Food groups and the likelihood of nonalcoholic fatty liver disease: a systematic review and meta-analysis

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Shortened version of the title: Food groups and NAFLD: meta-analysis

Keywords: nonalcoholic fatty liver disease, liver steatosis, risk of NAFLD, diet, food groups, meta-analysis, systematic review

Abbreviations used: NAFLD, nonalcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; ROBINS-I, risk of bias in non-randomized studies of interventions; PUFA, n-3 polyunsaturated fatty acids; EPA, eicosapentaenoic acid; DHA, docosahexaenoid acid; HOMA-IR, homeostasis model assessment for insulin resistance; ALT, alanine aminotransferase; FFQ, food frequency questionnaire; BDHQ, brief-type self-administrated diet questionnaire.

This peer-reviewed article has been accepted for publication but not yet copyedited or typeset, and so may be subject to change during the production process. The article is considered published and may be cited using its DOI 10.1017/S0007114520000914

The British Journal of Nutrition is published by Cambridge University Press on behalf of The Nutrition Society
ABSTRACT

Dietary habits have been implicated in the development and severity of nonalcoholic fatty liver disease (NAFLD). Several epidemiologic studies attempted to assess the relationship between food groups and the likelihood of NAFLD, but these results were conflicting. The present meta-analysis was conducted to assess the association between food groups and the likelihood of NAFLD. Published literature were retrieved and screened from MEDLINE, EMBASE and Web of Science. Out of 7892 retrieved articles, 24 observational studies (15 cross-sectional studies and 9 case-control studies) met our eligibility criteria and were finally included in this systematic review and meta-analysis. Consumption of both red meat and soft drinks contributed to a positive association with NAFLD. Inversely, nut consumption was negatively associated with NAFLD. There were no significant influences on the likelihood of NAFLD about consuming whole grains, refined grains, fish, fruits, vegetables, eggs, dairy, and legumes. This meta-analysis suggests that individuals who consumed more red meat and soft drinks may have a significantly increased likelihood of NAFLD, whereas higher nut intake may be negatively associated with NAFLD. Further prospective studies are required to assess the association between food patterns and NAFLD.
Introduction

With the rising prevalence of obesity, diabetes mellitus and metabolic syndrome, nonalcoholic fatty liver disease (NAFLD) has been considered the most common liver disease which affect 20%-30% of the worldwide population\(^1\). NAFLD is characterized by the accumulation of hepatic fat greater than 5% and not caused by excessive alcohol consumption, use of hepatotoxic medications or other established liver diseases\(^2\). It encompasses a spectrum of liver damage that can progress from simple steatosis to nonalcoholic steatohepatitis (NASH), hepatic fibrosis and cirrhosis. Approximately 30% of patients with simple steatosis progress to NASH, which can potentially progress to fibrosis/cirrhosis and eventually lead to hepatocellular carcinoma\(^3\).

Metabolic changes, including insulin resistance and impaired lipid metabolism, have been identified as the molecular pathogenesis of NAFLD\(^4\). NAFLD, which is similar to metabolic diseases such as obesity, inflammation, insulin resistance and type 2 diabetes, is considered to be a liver component of metabolic syndrome\(^5\). Western dietary pattern characterized by higher loads of calories, saturated fat, fructose, sugar-sweetened beverages and refined carbohydrates is associated with weight gain, obesity and more recently with NAFLD\(^6\). Although there is currently no consensus on the pharmacological treatment of NAFLD, the international guidelines recommend that lifestyle modification associated with weight loss should be an integral part of the treatment of NAFLD\(^7\).
Lifestyle modifications include achieving weight loss, increasing physical activity and acquiring healthy dietary pattern\(^8\). Although weight loss is an important approach for the management of NALFD, extreme dietary intervention for the purposes of weight loss, such as very low carbohydrate diet (VLCD) may increase insulin resistance and exacerbate NAFLD even if it can reduce body weight\(^9\). Also, achieving weight loss and maintaining it is often difficult for the most obese patients\(^{10}\). On the other hand, it has been shown that obese or lean patient with NAFLD benefit more from a healthy diet than from weight reduction\(^{11}\), suggesting that healthy diet patterns play an important role in the prevention and management of NAFLD. In view of this, several studies assessed the relationship between these food groups and the likelihood of NAFLD, but results were conflict\(^{12-18}\). Thus, to gain a better understanding of the relationship between NAFLD and dietary factors, we searched literatures according to dietary guidelines and guidelines for the prevention and treatment of NAFLD to evaluate the association of the following 11 food groups including refined grains, whole grains, red meat, fish, vegetables, fruits, dairy, legumes, eggs, nuts and soft drinks, with the likelihood of NAFLD by this meta-analysis\(^{6,19,20}\).

**Method**

This meta-analysis was registered through the International Prospective Register of Systematic Reviews (PROSPERO) as CRD42019120766. This study was reported according to the Meta-analysis Of Observational Studies in Epidemiology (MOOSE)
statement and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Similarly, it followed the recommendations of the Cochrane Collaboration Handbook. We employed the PICO format (population, intervention, comparison, outcome) to answer the research question: “Are food groups (refined grains, whole grains, red meat, fish, vegetables, fruits, dairy, legumes, eggs, nuts and soft drinks) associated with the occurrence of NAFLD”. Population: Adults with NALFD; Intervention: food groups (refined grains, whole grains, red meat, fish, vegetables, fruits, dairy, legumes, eggs, nuts and soft drinks); Comparison: Adults without NAFLD; O: The occurrence of NAFLD.

**Search strategy**

An electronic search was conducted in the MEDLINE, EMBASE and Web of Science databases with no restrictions to time, language, and publication type. Observational studies addressing the association between food groups and NAFLD were eligible. The following search terms were combined to design the search strategy: “Grain,” “whole grain,” “refined grain,” “cereal,” “coarse cereal,” “meat,” “red meat,” “white meat,” “pork,” “beef,” “poultry,” “domestic fowl,” “fish,” “diary,” “milk,” “yogurt,” “soy,” “legumes,” “natto,” “tofu,” “egg,” “vegetable,” “fruit,” “nut,” “soft drink,” “carbonate beverage,” “carbonated drinks,” “sugar beverage,” “soda,” “nonalcoholic fatty liver disease,” “NAFLD,” “nonalcoholic steatohepatitis,” “liver steatosis,” “fatty liver,” “hepatic steatosis,” “nutritional profile,” “nutritional intake,” “dietary pattern,” “dietary intake,” “diet,” “nutrition,” “food.” Duplicate publications were removed.
Our two investigators, HKY and LYT, independently screened the literatures by title, abstract, and full text, respectively. When the selected literatures were identical, the agreement was reached; any disagreement were resolved by consulting the third investigator (TSH). We also manually searched the additional relevant articles from reference lists of retrieved articles.

**Inclusion and exclusion criteria**

Inclusion criteria were as follows. 1) participants: adult participants; 2) observational studies: cohort studies, case-control studies or cross-sectional studies that investigated food groups (whole grains, refined grains, vegetables, fruits, soft drinks, fish, red meat, nuts, milk, eggs, legumes) in relation to the likelihood of NAFLD; 3) diagnosis: NAFLD diagnosis that was determined by ultrasound (diffused echogenicity of the liver or increased echogenicity compared to the renal cortex), or by abdominal CT scan (L/S ratio≤1.1, the L/S ratio was calculated from the mean of the liver and spleen measurements) or by MDCT scan (a value of the liver to phantom ratio<30.0), or by MRI (quantified liver fat content), or by H-MRS (intrahepatic triglyceride content more than 5%) or compatible liver histology\(^{(24-28)}\).

Exclusion criteria: (1) animal studies; (2) adolescents or pregnancy women; (3) present of hepatitis B surface antigen, antibody against hepatitis C or human immunodeficiency virus; (4) excess consumption of alcohol (more than 20 g/day in women or 30 g/day in men) or potentially hepatotoxic drugs (tamoxifen, steroids, amiodarone); (5) other factors which caused hepatic steatosis such as inflammatory
Data extraction and Risk of bias

Two investigators (HKY & LYT) independently extracted and summarized data from each study. Any discrepancies were resolved by consulting the third investigator (TSH). The quality of the included trials was assessed by the Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool\(^{(29)}\). It contains seven domains that rank the studies as low, moderate, serious, or critical serious. According to ROBINS-I guidance, if a study is ranked low in all domains, it is considered low risk of bias; if it is ranked low or moderate in all domains, it is considered moderate risk of bias; if it is ranked serious in at least one domain, it is considered serious risk of bias; if it is ranked critical in at least one domain, it is considered serious risk of bias\(^{(29)}\). All included studies were assessed by two researches (GX and ZL), and discrepancies were resolved by consulting the third investigator (TSH).

Statistical analysis and data synthesis

We analyzed the data using Stata release 15.1 (Stata Corp, College Station, Texas). The results were expressed in terms of OR and 95%CI. In order to evaluate the weight of each study, the standard error of the logarithmic OR of each study was calculated and taken as the estimated variance of the logarithmic OR. The inverse variance method was adopted\(^{(30)}\). Before inclusion in the overall meta-analysis, the results of
gender stratification were summarized using fixed-effects model. Different study type (cross-sectional study or case-control studies or RCT or cohort study) were analyzed separately.

Statistical heterogeneity was evaluated by Cochran's Q-test and $I^2$ statistics, and $P<0.1$ and $I^2>50\%$ was considered as significant heterogeneity$^{(31)}$. If the heterogeneity was acceptable ($I^2\leq50\%$), a fixed-effects model was conducted to calculate the pooled OR. Otherwise, a random-effects model was adopted. We used "metan logor loglb logub, label(namevar=author, yearvar=year) by(study) fixed eform" command to combine studies without significant heterogeneity ($I^2\leq50\%$); and used "metan logor loglb logub, label(namevar=author, yearvar=year) by(study) random eform" command to combine studies with significant heterogeneity ($I^2>50\%$). If the number of studies is greater than 5, the causes of heterogeneity were investigated by subgroup analysis based on geographic location (Asia, Europe and America), number of cases ($\geq$1000 versus <1000) and dietary assessment method (validated versus non-validated). In addition, sensitivity analysis was performed for low-bias studies (if the number of studies >5). According to the Cochrane Handbook, if $\geq$10 studies are available, we explore publication bias by using Eggers tests and funnel plots$^{(32, 33)}$.

Results

A total of 7892 potentially relevant articles were identified through literature searching in MEDLINE, EMBASE and Web of Science, and 2322 duplicate articles
were excluded. The remaining 5570 articles underwent a title and abstract screening, and 5499 were further excluded as they did not fulfill the inclusion criteria.

In total, 71 articles remained for full-text evaluation. Among them, 47 articles were excluded because 7 were review articles, 8 were about adolescents, 24 were without the relevant exposure/outcomes, and 8 did not conform to the relevant study design. Finally, 24 articles were identified and included in this systematic review and meta-analysis. The study selection process was described in Figure 1. Among them, 15 were cross-sectional studies and 9 were case-control studies. Of the studies, 17 studies were conducted in Asia (9 in China, 1 in South Korea, 2 in Iran, 3 in Israel and 2 in Japan), 5 in European (3 in Greece, 2 in Italy), and 2 in America. The main characteristics of the included studies are illustrated in Supplementary Table 1 and Table 2.

**Quality assessment**

15 studies were evaluated to have a low risk of bias, and 9 studies had a moderate risk of bias. The quality of included studies ranged from low to moderate risk of bias as shown in Supplementary Table 3. Bias risk of each domain of the included studies is also shown in Supplementary Table 3.

**Red meat**

A total of the 8 studies assessed the effect of red meat consumption on the likelihood of NAFLD, which include 7 cross-sectional studies (with 5141 cases) and 1 case control study (with 2974 cases). Meta-analysis results from 7
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homogeneous cross-sectional studies ($I^2=48.7\%$, $P=0.069$) showed a positive association between red meat consumption and the likelihood of NAFLD (OR=1.121; 95% CI=1.042, 1.207; $P=0.002$) (Figure 2). Also, the result from the case-control study found a positive association (OR=1.150; 95% CI=1.023, 1.293; $P=0.020$).

Further, subgroup analyses were conducted by risk of bias, geographic location, number of cases, and dietary assessment. Except for the 2 studies with ≥1000 cases by which the pooled result showed no association of red meat consumption with the likelihood of NAFLD ($I^2=0.0\%$, P-heterogeneity=0.340; OR=1.005; 95% CI=0.967, 1.150; $P=0.227$), the results still showed the positive associations between red meat consumption and the likelihood of NAFLD in the studies with low risk of bias and <1000 cases, and in the studies from the analyses by geographic location and dietary assessment. Evidence of significant heterogeneity in subgroup analysis was only found in the studies with validated dietary assessment ($I^2=56.4\%$) (Supplementary Table 4).

**Soft drinks**

A total of 7 studies assessed the effect of soft drinks consumption on the likelihood of NAFLD, which include 6 cross-sectional studies (with 9887 cases) and 1 case-control study (with 60 cases)\(^{(12, 34, 38, 40, 41, 46, 49)}\). Meta-analysis results from 6 homogeneous cross-sectional studies ($I^2=25.3\%$, $P=0.245$) showed that soft drink consumption was positively correlated with the likelihood of NAFLD (OR=1.294; 95% CI=0.191, 1.406; $P=0.000$) (Figure 3). However, the result from the case-control study found no
association between soft drink intake and the possibility of NAFLD (OR=2.000; 95% CI= 0.894, 4.472; P=0.091).

Stratified by risk of bias, geographic location, number of cases, and dietary assessment in subgroup analyses, the results still indicated the positive correlations between beverage intake and the likelihood of NAFLD. Evidence of no significant heterogeneity was found in subgroup analysis (Supplementary Table 5).

**Nut**

A total of 5 studies assessed the effect of nuts consumption on the likelihood of NAFLD, which include 2 cross-sectional studies (with 4737 cases) and 3 case-control studies (with 768 cases)\(^{15, 34, 35, 39, 51}\). A negative association of nut intake with the possibility of NAFLD was observed among cross-sectional studies (I\(^2\)=0.0%, P-heterogeneity=0.472; OR=0.837; 95% CI=0.727, 0.965; P=0.014) and case-control studies (I\(^2\)=42.6%, P-heterogeneity=0.175; OR=0.943, 95% CI=0.907, 0.980; P=0.003) (Figure 4).

**Whole grains**

A total of 3 studies assessed the effect of whole grains consumption on the likelihood of NAFLD, which include 2 cross-sectional studies (with 2394 cases) and 1 case-control study (with 73 cases)\(^{14, 36, 37}\). No significant association between whole grains consumption and the likelihood of NAFLD was observed among cross-sectional studies (I\(^2\)=0.0%, P-heterogeneity=0.965; OR=0.990; 95% CI=0.965, 1.015; P=0.439) and case-control study (OR: 1.029; 95% CI: 0.993, 1.067; P=0.119) (Figure 5).
Refined grains

A total of 6 studies assessed the effect of refined grains consumption on the likelihood of NAFLD, which include 4 cross-sectional studies (with 3509 cases) and 2 case-control studies (with 207 cases). No significant association between refined grains consumption and the likelihood of NAFLD was observed among cross-sectional studies ($I^2=68.4\%$, $P$-heterogeneity=0.023; OR=0.973; 95% CI=0.769, 1.230; $P=0.818$) and case-control study ($I^2=85.6\%$, $P$-heterogeneity=0.008; OR: 1.050; 95% CI: 0.880, 1.253; $P=0.591$). (Figure 6).

Fish

A total of 6 studies assessed the effect of fish consumption on the likelihood of NAFLD, which include 5 cross-sectional studies (with 2780 cases) and 1 case-control study (with 134 cases). Meta-analysis results from 5 heterogeneous cross-sectional studies($I^2=69.4\%$, $P=0.011$) showed no significant association between fish consumption and the likelihood of NAFLD (OR=0.908; 95% CI=0.647, 1.276; $P=0.579$) (Figure 7). However, the result from the case-control study showed fish consumption was negatively association with the possibility of NAFLD(OR=0.845; 95% CI= 0.751, 0.950; $P=0.005$).

Fruits

A total of 8 studies assessed the effect of fruits consumption on the likelihood of NAFLD, which include 6 cross-sectional studies (with 11861 cases) and 2 case-control studies (with 2168 cases). There was no significant
association between fruits intake and the likelihood of NAFLD among cross-sectional studies ($I^2=68.0\%$, P-heterogeneity=0.008; OR=0.991; 95% CI=0.844, 1.163; P=0.907) (Figure 8) and case-control studies ($I^2=37.4\%$, P-heterogeneity=0.206; OR=0.899; 95% CI: 0.802, 1.007; P=0.066) (Figure 9).

In subgroup analysis, the pooled result from the studies with <1000 cases showed a negative correlation between fruits intake and the likelihood of NAFLD ($I^2=0.0\%$, P-heterogeneity=0.437; OR: 0.651; 95% CI: 0.483, 0.878; P=0.005), whereas the results of all other subgroup analyses were consistent with the above overall analysis. Evidence of significant heterogeneity was still observed in the stratified analyses of the Asian studies ($I^2=74.4\%$), the studies with $\geq 1000$ cases ($I^2=55.2\%$), and the studies with validated dietary assessment ($I^2=72.2\%$) (Supplementary Table 6).

**Vegetables**

A total of 8 studies assessed the effect of vegetables consumption on the likelihood of NAFLD, which include 6 cross-sectional studies (with 4523 cases) and 2 case-control studies (with 3074 cases)\textsuperscript{14, 15, 34, 36, 38, 44, 45, 47}. There was no significant association between vegetables intake and the likelihood of NAFLD among cross-sectional studies ($I^2=50.0\%$, P-heterogeneity=0.075; OR=1.005; 95% CI=0.976, 1.035; P=0.725) and case-control studies ($I^2=0.0\%$, P-heterogeneity=0.884; OR=0.993; 95% CI: 0.897, 1.1000; P=0.898) (Figure 10).

In subgroup analysis, the pooled result from the studies with <1000 cases showed a negative correlation between vegetables intake and the likelihood of NAFLD
(I²=0.0%; P-heterogeneity=0.398; OR: 0.696; 95% CI: 0.528, 0.916; P=0.010), whereas the results of all other subgroup analyses were consistent with the above overall analysis. Evidence of significant heterogeneity was still found in the stratified analyses of the Asian studies (I²=60.0%) and the studies with validated dietary assessment (I²=59.8%) (Supplementary Table 7).

**Eggs**

A total of 3 studies assessed the effect of eggs consumption on the likelihood of NAFLD, which include 2 cross-sectional studies (with 2131 cases) and 1 case-control study (with 169 cases). Neither cross-sectional studies (I²=0.0%, P-heterogeneity=0.532; OR: 0.969; 95% CI: 0.815, 1.153; P=0.722) nor case-control study (OR=0.966; 95% CI=0.453, 2.060; P=0.929) showed the association between eggs consumption and NAFLD (Figure 1).

**Dairy**

A total of 4 studies assessed the effect of dairy consumption on the likelihood of NAFLD, which include 3 cross-sectional studies (with 6789 cases) and 1 case-control study (with 143 cases). Meta-analysis results from 3 heterogeneous cross-sectional studies (I²=55.7%, P=0.105) showed no significant association between dairy consumption and the likelihood of NAFLD (OR=0.954; 95% CI=0.824, 1.104; P=0.524) (Figure 12). However, the result from the case-control study showed dairy consumption was positively association with the possibility of NAFLD (OR=1.192; 95% CI= 1.002, 1.419; P=0.048).
Legumes

A total of 4 studies assessed the effect of legumes consumption on the likelihood of NAFLD, which include 3 cross-sectional studies (with 2614 cases) and 1 case-control study (with 196 cases)\(^{(13, 14, 34, 36)}\). Meta-analysis results from 3 homogeneous cross-sectional studies\((I^2=0.0\%, \ P=0.507)\) showed no significant association between legumes consumption and the likelihood of NAFLD \((OR=0.943; \ 95\% \ CI=0.877, 1.014; \ P=0.115)\) (Figure 13). However, the result from the case-control study showed legumes consumption was negatively associated with the possibility of NAFLD\((OR=0.730; \ 95\% \ CI= 0.637, 0.836; \ P=0.000)\).

Sensitivity analyses

In the sensitivity analyses, the findings from the studies with low risk of bias suggest a stronger positive association between red meat \((I^2=0.0\%, \ P\)-heterogeneity\(=0.817; \ OR: \ 1.218; \ 95\% \ CI: \ 1.018, 1.458; \ P=0.031)\) and soft drinks \((I^2=0.0\%, \ P\)-heterogeneity\(=0.880; \ OR: \ 1.575; \ 95\% \ CI: \ 1.133, 2.189; \ P=0.007)\) intake and the possibility of NAFLD (Supplementary Table 4 and 5). Moreover, an inverse association was found by sensitivity analysis between vegetables consumption and NAFLD \((I^2=10.2\%, \ P\)-heterogeneity\(=0.291; \ OR: \ 0.574; \ 95\% \ CI: \ 0.353, 0.932; \ P=0.025)\) in the studies with low risk of bias (Supplementary Table 7).
Discussion

In this meta-analysis, the results revealed that intake of red meat and soft drink was associated with an increased the likelihood of NAFLD, whereas intake of nut was negatively associated with the possibility of NAFLD. It is noteworthy that most foods included in the meta-analysis (whole grains, refined grains, fish, fruits, vegetables, eggs, dairy, and legumes) may have no significant effect on the likelihood of NAFLD.

To our knowledge, this is the first meta-analysis investigating the relationship between food groups (refined grains, whole grains, fish, red meat, vegetables, fruits, soft drinks, eggs, legumes, nuts and dairy) and the likelihood of NAFLD. The pooled results of our meta-analysis are in accordance with other systematic review and meta-analysis, indicating that consumption of red meat and sugar- and artificially sweetened soda is positively associated with NAFLD\textsuperscript{53, 54}. Firstly, red meat rich in saturated fat increases hepatic lipid accumulation and insulin resistance via reducing lipid oxidation and increasing lipid synthesis\textsuperscript{55, 56}. Additionally, heme-iron intake reduces insulin sensitivity through cellular oxidation stress\textsuperscript{57}. Red meat is often processed with a lot of sodium and preserved with nitrites, which is related to increased the likelihood of insulin resistance and NAFLD\textsuperscript{58, 59}. Secondly, several studies also have shown that higher consumption of soft drinks is associated with a greater likelihood of NAFLD and a series of metabolic syndromes\textsuperscript{60, 61}. Soft drinks provide a large amount of sugar and excessive calories, which led to rapidly increased insulin level and postprandial glucose\textsuperscript{60, 62}. Lebda and colleagues stated that
long-term intake of soft drinks is prospectively associated with the level of ALT which represents liver inflammation\(^{(63)}\).

Consistent with other studies, our meta-analysis shows that nut consumption reduces the likelihood of NAFLD. A study with 12946 participants indicated that nut consumption was positively associated with healthier nutrition and lifestyle\(^{(64)}\); another study displayed that risk factors associated with NAFLD and cardiovascular disease were improved after regular nut consumption\(^{(65)}\).

However, the current research still fail to reach a consistent conclusion on the possibility of NAFLD with intake of fish, legumes, fruits, vegetables, and dairy. In the cross-sectional studies, the pooled results showed that no significant associations were observed between consumption of both fish (OR=0.908) and legumes (OR=0.943) and the likelihood of NAFLD; but in the case-control studies, the results showed consumption of both fish (OR=0.845) and legumes (OR=0.730) decreased the possibility of NAFLD. In the cross-sectional studies and the case-control studies, the pooled results showed no significant associations between intake of both fruits and vegetables and the likelihood of NAFLD; but in the cross-sectional studies with <1000 cases, the pooled results showed that consumption of both fruits (OR=0.651) and vegetables (OR=0.696) significantly reduced the possibility of NAFLD. Moreover, in the cross-sectional studies with low risk of bias, the pooled results showed that intake of vegetables (OR=0.574) also reduced the possibility of NAFLD.

On the contrary, in the cross-sectional studies, the pooled results showed that no significant association was observed between dairy consumption and the likelihood of
NAFLD, but in the case-control study, the result showed that dairy consumption increased the possibility of NAFLD (OR=1.192)\(^{(50)}\). Taken together, the above findings suggest that higher consumption of fish, legumes, fruits, and vegetables appeared to have a protective trend against NAFLD likelihood, while intake of more milk may be an adverse effect on the likelihood of NAFLD.

Omega-3 PUFAs in fish and isoflavones in legumes have been shown to reduce lipid accumulation and liver enzyme levels, to improve insulin sensitivity, and to have anti-inflammatory effects, and thus are associated with the prevention of the development of hepatic steatosis, NAFLD, NASH, and fibrosis\(^{(66-68)}\). Fruits and vegetables are rich in fiber, antioxidants such as polyphenols, which help prevent the occurrence of NAFLD. In addition to the antioxidant effect, polyphenols also have beneficial effects on metabolic homeostasis in vivo and in vitro NAFLD model, with anti-inflammatory and anti-fibrosis effects. In general, they inhibit de novo fat synthesis and stimulate β-oxidation in the liver\(^{(69)}\). On the other hand, the case-control study \(^{(50)}\) as mentioned above found that dairy products (mainly referring to cheese) increased the likelihood of NAFLD. This may be related to the fact that cheese contains more saturated fatty acids that increases liver steatosis \(^{(39)}\). More studies are needed to further confirm the relationship between fish, legumes, fruits, vegetables, and dairy products and the likelihood of NAFLD.

In recent years, on the basis of the components of the Mediterranean diet, the literature reports its beneficial effects in preventing major chronic diseases, including obesity, diabetes, cardiovascular diseases, and some forms of cancers\(^{(70-73)}\). More
importantly, a growing body of evidence has supported the idea that the Mediterranean diet, associated with exercise and cognitive behavior therapy, may be the reference nutritional profile for the prevention and the treatment of NAFLD patients\(^{74-76}\). It is characterized by an abundance of consumption of whole grains, vegetables, fruits, legumes, nut, and olive oil (rich in monounsaturated-fat); a moderate intake of fish and poultry; low consumption of red/processed meat and dairy products; and low to moderate consumption of alcohol during meals\(^{75}\). From our meta-analysis results, a high to moderate intake of nut, legumes, fish, egg, whole grains, and vegetables, and low consumption of red meat and soft drinks should be recommended for patients with NAFLD, which is roughly similar to the diet composition of the Mediterranean diet. At present, Mediterranean diet is the latest recommended dietary pattern for NAFLD patients in EASL-EASD-EASO clinical practice guidelines\(^6\).

Most of the studies measured foods intake with a food frequency questionnaire (FFQ), which is easy for the administration to assess long-term habitual food consumption. It contains numerous food items with specific serving sizes and frequency categories and has the following advantages: firstly, since the questionnaire is structured, it is convenient and simple; secondary, the implementation is simple and easy to understand, and the participation rate of subjects is high; thirdly, it can be used to analyze the correlation between specific nutrients or related foods and diseases. However, there are some limitations. Firstly, it may cause bias due to errors in the estimation of portion sizes; secondary, cooking methods and seasoning dosage are not
easy to estimate, there may be a large error range. Although the debate about the utility of FFQ in nutritional epidemiological studies is often polarized, dietary data derived from it has proven useful in addressing important research questions\(^{(77)}\). Of the 24 studies included in our meta-analysis, 21 studies used FFQ to investigate dietary intake. Since the implementation is simple and the content design is easy to understand, subjects will be more willing to cooperate, thus guaranteeing the reliability of the results of this meta-analysis.

Some strengths of this meta-analysis are as follow: (1) we investigated a variety of foods; (2) all the studies included in our meta-analysis were low to moderate bias risk; (3) all the studies included in our meta-analysis used multiple logistic regressions to reduce the effect of confounders on the correlation of NAFLD with food consumption. However, several limitations of this meta-analysis should be note. First, because the overall number of studies included was small, subgroup and sensitivity analyses were limited to four of the 11 food groups (red meat, soft drinks, fruits, and vegetables). Consistent with this, publication bias could not be tested as the overall low number of included studies. Also, the results of several food groups may be bias due to too few studies included (eggs=3 studies, dairy=4 studies, legumes=4 studies, whole grains=3 studies). Lastly, since most studies do not stratify food intake, it is not possible to perform linear or nonlinear dose-response of different food groups. Also, the included studies used different units or different standards to measure food groups.

In summary, this meta-analysis with 24 studies identified 11 food groups associating the likelihood of NAFLD. The results were broadly consistent with the current dietary
recommendation for the management of NAFLD. Larger and more precise studies are required to further assess the association and the underlying mechanisms between food groups and the possibility of NAFLD.

Acknowledgments

The authors’ contributions were as follow— all authors designed the research (project conception, development of the overall research plan) and approved the final manuscript; HKY and LYT designed and conducted research (conduct the systematic search, screened the literature and extracted the data); HKY: completed the first draft of the manuscript; GX and ZL analyzed the data and performed the statistical analyses; SHT had primary responsibility for final content; ZL critically reviewed the manuscript. None of the other authors reported a conflict of interest related to the study.
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Figure Legends

Figure 1. Flow diagram of literature search and study selection
Figure 2. Fixed-effects meta-analysis of cross-sectional studies that examined red meat consumption and NAFLD risk. Weights are from fixed-effects analysis. ES, effect size.
Figure 3. Fixed-effects meta-analysis of cross-sectional studies that examined soft drinks consumption and NAFLD risk. Weights are from fixed-effects analysis. ES, effect size.
Figure 4. Fixed-effects meta-analysis of prospective studies that examined nut consumption and NAFLD risk. Weights are from fixed-effects analysis. ES, effect size.
Figure 5. Fixed-effects meta-analysis of cross-sectional studies that examined nut consumption and NAFLD risk. Weights are from fixed-effects analysis. ES, effect size.
Figure 6. Random-effects meta-analysis of prospective studies that examined refined grains consumption and NAFLD risk. Weights are from random-effects analysis. ES, effect size.
Figure 7. Random-effects meta-analysis of cross-sectional studies that examined fish consumption and NAFLD risk. Weights are from random-effects analysis. ES, effect size.
Figure 8. Random-effects meta-analysis of cross-sectional studies that examined fruits consumption and NAFLD risk. Weights are from random-effects analysis. ES, effect size.
Figure 9. Fixed-effects meta-analysis of case-control studies that examined fruits consumption and NAFLD risk. Weights are from fixed-effects analysis. ES, effect size.
Figure 10. Fixed-effects meta-analysis of prospective studies that examined vegetables consumption and NAFLD risk. Weights are from fixed-effects analysis. ES, effect size.
Figure 11. Fixed-effects meta-analysis of cross-sectional studies that examined eggs consumption and NAFLD risk. Weights are from fixed-effects analysis. ES, effect size.
Figure 12. Random-effects meta-analysis of cross-sectional studies that examined dairy consumption and NAFLD risk. Weights are from random-effects analysis. ES, effect size.
Figure 13. Random-effects meta-analysis of cross-sectional studies that examined legumes consumption and NAFLD risk. Weights are from random-effects analysis. ES, effect size.