

Dietary Patterns and Hyperuricemia in Adult Subjects: A Systematic Review and Meta-Analysis of Observational Studies

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Abstract: Dietary patterns have been found to be related to hyperuricemia (HUA) in some studies, and it is necessary to gather evidence on the role of nutrition in HUA to provide advice and guidance for the management of chronic diseases. The aim of this systematic review and meta-analysis was to investigate the correlation between dietary patterns and HUA risk. We searched seven electronic databases up to 31 January 2023 for studies that investigated adherence to the “Healthy” pattern and “Meat/Western” pattern in relation to HUA. Estimates were pooled using random-effects models with stratification by observational study, heterogeneity and publication bias were evaluated. 10 observational studies that identified the “Healthy” and the “Meat/Western” dietary patterns were included in the meta-analysis. The “Healthy” pattern was associated with the reduction of HUA risk (odds ratio (OR) = 0.73; 95% confidence interval (CI): 0.61–0.88) and significantly decreased it in cohort study (OR=0.79; 95% CI: 0.72–0.86) and in Eastern countries (OR=0.79; 95% CI: 0.64–0.98) and Western countries (OR=0.53; 95% CI: 0.30–0.92). The “Meat/Western” pattern was related to increased HUA risk (OR=1.26; 95% CI: 1.17–1.37) and the association still existed in the stratified analysis by study design. The “Healthy” and “Meat/Western” patterns are significantly associated with the reduction and elevation of HUA risk, respectively. This provides a reasonable evidence base to evaluate the role of dietary interventions to prevent HUA.

Keywords: Dietary Pattern, Hyperuricemia, Adult, Systematic Review, Meta-Analysis

1. Introduction

Hyperuricemia (HUA) is a metabolic disorder caused by purine metabolism. In recent years, the prevalence of HUA was skyrocketing speedily around the world with economic growth and lifestyle changes. [1, 2] Previous studies showed that HUA is considered to be an important risk factor for some chronic diseases, such as hypertension, [3] diabetes, [4] metabolic syndrome, [5] chronic kidney disease [6] and cardiovascular disease. [7] Moreover, genetic, environment and alcohol consumption, especially diet may increase the risk of developing HUA. [8-11] There is evidence that diet and nutrients are crucial to the management of HUA. [8] Due to

the correlation between diet and nutrients, it may be difficult to determine the specific effects of various aspects of diet, and may be partially confounded by the effects of other food ingredients. [12]

Nutritional epidemiology studies demonstrated the correlation between diet and the risk of HUA, focusing primarily on individual foods and nutrients rather than on diet combinations and nutrients interactions. [12, 13] In this context, dietary patterns represent comprehensive dietary variables, studying the relationship between diet and chronic diseases, and evaluating the impact of overall diet. [12] A cohort study showed that adherence to a Mediterranean diet can reduce the risk of HUA, [14] and a cross-sectional study showed that adherence to the ‘animal products and fried foods

pattern' and 'soyabean products and fruit pattern' were significantly associated with an increase and decrease in the risk of HUA, respectively. [15] Whereas, in another Taiwan study, no significant association was found between vegetable and fruit patterns and serum uric acid level. [16] Given the inconsistencies in these results, the impact of dietary patterns on HUA is still unclear. To date, systematic reviews and meta-analysis that can help draw conclusions from these studies have not been reported. Therefore, we conduct a systematic reviews and meta-analysis to identify the major dietary patterns and assess the relationship between dietary patterns and HUA risk in the adult population.

2. Methods

This meta-analysis was conducted in accordance with the MOOSE (Meta-analysis of Observational Epidemiological Studies) guidelines [17] and PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) statement. [18]

2.1. Search Strategy and Data Source

A comprehensive literature search, without restrictions, was conducted up to 31 January 2023 through PubMed (<http://www.ncbi.nlm.nih.gov/pubmed/>), Web of Science (<http://wokinfo.com/>), Cochrane (<https://www.cochranelibrary.com/>), Embase (<https://www.embase.com/>), Medicine (<https://www.medicines.com/>), ScienceDirect (<https://www.sciencedirect.com/>) and Medline (<https://www.medline.com/>) databases to determine all the original papers on the correlation of dietary patterns with HUA risk. The following search medical subject headings (MeSH) and key words were included in the literature search: ("Hyperuricemia" OR HUA OR "Serum uric acid") AND ("Dietary pattern" OR "Food pattern" OR "Diet pattern" OR "Nutrient pattern" OR "Dietary score" OR "Food score" OR "Diet score" OR "Dietary index" OR "Diet index" OR "Dietary habits" OR "Food diversity" OR "Diet diversity" OR "Diet variety" OR "Dietary factors") AND ("Factor analysis" OR "Principal component analysis" OR "Cluster analysis" OR "Exploratory factor analysis" OR "Reduced rank regression" OR "Principal component factor analysis" OR "Data-driven approach").

The reference lists of selected articles and recent relevant reviews to determine possible other correlative publications were manually examined by us.

2.2. Inclusion and Exclusion Criteria

The inclusion criteria were as follows: (a) evaluated the association between dietary patterns and HUA risk in adults; (b) observational study; (c) provided relevant data, including odds ratio (OR), relative risk (RR) or hazard ratio (HR) estimates with 95% confidence intervals (CIs); (d) published in English.

The exclusion criteria were as follows: (a) no measure of

whole diet (e.g., dietary screeners or individual questions); (b) low-quality studies, duplicate studies, individual case reports and studies without available data.

Two researchers independently selected, extracted, and assessed the quality of each potentially included study. Inconsistent views were resolved through discussion or in consultation with the third author. Although background information was useful, reviews and meta-analysis were excluded. No studies were excluded because of weak design or data quality.

2.3. Data Extraction and Quality Assessment

We extracted the following information for each selected study: first author's last name, year of publication, country, study design, sample size (if possible, number of cases and controls; cohort size and event cases), population characteristics (gender, age), follow-up time of cohort studies, HUA assessment method, dietary assessment and dietary patterns recognition methods (FA, PCA and PCFA), the method for evaluating the dietary characteristics, the name and characteristics of dietary patterns, cutoff points for adherence to the different categories of the dietary patterns (tertile, quartile and quintile), 95% CIs risk estimates for the different categories of adherence, and confounders adjustment. When multiple estimates were mentioned in the paper, we excluded those adjusted for the most confounders.

The Newcastle-Ottawa Scale was used to assess the quality of studies, which judges each study on three fields: the selection of the study groups; the comparability of the groups; and the determination of the outcome of interest. The scale allowed a range of points from 0 to 9, with higher scores indicating the better quality.

2.4. Statistical Analysis

The estimated overall effect-size statistic was the average of the logarithm of the observed OR (approximated to RR, if necessary) related to the highest vs. the lowest level of adherence to the different dietary patterns. The random-effects model was used to compute the summary OR and 95% CIs. Ultimately, the two most common dietary patterns were identified in 10 studies. [14, 15, 19-26] The first dietary pattern, called "Healthy", was characterized by a high intake of vegetables and fruit, poultry, fish, and whole grains. [27] Generally, the Mediterranean diet was also defined as a healthy eating pattern. [28] The selected articles marked this pattern as "Mediterranean", [14, 19, 25] "Vegetable and fruit", [26] "Vegetable", [22, 23] "Traditional Chinese", [24] "Plant-based", [21] "Soybean products and fruit". [15]

The second dietary pattern, named "Meat/Western", had a high intake of red meat, processed meat, animal fat, eggs and sweets. [27] The included articles marked this pattern as "Western", [15] "Animal food", [22, 23] "Meat food", [24] "Animal products", [21] "ultra-processed foods". [20]

The Cochran's Q statistic based on chi-square test and the I^2 statistic were used to assess heterogeneity in results across studies. [29] The I^2 statistic yields results ranged from 0% to

100% ($I^2=0\%-25\%$, no heterogeneity; $I^2=25\%-50\%$, moderate heterogeneity; $I^2=50\%-75\%$, large heterogeneity; and $I^2=75\%-100\%$, extreme heterogeneity). [30] If the probability of publication depends on the results of the study, the meta-analysis results may be biased. The methods of Begg and Mazumdar [31] and Egger et al. [32] were used to examine publication bias. If a potential bias was detected, a sensitivity analysis was further performed to evaluate the robustness of combined effect estimates, as well as the possible effect of the bias, and to correct the bias. A sensitivity analysis was also performed to investigate the impact of a single study on the overall risk estimate by omitting one study per round. In addition, the cumulative meta-analysis was conducted by updating the pooled estimate of the treatment effect each time trial results with a more recent publication date were added. A correlation P-value less than 0.05 was considered statistically significant. The results of the meta-analysis were displayed in the form of a graph with forest plots representing the effect size in OR and the corresponding 95% CIs. The analyses were conducted using the Stata version 11.0 (StataCorp, TX, USA).

3. Results

3.1. Literature Search

The primary literature search through PubMed (n=2126), Web of Science (n=340), Embase (n=162), Medline (n=84), Medicine (n=16), Cochrane (n=3) and ScienceDirect (n=2) databases identified a total of 2733 articles. Among these, duplicates (n=852) were excluded, 1726 articles were removed as not reporting the correlation between dietary patterns and the finding of interest and 133 studies were excluded after reading through the article titles and abstracts (Figure 1). Subsequently, 11 papers were removed, including reviews (n=4), Dietary Approaches to Stop Hypertension (DASH) (n=1), animal studies (n=2), adolescents (n=1) and studies that did not use FFQ/24h recall questionnaire (n=3). Therefore, 10 studies were included to identify different dietary patterns in the systematic review and meta-analysis at the end of the selection process. [14, 15, 19-26]

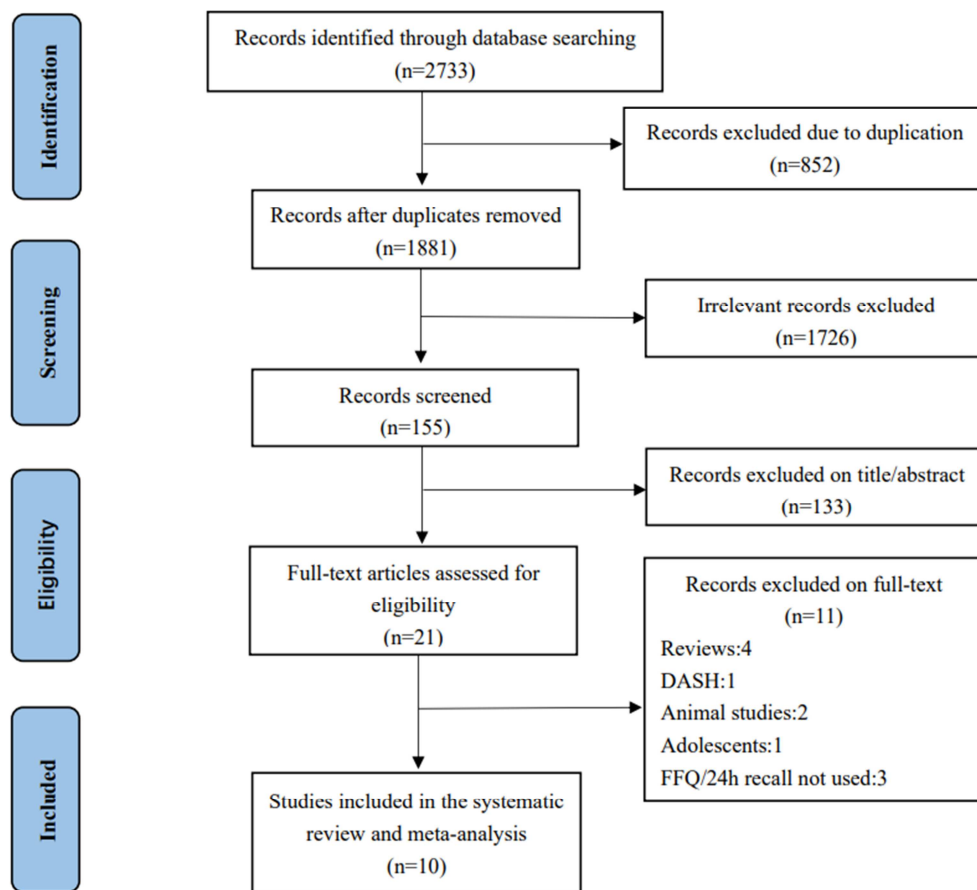


Figure 1. Flow diagram of the systematic literature search on dietary patterns and HUA risk. Hyperuricemia (HUA).

3.2. Study Description

Table 1 shows the general characteristics of the 10 studies that assessed the correlation between adherence to the dietary patterns with HUA risk.

These studies were published between 2011 and 2021. Seven studies were performed in China, [15, 20-24, 26] two in Greece, [19, 25] and one each in Spain. [14] Three were cohort studies, [14, 20, 23] two were case-control study [15, 22] and all others were cross-sectional studies. [19, 21, 24-26] All

studies assessed the risk of HUA on women and men together and used a food frequency questionnaire (FFQ; 22 to 168 items) [14, 15, 19-26] to collect dietary information. In addition, one study also used an EPIC-Greek FFQ. [19] One study [25] derived dietary patterns through MedDietScore, another study [26] used a “Maximum likelihood method”,

while all the other studies used a posteriori method (PCA, PCFA, EFA and FA) to derive dietary patterns. Six studies [15, 21-24, 26] reported the relation between HUA risk and three different dietary patterns and four studies [14, 19, 20, 25] only considered one dietary pattern.

Table 1. Main characteristics of studies included in the systematic review and meta-analysis on dietary patterns and Hyperuricemia.

First Author Year Location	Study Design, Name, and Population Cases/Control s Follow-Up Incident Cases Age	Assessment of Hyperuricemia	Dietary Pattern Assessment and Identification Method	Dietary Pattern Type and Characteristics	Pattern Score	OR/RR (95%CI)	Matched or Adjusted Variables	Quality assessment
Zhang et al. [23], 2021, China	Cohort Tianjin Chronic Low-grade Systemic Inflammation and Health (TCLSIH) study 20766 subjects 10391 men 10375 women Age \geq 18 Mean follow-up: 4.2 4389 incident cases	- Men: SUA ¹ >420 mmol/L - Women: SUA >350 mmol/L	81-item FFQ ² PCA ³ Varimax rotation EIG ⁴ \geq 1.5 Loading \geq 0.45 3 factors VE ⁵ 29.2%	1. Vegetable: celery, cucumber, Chinese cabbage, green leafy vegetables, pumpkin, and carrot 2. Sweet food: strawberry, kiwi fruit, persimmon, grape, pineapple, Western-style pastry, cakes, sweets, and candied fruits 3. Animal food: animal organs, animal blood, animal liver, preserved eggs and sausage	Quartile 1 Quartile 4 Quartile 1 Quartile 4 Quartile 1 Quartile 4	1.00 (Reference) 0.79 (0.72-0.87) 1.00 (Reference) 1.22 (1.12-1.33) 1.00 (Reference) 1.24 (1.13-1.37)	Sex, age, BMI ⁶ , smoking status, alcohol consumption status, education levels, employment status, household income, physical activity, family history of disease, depressive symptoms, HUA ⁷ , hypertension, hyperlipidemi a, diabetes, total energy intake and each other dietary pattern scores, glomerular filtration rate and high-sensitiv ity C-reactive protein Age, sex, BMI, smoking, alcohol and coffee intake, insulin resistance index (HOMA-IR), serum creatinine, and presence of hypertension Age, gender, BMI, smoking, drinking, hypertension,	6
Kontogianni et al. [19], 2012, Greece	Cross-sectional ATTICA study 2380 subjects 1163 men Aged 45 \pm 13 1217 women Age 44 \pm 14	- Men: SUA >7.0 mg/dL - Women: SUA >6.0 mg/dL	156-item FFQ and EPIC-Greek FFQ 9 food groups	Mediterranean: non-refined cereals, potatoes, fruit, vegetables, legumes, fish, red meat and products, poultry, full-fat dairy products	Quartile 1 Quartile 4	1.00 (Reference) 0.30 (0.11-0.82)	Age, sex, BMI, smoking, alcohol and coffee intake, insulin resistance index (HOMA-IR), serum creatinine, and presence of hypertension Age, gender, BMI, smoking, drinking, hypertension,	7
Liu et al. [21], 2018, China	Cross-sectional 1893 subjects 906 males 987 females Age 18-96	- Men: SUA \geq 420 μ mol/L - Women: SUA \geq 360 μ mol/L	52-item FFQ 18 food groups PCFA ⁸ Varimax rotation EIG \geq 1	1. Plant-based: vegetables, fruits, mushroom, algae food, legumes, nuts, brawn, and	Tertile 1 Tertile 3 Tertile 1 Tertile 3	1.00 (Reference) 1.03 (0.84-1.26) 1.00 (Reference)	Age, sex, BMI, smoking, drinking, hypertension,	6

First Author Year Location	Study Design, Name, and Population Cases/Control s Follow-Up Incident Cases Age	Assessment of Hyperuricemia	Dietary Pattern Assessment and Identification Method	Dietary Pattern Type and Characteristics	Pattern Score	OR/RR (95%CI)	Matched or Adjusted Variables	Quality assessment
He et al. [24], 2017, China	Cross-sectional Nutrition and Health Study 1204 subjects 743 males 461 females Age 45-59	- Men: SUA ≥ 420 $\mu\text{mol/L}$ - Women: SUA ≥ 360 $\mu\text{mol/L}$	Loading ≥ 0.35 3 factors VE 34.22%	bacon 2. Animal products: fish, animal giblets, fresh meat, wheat products 3. Mixed food: rice, cereal, tubers, snack, dessert, eggs, and animal giblets	Tertile 1 Tertile 3	1.34 (1.06-1.70) 1.00 (Reference) 0.97 (0.78-1.20)	hyperlipidemia	7
				1. Traditional Chinese: rice and rice products, coarse grains, starchy tubers, vegetables, pickled vegetables, pork, soybean and soybean products, and tea 2. Meat food: poultry, beef/mutton, processed and cooked meat, eggs, fats/oil, snacks and fast food, milk and dairy, cake and biscuits, and soft drinks 3. Mixed food: wheat and wheat products, vegetables, mushroom, fresh fruits, pork, fish and shrimps, seafood, and caffeinated beverages	Quartile 1 Quartile 4 Quartile 1 Quartile 4	1.00 (Reference) 0.82 (0.426-0.922) 1.00 (Reference) 1.48 (1.120-2.097)	Gender, age, education level, physical activity level, smoking status, alcohol use, hypertension, BMI and total energy intake	
				56-item FFQ PCFA Varimax rotation EIG ≥ 1.5 Loading ≥ 0.3 3 factors VE 28.1%	Quartile 1 Quartile 4	1.00 (Reference) 1.24 (0.925-1.835)		
Xia et al. [22], 2018, China	Case-control TCLSIH 2844 subjects Cases: 1422 Mean age: 40.85 Controls: 1422 Mean age: 40.58	- Men: SUA > 7.0 mg/dL - Women: SUA > 6.0 mg/dL	100-item FFQ 5 food groups FA ⁹ Varimax rotation EIG ≥ 1.0 Loading ≥ 0.3 3 factors VE 22.6%	1. Sweet: candied fruits, cakes and ice cream 2. Vegetable: vegetables, soya products and coarse cereals 3. Animal foods: animal organ, seafood and processed meat products	Quartile 1 Quartile 4 Quartile 1 Quartile 4 Quartile 1 Quartile 4	1.00 (Reference) 1.10 (0.89-1.37) 1.00 (Reference) 0.88 (0.71-1.09) 1.00 (Reference) 1.50 (1.20-1.87)	The scores of other two dietary patterns	7
				1. Animal products and fried food: pork, eggs, animal giblets, poultry and fried wheat	Tertile 1 Tertile 3 Tertile 1 Tertile 3	1.00 (Reference) 2.15 (1.22-3.76) 1.00 (Reference) 1.46 (0.78-2.71)	Age, sex, education level, physical activity, smoking	
				33-item FFQ 20 food groups FA Varimax rotation EIG ≥ 1.5 Loading ≥ 0.3				
Zhang et al. [15], 2012, China	Case-control 374 adults Age: 20-59 Cases: 187 93 men 94 women	- Males: SUA > 7.0 mg/dL - Females: SUA > 6.0 mg/dL	33-item FFQ 20 food groups FA Varimax rotation EIG ≥ 1.5 Loading ≥ 0.3	1. Animal products and fried food: pork, eggs, animal giblets, poultry and fried wheat	Tertile 1 Tertile 3 Tertile 1 Tertile 3	1.00 (Reference) 2.15 (1.22-3.76) 1.00 (Reference) 1.46 (0.78-2.71)	Age, sex, education level, physical activity, smoking	7

First Author Year Location	Study Design, Name, and Population Cases/Control s Follow-Up Incident Cases Age	Assessment of Hyperuricemia	Dietary Pattern Assessment and Identification Method	Dietary Pattern Type and Characteristics	Pattern Score	OR/RR (95%CI)	Matched or Adjusted Variables	Quality assessment
Tsai, et al. [26], 2012, China	Controls: 187 92 men 95 women		3 factors VE 36.1%	products while low in vegetables and fruits 2. Western: beef, lamb, cake, and beverages, including juice and alcoholic beverages 3. Soybean products and fruit: soybean products, fruits, vegetables and starchy tubers	Tertile 1 Tertile 3	1.00 (Reference) 0.32 (0.19-0.57)	status, drinking status and BMI	
	Cross-sectional 266 adults 147 men 119 women	NR ¹⁰	38-item FFQ 14 food groups EFA ¹¹ “Maximum likelihood method” Loading ≥0.35 3 factors	1. Uric acid-prone: meat, seafood, organ meat, eggs and beverages 2. Fish and fried food: fried foods and fish 3. Vegetable and fruit: soy products, white vegetables, dark vegetables and fruit Mediterranean: “beneficial” foods olive oil, vegetables, legumes, fruit, nuts, fish and seafood, white meat instead of red meat, sofrito (tomato, onion, spices, garlic, and simmered with olive oil), and red wine; “detrimental” foods red meat, fat-rich dairy products, commercial pastries and snacks, artificially sweetened beverages Mediterranean: meat and meat products, fish and fish products, poultry, milk and other dairy products, fruits, vegetables, greens, legumes,	Quartile 1 Quartile 4 Quartile 1 Quartile 4 Quartile 1 Quartile 4	1.00 (Reference) NR 1.00 (Reference) NR 1.00 (Reference) NR	Age, gender, body mass index, sites, systolic and diastolic blood pressure, smoking status, medication for uric acid lowering, exercise, total energy and alcohol age, BMI, recruitment center; current smokers, former smokers, physical activity, educational level blood pressure, total energy intake, caffeine intake, antihypertensi ve agents, oral hypoglycemic agents, allopurinol use, and prevalence of diabetes	6
	cohort PREvención con Dieta MEDiterránea study 4449 subjects 1937 men Aged 55-80 2512 women Age 60-80 follow-up: 5	- Men: SUA >7.0 mg/dL - Women: SUA >6.0 mg/dL	137-item FFQ 14 food groups		Quintile 1 Quintile 5	1.00 (Reference) 0.77 (0.62-0.97)		7
Chrysoshoou et al. [25], 2011, Greece	Cross-sectional IKARIA study 673 subjects 257 males Age 75±7 281 females Age 75±6	- Men: SUA >7.0 mg/dL - Women: SUA >6.0 mg/dL	FFQ 12 food groups		MEN Tertile 1 Tertile 3 WOMEN Tertile 1 Tertile 3	1.00 (Reference) 0.43 (0.25-0.77) NR	age, gender, physical activity status, smoking habits and BMI	6

First Author Year Location	Study Design, Name, and Population Cases/Control s Follow-Up Incident Cases Age	Assessment of Hyperuricemia	Dietary Pattern Assessment and Identification Method	Dietary Pattern Type and Characteristics	Pattern Score	OR/RR (95%CI)	Matched or Adjusted Variables	Quality assessment
Zhang et al. [20], 2021, China	Cohort Tianjin Chronic Low-grade Systemic Inflammation and Health (TCLSIH) study 18444 subjects 9086 men 9358 women Age 18-90 Mean follow-up: 4.2 3750 incident cases	- Men: SUA >7.0 mg/dL - Women: SUA >6.0 mg/dL	100-item FFQ PCA Varimax rotation Loading	refined and non-refined cereals, coffee, tea and soft-drinks ultra-processed foods: instant noodles, bread, sausages, preserved egg, western-style pastries or cakes, cookies (biscuits), Chinese pastries or cakes, sweets, candies (confectionery), preserves (jams), ice cream, soft drinks, and fruit and vegetable drinks.	Quartile 1 Quartile 4	1.00 (Reference) 1.16 (1.05-1.28)	Sex, age, BMI, smoking status, alcohol consumption status, education levels, employment status, household income, physical activity, depression symptoms, family history of disease, hypertension, hyperlipidemi a, and diabetes, metabolic syndrome, total energy intake, dietary patterns (ultra-process ed food consumption was not included in the calculation), baseline serum uric acid and glomerular filtration rate.	7

¹Serum Uric Acid (SUA); ²Food Frequency Questionnaire (FFQ); ³Principal Component Analysis (PCA); ⁴Eigenvalues (EIG); ⁵Variance Explained (VE); ⁶Body Mass Index (BMI); ⁷Metabolic Syndrome (MetS); ⁸Principal Component Factor Analysis (PCFA); ⁹Factor Analysis (FA); ¹⁰Not Reported (NR); ¹¹Exploratory factor analysis (EFA).

3.3. Meta-Analysis

We identified two common dietary patterns with the characterization of vegetables and fruits, poultry, fish, whole grains, red meat, processed meat, animal fat, eggs and sweets: “Healthy” and “Meat/Western” patterns. The overall analysis showed a significant reduction in the risk of HUA associated with the adherence to the “Healthy” pattern (OR=0.73; 95% CI: 0.61–0.88) and a significant increase in the risk of HUA associated with the adherence to the “Meat/Western” pattern (OR=1.26; 95% CI: 1.17–1.37) (Figure 2).

3.4. Subgroup Analysis

In the meta-analysis of “Healthy” pattern, the stratification design of the study showed that the risk of HUA was significantly reduced only in the cohort studies. Based on a stratification analysis of geographic location, the risk of HUA in Eastern countries (OR=0.79; 95% CI: 0.64–0.98) and Western countries (OR=0.53; 95% CI: 0.30–0.92) was significantly reduced. Furthermore, Asia and Europe have shown similar results stratified by geographic area. However, in the “Meat/Western” pattern meta-analysis, when stratified

by study design, the risk of HUA was significantly increased in cohort (OR=1.20; 95% CI: 1.12–1.29), cross-sectional (OR=1.39; 95% CI: 1.15–1.68) and case control (OR=1.50; 95% CI: 1.21–1.84) studies (Table 2).

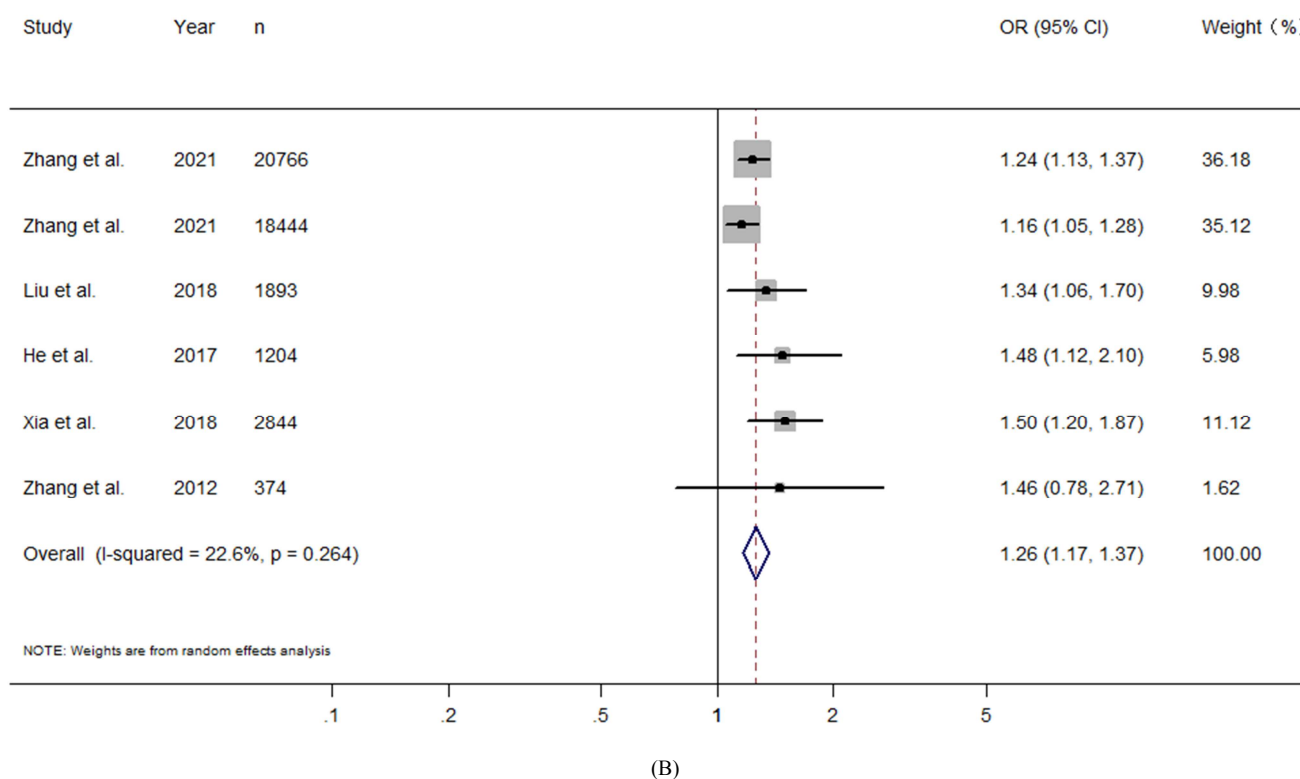
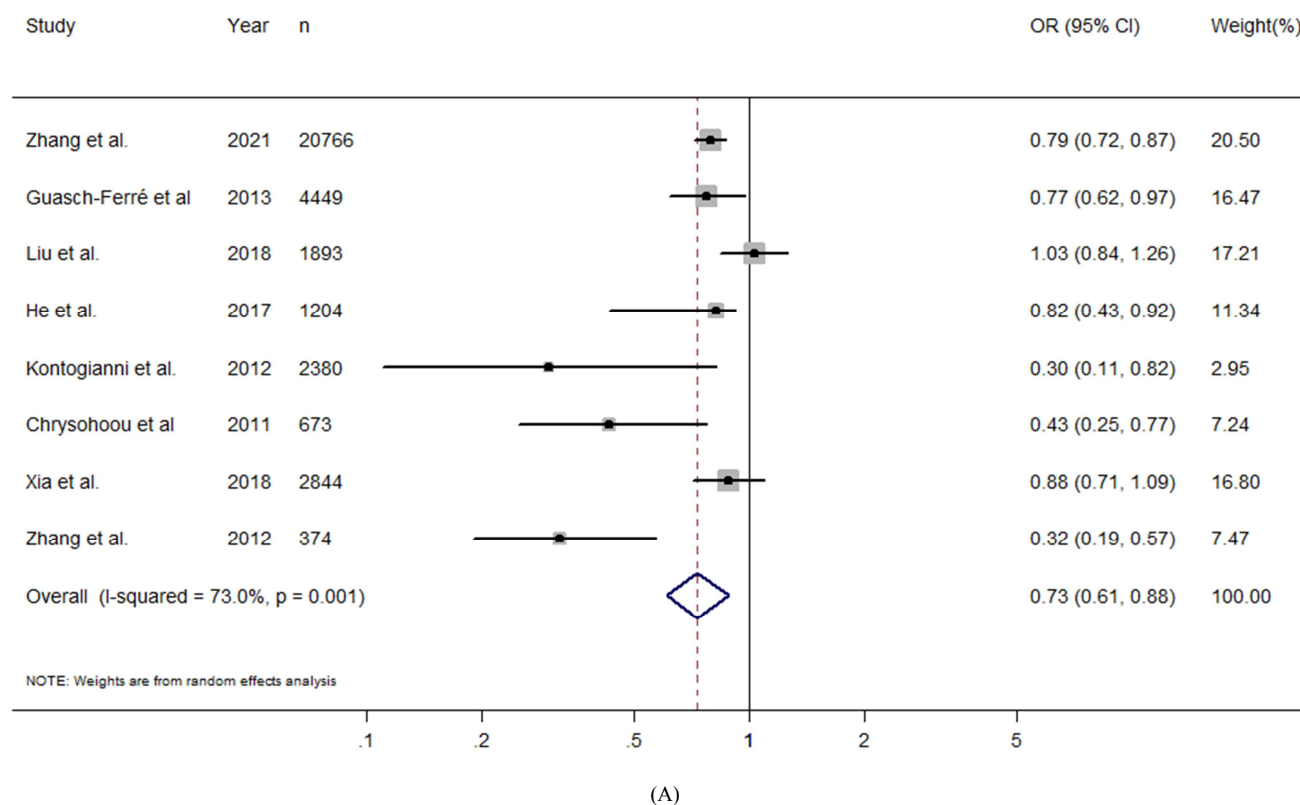


Figure 2. Forest plots of the association between “Healthy” (A) and “Meat/Western” (B) dietary patterns and HUA risk.

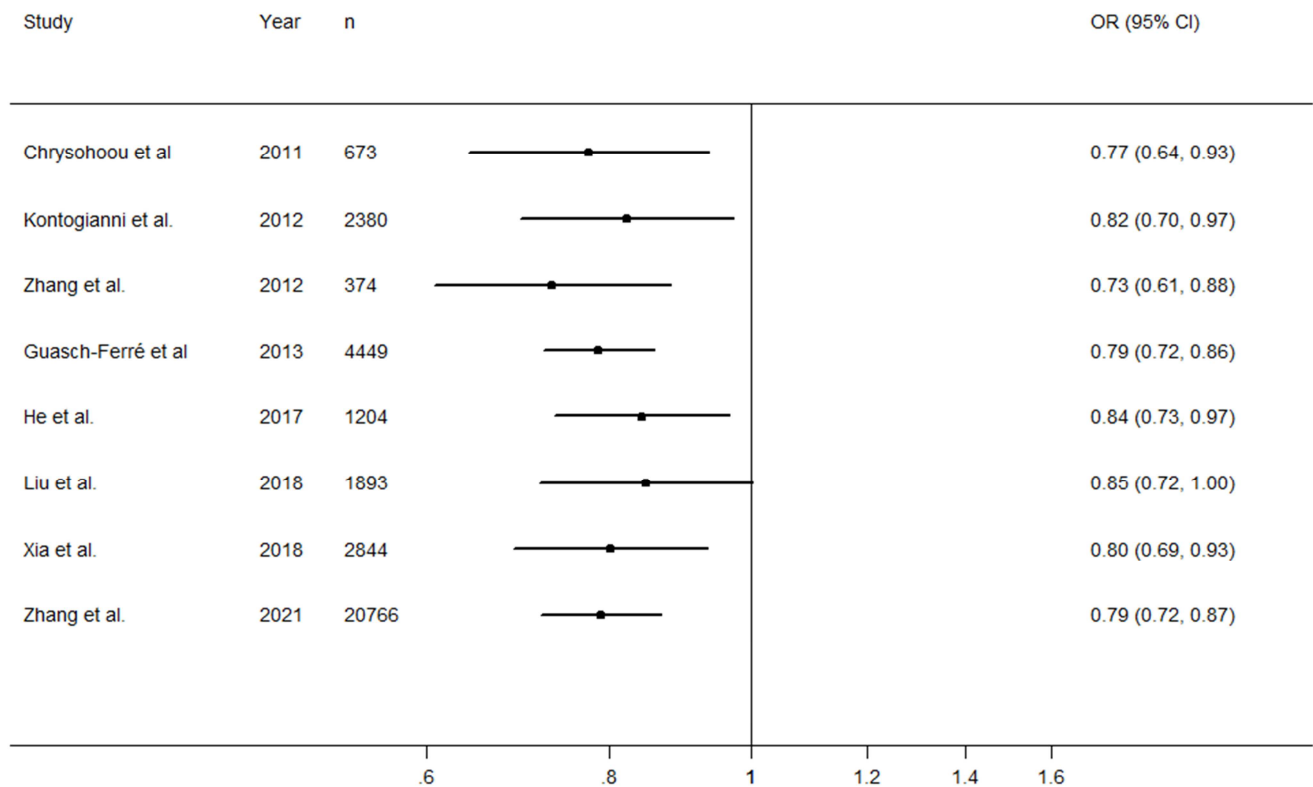
Table 2. Results of stratified analysis of the association between “Healthy” and “Meat/Western” dietary patterns and HUA risk.

Dietary Patterns	Combined Risk Estimate		Test of Heterogeneity		
	OR (95%CI)	P	Q	I ² %	P
“Healthy”					
All (n=8)	0.73 (0.61-0.88)	0.001	25.96	73.00	0.001
Study design					
Cohort (n=2)	0.79 (0.72-0.86)	<0.001	0.04	0.00	0.836
Cross-sectional (n=4)	0.66 (0.42-1.06)	0.084	13.08	77.10	0.004
Case control (n=2)	0.55 (0.20-1.47)	0.234	11.31	91.20	0.001
Geographic location					
Eastern countries (n=5)	0.79 (0.64-0.98)	0.032	17.14	76.70	0.002
Western countries (n=3)	0.53 (0.30-0.92)	0.024	6.28	68.10	0.043
Geographic area					
Asia (n=5)	0.79 (0.64-0.98)	0.032	17.14	76.70	0.002
Europe (n=3)	0.53 (0.30-0.92)	0.024	6.28	68.10	0.043
“Meat/Western”					
All (n=6)	1.26 (1.17-1.37)	<0.001	6.46	22.60	0.264
Study design					
Cohort (n=2)	1.20 (1.12-1.29)	<0.001	0.90	0.00	0.344
Cross-sectional (n=2)	1.39 (1.15-1.68)	0.001	0.25	0.00	0.620
Case control (n=2)	1.50 (1.21-1.84)	<0.001	0.01	0.00	0.936

3.5. Cumulative Meta-Analysis

The cumulative meta-analysis of studies reported since 2011 shows the expected progressive accuracy of CI has improved with the addition of the new studies (Figure 3). After inclusion of the first studies, the cumulative meta-analysis showed a significant reduction in the risk of HUA associated with adhering to the “Healthy” pattern and a significant improvement in the risk of HUA associated with adhering to the “Meat/Western” pattern. Notably, there was no

significant difference in reducing HUA risk associated with adhering to the “Healthy” pattern via including 2018 (Liu et al.) study. With the inclusion of further studies reported from 2018 (Xia et al.) to 2021 (OR=0.79; 95% CI: 0.72–0.87), the cumulative meta-analysis indicated a slight reduction in HUA risk associated with adhering to the “Healthy” pattern. Nevertheless, there was a significant augmentation in HUA risk associated with adhering to the “Meat/Western” pattern when the study reported in 2018 (Xia et al.) (OR=1.27; 95% CI: 1.16–1.38) was included.



(A)

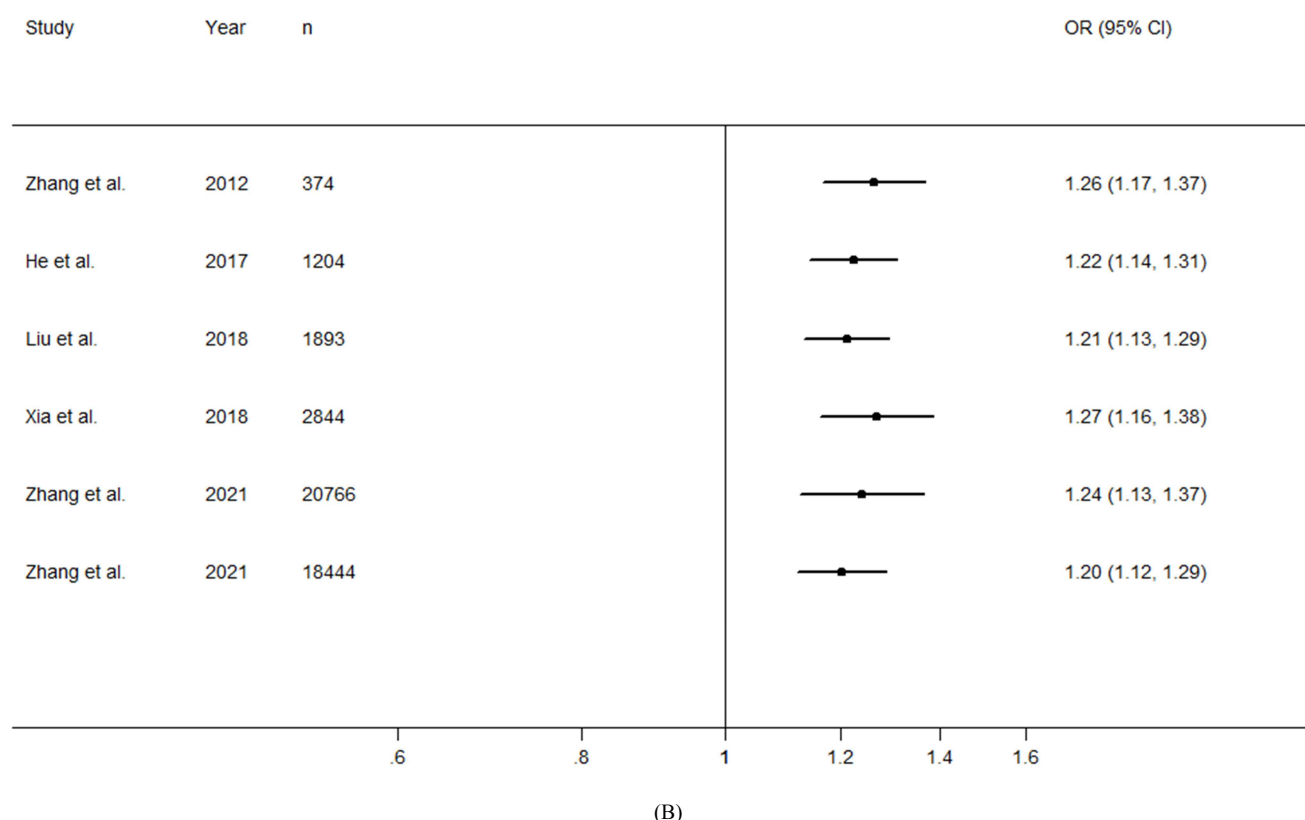


Figure 3. Cumulative meta-analysis according to the publication year of “Healthy” (A) and “Meat/Western” (B) dietary patterns.

3.6. Sensitivity Analysis and Publication Bias

All the sensitivity analyses have shown the stability of our results, and no substantial modification have been made to the estimates in any single study. When the abnormal value study of Zhang et al. [15] (OR=0.32; 95% CI: 0.19–0.57) was deleted from the “Healthy” pattern analysis, the risk estimate slightly changed. Additionally, when the outlier study of Zhang et al. [20] (OR=1.16; 95% CI: 1.05–1.28) was removed from the “Meat/Western” pattern analysis, there were also minor changes in the risk estimates.

In the meta-analysis of the “Healthy” pattern ($p=0.162$) and “Meat/Western” pattern ($p=0.072$), the Egger’s test did not detect publication bias in the overall analysis.

4. Discussion

Our systematic review and meta-analysis explored the influence of dietary patterns on HUA risk. According to literature, several different health results were related to western and healthy dietary patterns. [27] Especially, the western dietary pattern increased the risk of chronic diseases, such as obesity, [33] chronic kidney disease, [34] coronary artery disease [35] and related metabolic diseases. [33]

Furthermore, the healthy dietary pattern was associated with lower risk of the major diet-related chronic diseases, including diabetes, [36, 37] cardiovascular disease, [38] some cancers [39] and cognitive decline and dementia. [40]

Considering the 8 included studies, two main dietary patterns (i.e. “Healthy” dietary pattern and “Meat/Western” pattern) were identified in adult population. The main finding of this observational study was that the “Healthy” dietary pattern showed a protective effect on HUA risk in the cohort study, and in Eastern and Western countries, and the “Meat/Western” pattern was associated with an elevated risk of HUA and the relationship still existed in the stratified analysis by study design. Similarly, several studies by He et al., [24] Liu et al., [21] Xia et al. [22] showed that a positive association between meat dietary pattern and HUA risk, whereas a healthy dietary pattern, such as Mediterranean diet, was associated with lower the risk of HUA. In this study, “Meat/Western” dietary pattern significantly increased HUA risk by 26%, by 48% in the study by He et al., [24] by 34% in the study by Liu et al. [21] and by 50% in the study by Xia et al.. [22] Moreover, HUA risk reduced by 27% through “Healthy” dietary pattern, while it decreased by 18% in the study by He et al. [24] and by 21% in the study by Zhang et al. [23]

According to our findings, the “Meat/Western” dietary pattern was associated with elevated HUA risk of 20% in the cohort study, 39% in cross-sectional study and 50% in case control study. “Healthy” dietary pattern significantly reduced HUA risk of 21% in the cohort study, of 21% in Eastern countries and of 47% in Western countries. Notably, the two dietary patterns indicated the consumption of food was influenced by the culture of different nations. [41, 42] In addition, there are other pre-defined typical dietary patterns

around the world, such as the Northern Europe dietary pattern is characterized by a high intake of fruit, vegetables, egg, fatty fish, low-fat dairy, legumes and oats; [43] the Dietary Approaches to Stop Hypertension (DASH) diet is characterized by a high intake of vegetables, fruit, dairy, beans and whole grains; [44] and the Iranian diet is characterized by a high intakes of dairy product, animal fat, sweets and organ meat. [45] These patterns influenced by culture, [46] socio-economic status and geographical area [47] play a crucial role in developing HUA. Our study mainly combined dietary patterns from Asian and Europe with widely vary eating habits, particularly, traditional dietary patterns from China, [15, 21-24, 26] from Greece [19, 25] and from Spain. [14] In fact, the traditional dietary pattern in China is characterized by high intake of fruits, vegetables, mushroom, algae food, legumes, nuts, rice and rice products, coarse grains, [15, 21-24, 26] and in Greece and Spain by full-fat dairy products, non-refined cereals, potatoes, red meat and products, fruit, vegetables, fish, poultry and legumes. [19, 25]

Our research also found that cumulative meta-analysis effectively presented the trend of two dietary patterns on HUA risk with the accumulation of data over time. A large number of observational studies have been conducted to address efficacy questions that previous trials had already clearly answered through cumulative meta-analysis. [48] For example, as reported by Zeng et al, [49] the association between trimethylamine N-oxide concentrations and kidney function was estimated by using cumulative meta-analysis. [49]

The “Meat/Western” pattern, characterized by high intake of sweets, fried foods, red and processed meat, carbonated beverages, and canned food, significantly increased HUA risk by 26%. To some extent, these foods may influence the developing of HUA risk, especially foods with pro-inflammatory properties, including red and processed meats, fried foods, and canned food which can increase inflammatory cytokines. [50] In reality, although no significant correlation between the most pro-inflammatory diet and HUA was found, [51] inflammatory factors may be related to insulin resistance and lipid disorders. [50]

In addition, this study demonstrated that the “Healthy” pattern significantly reduced HUA risk by 27%. The healthy patterns tended to include the consumption of foods with high intake of olive oils, chicken and fish, fruits, vegetables and n-3 fatty acids, which could contribute to explain the positively association between the “Healthy” pattern and HUA risk. Indeed, adherence to healthy dietary patterns was significantly inverse associated with the risk of MetS, obesity, hypertension, diabetes, inflammation, insulin resistance. [45, 52] The beneficial effect might be attributed to higher amounts of antioxidants including vitamin C, vitamin E, flavonoids, some plant proteins, carotenoids, isoflavone, monounsaturated and polyunsaturated fatty acids. [45, 53, 54]

5. Strengths

This study has a few strengths. First, to our knowledge, this

is the first study in adult population to assess the relationship between dietary patterns and HUA risk. Second, a relatively large number of subjects were included in our study, reducing sampling error to a large extent and allowing a greater likelihood to draw reasonable conclusions. Third, the ORs adjusted for the most confounders were extracted to make the results more reliable in the original studies.

6. Limitations

Nevertheless, our study also has several limitations. First, in addition to the “Healthy” and “Meat/Western” dietary patterns discussed in this meta-analysis, the developing of HUA risk may be related to other dietary patterns. Second, the cross-sectional nature of many included studies prevents us from making a causal inference. Third, our analysis only included the OR for the highest and the lowest quantile of healthy or western dietary patterns, limiting the assessment of the existence of any trends.

7. Conclusion

The study demonstrates that adherence to the “Healthy” pattern characterized by high consumption of fruits, vegetables, whole grains, low and non-fat dairy and lean protein, can contribute to both the prevention and the treatment of HUA, whereas a positively association on HUA is attributed to the “Meat/Western” pattern. These findings should aim to develop dietary guidelines for adult population and to provide guidance for healthy dietary patterns, and encourage people in the risky pattern to change their dietary structure to both the prevention and control of HUA. For further advance research, more prospective studies are needed to substantiate these findings.

Author Contribution

Can Liu conceived the study question, and contributed to the study design, supervision of data extraction, data analysis and interpretation, writing and revising the manuscript. Xiaolong Li and Feifei Li screened articles and extracted data. All authors read and approved the final manuscript.

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