mass index (BMI) was calculated. Trace element dietary intake data were collected from the complete dietary data of the first-day and the second-day total nutrients. Smoking and alcohol data were from Alcohol Use and Smoking – Cigarette/Tobacco Use – Adult), drinking alcohol (Drinking alcohol at least 12 times per year or not). Ethical approval is exempted.

Psoriasis Definition

Psoriasis status was determined by the response to the question "Have you ever been told by a doctor or other health care professional that you had psoriasis?" in the "medical conditions" section of the questionnaire data in 2011–2012 and 2013–2014, and the self-reporting way has been used to estimate the prevalence of psoriasis in the US population.[10,11]

Laboratory Procedure Manual of Cu, Se and Zn in Serum

Blood sample was collected from participants by a phlebotomist at the MEC. The operators determined the amount of blood drawn according to age, and the blood was processed and divided into vials and stored in MEC. These vials were then refrigerated or frozen and shipped to laboratories across the United States.

The concentration of Cu, Se, and Zn in serum was measured by Inductively coupled plasma dynamic reaction cell mass spectrometry in Inorganic Radiation Analytical Toxicology, Division of Laboratory Sciences, National Center for Environmental Health.

Generally speaking, experimenters should draw trace metals tube the second time or after if experimenters want to draw more than one vacuum blood from a person. Get the blood pumped into a pre-screened 7 mL vacuum container through a stainless-steel needle. Allow the blood in the stoppered vacutainer clot for 30–40 minutes, no more than 60 minutes at most. Centrifuge it for 10 minutes at 2400 rpm without opening the vacutainer. Remove the serum from the clot with a pre-screened serum separator. Pour the serum in the serum separator into pre-screened polyethylene vials under a laminar flow hood. Experimenters should transport and store Serum specimens at ≤ 4 °C. Once received, experimenters can freeze them at ≤ -20 °C until time for analysis. After experimenters take out the aliquot sample for analysis, they should control the remaining part of the sample to refreeze at the temperature of ≤ -20 ° C, to ensure that the samples that are thawed and refrozen for many times will not be affected.

Finally, we review the data and send incomplete data or imperfect values to the performing lab for identification. The NHANES quality assurance and quality control protocols conform to the 1988 Clinical Laboratory Improvement Act mandates.

Other Covariates

The following variables were considered potential confounding factors: gender, age, marital status, BMI, the ratio of family income to poverty, smoking, drinking alcohol. All these covariates were obtained from demographics data and questionnaire data (Alcohol Use and Smoking – Cigarette/Tobacco Use – Adult).[12]

Statistical Analysis

Our research combined two cycles and weighted the data. Continuous variables with normal distribution were described as mean ± standard error and Student's t-tests was utilized between psoriasis and non-psoriasis groups. Categorical variables were described in terms of number (percentage) and $\chi 2$ test was used between the two groups.

Subgroup analyses and interaction tests were conducted to test the robustness of associations between daily intake Se with psoriasis in different subgroups. The dose–response analysis was also conducted by sex and BMI that contribute to discrepancies in the prevalence of psoriasis.

The results are expressed by the odds ratio (OR) with a 95% confidence interval (CI) and p-value. The study deemed that $p<0.05$ is statistically significant.

The recommended sample weights, sampling units and strata was used in this analysis because of the stratified, multistage probability sample design of NHANES.

IBM SPSS Statistics 22 and EmpowerStats (http:// www.empowerstats.com) were used for statistical analyses.

Results

Characteristics of the Study Population

2011–2012 and 2013–2014 data from NHANES contained 19,932 individuals, 7512 without response to psoriasis and 3189 with age >60 or age <16 were deleted, finally 9231 individuals were included, and divided into psoriasis (n=221) and non-psoriasis (n=9010) groups. The demographic data of the two groups are presented in Table 1. The participants in psoriasis group had an older mean age, a larger waist circumference and a higher proportion of active smokers than those in the control group. More than 50% of the psoriasis population were of non-Hispanic White and more of them were born in 50 US states or Washington, DC compared to the control group.

Variability of Serum Level and Dietary Intake of Trace Elements in Psoriasis and Non-Psoriasis Populations

Group comparisons (weighted by the number of participants in each group) suggested that there is no difference on serum concentrations of Cu, Se, and Zn between the two groups. For dietary intake level of trace elements, only Se in the psoriasis group was lower than that of the non-psoriasis group, while the decrease did not influence the serum concentration of Se (Table 2).

Dietary Intake and Serum Levels of Trace Elements and the Risk of Psoriasis

Table 3 shows the risk of psoriasis in subgroups by dietary intake and serum levels of trace elements. No association was found between serum Se, Cu levels and the prevalence of kidney stones overall, and in stratified analysis by sex and BMI. Only the man subgroup taking high dose of Se has a decreased risk of psoriasis compared to the subgroup taking low dose of Se (P=0.034).

Our research further used trend tests to examine the dose–effect relationship between the dietary intake and serum levels of Se and the prevalence of psoriasis by smooth curve fitting plot with dose as the horizontal axis and prevalence as the vertical axis, and a scatter plot. However, no linear and non-linear and relationship were found (data are not shown).

Table 1 Demographic Data of the Populations

Variable	Psoriasis (n=221)	Non-Psoriasis (n=9010)	P value
Age (years)a	42.7±1.1	37.8±0.4	0.0002***
BMI (kg/m²)a	29.6±0.7	28.6±0.2	0.1353
Waist circumference (cm)	100.4±1.6	97.0±0.4	0.0439*
Gender, n (%)			0.6585
Male	104 (47.06)	4396 (48.79)	
Female	117 (52.94)	4614 (51.21)	
Marital status, n (%)			0.7290
Married	97 (43.89)	3736 (41.47)	
Never married	50 (22.62)	2061 (22.87)	
Others	63 (28.51)	1912 (21.22)	
Race, n (%)			<0.0001*
Mexico American	12 (5.43)	1251 (13.88)	
Other Hispanic	21 (9.50)	868 (9.63)	
Non-Hispanic White	120 (54.30)	3129 (34.73)	
Non-Hispanic Black	27 (12.22)	2166 (24.04)	
Non-Hispanic Asian	41 (18.55)	1596 (17.71)	
Birth country, n (%)			<0.0001*
Born in 50 US states or Washington, DC	176 (79.64)	6342 (70.39)	
Others	45 (20.36)	2662 (29.54)	
Education level, n (%)			0.0328*
Less than 9th grade	11 (4.98)	520 (5.77)	
9–11th grade	33 (14.93)	1882 (20.89)	
High school graduate	46 (20.81)	2071 (22.99)	
Some college or AA degree	64 (28.96)	2473 (27.45)	
College graduate or above	67 (30.32)	2060 (22.86)	
Had at least 12 alcohol drinks/1 year, n (%)			0.6762
Yes	139 (62.90)	5256 (58.34)	
No	43 (19.46)	1911 (21.21)	
Smoke, n (%)			<0.0001***
Every day	43 (19.46)	1515 (16.81)	
Some days	4 (1.81)	363 (4.03)	
Not at all	50 (22.62)	1272 (14.12)	
BMI grade (kg/m²), n (%)			0.0633
Underweight (<18)	1 (0.45)	137 (1.52)	
Normal weight (18.0–24.9)	52 (23.53)	3005 (33.35)	
Overweight (25.0–29.9)	70 (31.67)	2538 (28.17)	
Obesity (≥ 30.0)	79 (35.75)	2952 (32.76)	
Family income ($), n (%)			0.2842
0–19,999	51 (23.08)	2162 (24.00)	
20,000–34,999	48 (21.72)	1914 (21.24)	
35,000–74,999	50 (22.62)	2238 (24.84)	
≥ 75,000	64 (28.96)	2259 (25.07)	

Notes: a, Mean±SE is used for continuous variables, and the P values are weighted; *P<0.05; ***P<0.001.
Abbreviations: n, number; BMI, body mass index; $, United States dollar.

Table 2 Comparison of Serum Concentrations and Dietary Intake Levels of Trace Elements Between Psoriasis and Non-Psoriasis Populations

Variables	Psoriasis (n=221)	Non-Psoriasis (n=9010)	P value
Serum level			
Se (μg/L)	131.0±3.0	129.8±0.8	0.6722
Cu (μg/dL)	115.9±3.7	117.9±1.1	0.5947
Zn (μg/dL)	81.7±2.6	82.8±0.6	0.6541
Cu/Zn	1.5±0.1	1.5±0.0	0.9697
Dietary intake			
Se (mcg/day)	103.4±6.3	120.6±1.1	0.0107*
Cu (mg/day)	1.3±0.1	1.3±0.0	0.7736
Zn (mg/day)	10.5±0.7	11.7±0.1	0.0787

Note: *P<0.05.
Abbreviation: n, number.

Table 3 Weighted Risk of Psoriasis by Dietary Intake and Serum Levels of Trace Elements

Parameters	OR (95% CI) of Psoriasis			P
Serum Se (μg/L)	<120	120–140	>140	
Overall	1.00	0.903 (0.524–1.556)	1.211 (0.668–2.195)	0.595
Men	1.00	0.929 (0.398–2.168)	0.908 (0.356–2.312)	0.977
Women	1.00	0.900 (0.441–1.838)	1.727 (0.796–3.746)	0.215
Normal weight	1.00	0.898 (0.429–1.882)	1.144 (0.508–2.577)	0.830
Overweight	1.00	0.900 (0.403–2.012)	1.326 (0.552–3.183)	0.651
Serum Cu (μg/dL)	<100	100–130	>130	
Overall	1.00	0.911 (0.521–1.592)	1.158 (0.648–2.069)	0.693
Men	1.00	0.733 (0.359–1.498)	0.000 (0.000-)#	0.696
Women	1.00	1.470 (0.482–4.482)	1.987 (0.682–5.794)	0.374
Normal weight	1.00	1.400 (0.669–2.928)	1.358 (0.582–3.170)	0.644
Overweight	1.00	0.357 (0.149–0.859)	0.577 (0.256–1.301)	0.070
Serum Zn (μg/dL)	<75	75–90	>90	
Overall	1.00	1.101 (0.648–1.872)	0.883 (0.478–1.631)	0.759
Men	1.00	0.992 (0.420–2.346)	0.883 (0.355–2.196)	0.953
Women	1.00	1.223 (0.622–2.404)	0.952 (0.402–2.250)	0.779
Normal weight	1.00	1.330 (0.623–2.837)	1.177 (0.506–2.738)	0.762
Overweight	1.00	0.969 (0.455–2.066)	0.667 (0.265–1.678)	0.660

(*Continued*)

Table 3 (Continued).

Parameters	OR (95% CI) of Psoriasis			P
Dietary intake of Se (mcg/day)	<75	75–150	>150	
Overall	1.00	0.789 (0.565–1.102)	0.695 (0.464–1.042)	0.179
Men	1.00	0.567 (0.333–0.967)	0.480 (0.268–0.858)	0.034*
Women	1.00	0.966 (0.629–1.484)	1.049 (0.577–1.905)	0.958
Normal weight	1.00	0.663 (0.411–1.070)	0.819 (0.485–1.385)	0.240
Overweight	1.00	0.937 (0.585–1.499)	0.587 (0.306–1.126)	0.240
Dietary intake of Cu (mg/day)	<1	1–2	>2	
Overall	1.00	1.294 (0.951–1.759)	0.998 (0.599–1.663)	0.214
Men	1.00	1.346 (0.828–2.186)	0.872 (0.416–1.828)	0.301
Women	1.00	1.309 (0.873–1.963)	1.344 (0.652–2.770)	0.388
Normal weight	1.00	1.505 (0.974–2.325)	0.974 (0.464–2.046)	0.134
Overweight	1.00	1.162 (0.749–1.803)	1.101 (0.543–2.234)	0.797
Dietary intake of Zn (mg/day)	<10	10–20	>20	
Overall	1.00	0.973 (0.721–1.313)	0.618 (0.338–1.129)	0.290
Men	1.00	0.830 (0.527–1.309)	0.582 (0.280–1.210)	0.327
Women	1.00	1.153 (0.769–1.728)	0.717 (0.223–2.308)	0.637
Normal weight	1.00	0.877 (0.573–1.341)	0.730 (0.345–1.546)	0.652
Overweight	1.00	1.124 (0.734–1.721)	0.527 (0.188–1.477)	0.352

Notes: #not enough data; *P<0.05.
Abbreviations: OR, odds ratio; CI, Confidence interval.

Discussion

Studies point out that trace elements including Se, Zn and Cu take vital roles in immunological and inflammatory reactions, while findings regarding serum levels of trace elements in psoriasis are contradictory. This study investigated the association between daily intake and serum levels Se, Zn and Cu and psoriasis, and our results indicate that there are no differences on daily intake of Se, Zn, and Cu and serum levels of Zn and Cu between psoriasis and healthy controls. However, the data showed that the population with psoriasis has a lower dose of dietary intake Se than the controls, and risk analysis showed that the men with Se daily intake >150 mcg/day has a decreasing risk for psoriasis compared to those daily intaking Se <75 mcg/day.

Se has antiproliferative and immune-modulating properties, and this active component can influence immune response and is involved in redox reactions which protect membranes from oxidative damage. Deficit of Se is one of the risk factors that may predispose to inflammatory disorders.[13] Low Se concentration was reported in psoriatic patients compared to controls,[7,14–16] no matter inactive psoriasis or active psoriasis,[17] and the decrease of Se was related to the alcohol[18] and arsenic[19] poisoning. However, no significant difference in serum Se levels between patients and controls was also observed.[20,21] Only one study reported an increase of Se level in psoriatic patients with different severity scores.[22]

A systematic review and meta-analysis published on 2020 collected data from 9 studies both in English and Chinese, including serum/plasma samples and hair samples, and it reported that a lower Se level was found in patients with psoriasis compared with controls (SMD = −0.62, 95% CI: −1.15 to −0.10), while severe patients had a higher Se level than mild patients in psoriasis (SMD = 0.72, 95% CI: 0.07–1.38).[23] The authors reported that the serum Se level in

psoriasis ranged from 42.90 ± 13.03 to 82 ± 29 μg/L, which is much lower than that in our study (131.0±3.0 μg/L), and the difference may rise from the various detection methods and origin countries of subjects. However, Chen et al[24] conducted a meta-analysis on literature from databases PubMed, Embase, Cochrane Library, Google Scholar, and Web of knowledge by 2018 confirmed that the serum Se level (6 publications with 634 psoriasis vs 360 controls) showed no remarkable difference between psoriasis and controls, which is consistent with our results.

A direct relation between Se intake and blood Se content was demonstrated,[25].[26] However, a few investigators also reported that Se intake could not predict blood Se concentration.[27,28] Yang et al[29] found that at higher Se-intakes the whole blood Se-level became less sensitive than the levels in tissue, including finger-nail and toe-nail, and confirmed a highly significant correlation between the Se-intake and the tissue-Se level, and also between the Se levels of various tissues, which the authors thought is convenient to convert the known tissue-Se level to the corresponding Se-intake.[29] Li et al[26] found that Se intake was obviously, the strongest predictor of Se concentration in tissues. It has been shown that the chemical form (inorganic form or organic form of Se) is an important determinant of its biological function as an essential nutrient, and the organic form of Se, such as seleno-proteins are essential for proper keratinocyte function and skin development.[30] While seleno-proteins are expressed in tissue-dependent distributions and levels in all cells of all vertebrates.[31] The above combined evidence suggested that the Se in tissue in organic form, not the serum Se, may play a significant role in the psoriasis.

In diet therapy for persons with psoriasis, the introduction of antioxidants such as Se is supposed to be important.[32] The RDAs for Se are 55 mcg in adult men and women in the USA and 60 to 70 mcg in pregnancy and during lactation,[33] which is much lower than the actual dose of daily intake in USA adults measured in our study. The results of our study showed the higher dose of Se intake (>150 mcg/day) could benefit males, which should be executed with caution as the upper tolerable level of Se intake is 300 mcg/day.[34]

Zn and Cu are two other critical trace elements for human body. Approximately 20% of the total Zn in the body is located in the skin. Zn along with Cu is involved in the normal keratinization processes of animal skin, and the protective role of Zn and Cu against oxidative stress may be against the damage caused by peroxidant-antioxidant imbalance in psoriasis.[7] So Zn and Cu elements are speculated to participate in the pathogenesis of psoriasis. However, the contradictory results of serum Zn and Cu serum levels in patients with psoriasis were also reflected in the study Investigators have noted a low Zn serum level in psoriasis,[15,35–37] while studies also found no statistically significant differences in serum Zn level between psoriatic patients and healthy control groups,[38–40] which is consistent with our results. In contrast, an increase of serum Zn level in psoriasis patients was reported by Butnaru et al[41] Elevated Cu serum levels have been reported in psoriatic patients compared to controls by Butnaru et al,[41] Tasaki et al,[42] Sheikh et al,[37] and Ala et al[38] In contrast, Bhatnagar et al reported that the reduced Cu levels in active and remissive phases of psoriasis,[43] and no difference was reported by Akbarzadeh et al.[40]

One study found that up-regulation of Cu/Zn SOD expression by NO establishes an inhibitory mechanism on keratinocyte proliferation,[44] which can be explained by the following results that Cu/Zn ratio was significantly higher in psoriasis patients compared to controls,[7,37] However, Butnaru et al[41] have presented contrast findings.

Few meta-analyses were conducted on trace elements, Lei et al[45] analyzed the data from English and Chinese documents from international and national electronic databases from 1988 to May 2016, and found that serum Cu levels were significantly increased ($Z = 4.02$, $P < 0.0001$; standardized mean difference [SMD], 1.23; 95% CI, 0.63 to 1.82), and serum Zn levels were significantly decreased ($Z = 2.95$, $P < 0.0001$; SMD, −1.35; 95% CI, −2.25 to - 0.45) in patients with psoriasis. However, Chen et al[24] conducted a meta-analysis confirmed that the serum Zn (19 Publication with 933 psoriasis vs 867 controls) level showed no remarkable difference between psoriasis and controls, which is consistent with our results. A system review published in 2020 showed no significant benefit of Zn treatment/supplementation on disease outcome.[46]

Our results showed that there is no association between the serum concentration and dietary intake of Zn and Cu, and the psoriasis, while a weak link between Se intake and psoriasis. Our results might provide evidence for regulation the dietary recommendations for patients with psoriasis, especially on trace elements.

The current study showed that the psoriasis group was significantly older with a bigger waist circumference, a higher education level, higher ratio of person with smoke in every day, and higher ratio of person born in USA and being non-Hispanic White. The social and cultural background and ethnic differences between the two groups influence the eating and living models, including the trace element intake. A gender-specific association of smoking on Se status was

observed, lower total serum selenium levels (~10%) were found in male smokers in comparison to male non-smokers.[47] Therefore, smoking may have an impact on our trace element levels.

As we know, it is the first time to explore the serum and dietary intake levels of three trace elements between psoriasis patients and healthy controls using a larger number of individuals from consecutive nationally representative surveys. However, several limitations also exist in the research: First, due to the limitations of research types, causal inference cannot be carried out. Second, dietary habits of participants may be changed because of research survey. Finally, we did not include all factors that affect trace elements in blood and diet.

In conclusion, this cross-section study showed that a high Se intake may benefit USA adults from psoriasis, especially for males, and the RAD might be considered to be modified with more reliable investigative clinical data.

Ethical Approval and Consent to Participate

According to Article 32 of "the Measures for Ethical Review of Life Science and Medical Research Involving Human Subjects", which was reviewed by the National Science and Technology Ethics Committee, approved by the State Council of China, and jointly promulgated by the National Health Commission, the Ministry of Education, the Ministry of Science and Technology and the State Administration of Traditional Chinese Medicine on Feb. 18, 2023: The use of human information data for conducting life science and medical research involving humans, which does not cause harm to the human body, does not involve sensitive personal information or commercial interests, may be exempted from ethical review. The specific situation is as follows: 1. The research is conducted using legally obtained public data or data generated through observation and does not interfere with public behavior 2. Use of anonymized data for research. This research is conducted using legally obtained public and anonymized data and does not interfere with public behavior. Therefore, this study is exempt from approval based on national legislation guidelines. All participants provided written informed consent.

Ethical Standards Disclosure

The data analyzed in this study is subject to the following licenses/restrictions: The data used in this study came from the National Health and Nutrition Examination Survey (NHANES, https://www.cdc.gov/nchs/nhanes/index.htm).

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This work was supported by Science and Technology Program of Guangzhou (202102080341 to ES).

Disclosure

Rui-lian Ding and Cheng Fu are co-first authors for this study. The authors declare that they have no conflicts of interest in this work.

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