

Does Consumption of Refined Carbohydrate Predict Incidence of Type Two Diabetes Mellitus? A Systematic Review and Meta-Analysis

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Abstract

Background: Type two diabetes mellitus (T2DM) is a highly prevalent health disorder among adult males and females worldwide. There is consistent evidence that unhealthy diets and physical inactivity play an important role in the development of T2DM. Many people consume refined carbohydrates as part of their daily meals. However, the evidence on whether refined carbohydrates predict T2DM is inconclusive.

Objective: To provide evidence on the association between refined carbohydrates and the incidence of T2DM.

Method: The literature search through PubMed, Embase, CINAHL and Scopus identified prospective cohort studies that associated refined carbohydrate intake with the incidence of T2DM in non-diabetic participants. We then summarized the evidence by using systematic review and meta-analysis.

Results: A systematic review and a meta-analysis were conducted for prospective cohort studies that examined the intake of refined carbohydrates and the incidence of type 2 diabetes. We included 16 articles in the systematic review. Of these 16 articles, only eight examined refined carbohydrates separately from other diets, so these eight were included in the meta-analysis. Our findings from the systematic review suggest heavily that a link exists between high consumption of refined carbohydrates, especially white rice, and the development of T2DM. In the meta-analysis, the random effects model of included studies suggests a positive linkage between refined carbohydrate intake and the incidence of T2DM with a pooled RR = 1.33, 95% CI [1.18, 1.48].

Conclusion: Consumption of high amounts of refined carbohydrates is significantly associated with the increased incidence of type 2 diabetes. Reducing refined carbohydrates and improved information about their risk and access to this information may prevent T2DM development worldwide.

Key words: Type two diabetes mellitus, refined carbohydrates

Introduction

Diabetes mellitus has become increasingly prevalent in recent years, which might indicate an actual increase in the number of individuals with this condition, or it might indicate that, over the past century, we have developed technology that is better able to detect diabetes mellitus (1). A total of 415 million adults people worldwide were estimated to have diabetes in 2015. If these trends continue, 642 million people will have diabetes by 2040 (2).

Diabetes is genetically driven; that is, it is thought to be passed on from parent to child. Type 2 diabetes mellitus (T2DM), which is the more prevalent form thereof, occurs amongst individuals once they reach middle age, while type 1 is a chronic condition that occurs amongst children or young adults and lasts throughout their lifetime (3). In the case of T2DM, then, while the hereditary factor is given much focus, there is also a certain degree of control that needs to be established in the diet of patients (4).

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There are certain arguments related to the regulation of diet amongst diabetic patients, most of which involve the control of sugar intake to maintain normal blood sugar levels (5,6). However, other studies have considered the intake of refined carbohydrates as a contributing factor towards blood sugar increase in diabetic patients as well (7). Either way, it has been well established that T2DM is at least partially genetic in nature, although certain environmental factors have also been counted as contributory towards its existence and, more importantly, towards its progression over time.

One of the issues with regard to the suggested environmental causes is the change in dietary habits worldwide. In contrast to the substantial fibre-based intake of earlier times, there has been an increase in the consumption of carbohydrates as well as processed and fat-based foods in the contemporary world (8), paired with a relatively sedentary lifestyle (9,10). A number of adverse effects can take place in the body with regard to various illnesses, and, despite its heritability (11), T2DM gains traction through such dietary and lifestyle choices, as is argued in many cases (12).

Refined carbohydrates are the result of a refining process in which fibres and valuable nutrients are extracted from grains and sugar at a processing plant (13). Upon consumption of these carbohydrates, which are rapidly digested and assimilated after the intake, postprandial blood glucose and insulin levels become elevated (14). Thus, on the glycaemic index (GI), which measures the potential of foods to elicit the postprandial elevation of blood sugar, refined carbohydrates have a very high score (GI = 70 or more) (15).

Various studies reported positive association between the consumption of refined carbohydrates and T2DM (16–19). However, such association has been considered significant in other study (20). A recent systematic review and a meta-analysis show that the inclusion of simple carbohydrates within the diet seems to have a major effect on the acquisition of T2DM (20). This review has been restricted to a single pattern: the consumption of white rice. Although this pattern has been found to relate to the risk of diabetes, the evidence is inconclusive. Thus, this systematic review and meta-analysis aims to summarize the evidence of published prospective cohort studies by evaluating the association between all different patterns of refined carbohydrates and T2DM. This is the first systematic review and meta-analysis that aims to assess the risk of refined carbohydrates to the incidence of T2DM conclusively.

Methodology:

Literature Search:

To identify published studies that examined the relationship between refined carbohydrate intake and T2DM, a systematic search was conducted on PubMed, Embase, CINAHL and Scopus for prospective cohort studies. The key terms for the search were “diabetesmellitus”, “type 2 diabetes mellitus” and “non-insulin dependent diabetes mellitus”, in combination with “refined carbohydrates,” or “dietary carbohydrates” and in combination with cohort studies, follow up (check supplementary search strategies). For further relevant articles, reference lists of articles were screened.

Study selection

The following inclusion criteria were applied: prospective cohort studies that examined the relationship between refined carbohydrate intake and T2DM, studies published up to July 2017, journals in the English language, participants aged 18 years and above, research carried out globally and studies that reported risk estimates (odds ratio or relative risk) with 95% confidence intervals.

Figure 1 demonstrates the study selection process and results. A total of 334 articles were identified through database searching, 89 of which were identified from PubMed, 115 from Embase, 39 from CINAHL and 91 from Scopus. Forty-one studies remained after exclusion of the duplicated articles and those studies that did not meet our inclusion criteria. Of these 41 published articles, we evaluated the full text and excluded 29 studies. Of these excluded articles, 16 studies did not have original data that could be extracted (letters and reviews articles) and 13 studies were irrelevant (no relevant outcome, no relevant exposure, no risk estimation and not in English). Finally, we identified 12 studies that matched the inclusion criteria. A manual search of references cited by these studies yielded four new eligible articles. Ultimately, 16 articles were included in the systematic review, of which only eight examined refined carbohydrates separately from other diets and, thus, were included in the meta-analysis. Of these eight studies included in the meta-analysis, men and women were examined separately in the study by Nanri et al, three independent cohort studies were conducted in the Sun et al's study and two types of refined carbohydrates were

examined separately in both the Hodge et al's and Villegas et al's studies. Thus, a total of 13 comparisons were included in the meta-analysis (supplementary figure 1).

Data extraction

From each study, the following information was extracted: study characteristics, including author names, publication year, study participants, incident cases, study location, follow-up period and person time. Participants' characteristics included age, sex, exposure to refined carbohydrates, assessment methods of dietary exposure, including reproducibility and validity, outcome (type 2 diabetes) and its measures and risk estimation for each category. Studies that had multiple cohorts or expressed data for men and women separately were considered to be independent and were extracted separately.

Quality assessment of the included studies

The quality of included studies was assessed using "The Risk Of Bias In Nonrandomized Studies-of Intervention (ROBINS-I) assessment tool for cohort-type studies"⁽²¹⁾. The results demonstrated that most studies obtained a score of 7 (maximum score of 7) except the Schulze et al's study that achieved a score of 6 and both the Nettleton et al's and Denova-Gutiérrez et al's studies that achieved scores of 5.

Assessment method of dietary intake and study outcomes:

For all included studies in this systematic review and meta-analysis, the information regarding dietary intake among participants was collected using a validated food frequency questionnaire (FFQ) designed to determine the average intake of food during the studies follow-up period.

The included studies measured the incidence of type 2 diabetes mellitus (T2DM), which was identified through many methods, including self-reports and a validated supplementary questionnaire, and then confirmed using various measures, such as medical records, the National Diabetes Data Group, the American Diabetes Association diagnostic criteria (1997), the World Health Organization criteria (1985, 1999), the use of antidiabetic medication, the Japan Diabetes Society diagnostic criteria (1982) for the Nanri et al's study in Japan and the enzymatic colorimetric for the Denova-Gutiérrez et al's study.

Statistical Analysis

All the cohort studies included in the meta-analysis used relative risks (RRs) as a measure of association except for those by Hodge et al, Nanri et al and Golozar et al, all of which used odds ratios (ORs) for their measurements. Due to a low incidence of T2DM in these studies (e.g., the incidence was 1.9% for Nanri et al, 1.2% for Hodge et al and 3.7% for Golozar et al, ORs were considered comparable to RRs as a measure of association.

All RRs that compared extreme categories of consumption were pooled by using a random effects model. Subsequently, a forest plot was produced for visual assessment of the multivariate-adjusted RRs and their concordant 95% confidence intervals. The evaluation of heterogeneity between studies was assessed by Cochrane's Q and I² statistical tests (where an I² value of 25% is indicative of low heterogeneity, 50% is moderate heterogeneity, 75% is high heterogeneity and $p < 0.05$ indicates a statistical significance for heterogeneity). Finally, a funnel plot was used to address any potential publication bias. All analysis was performed by using MetaXL statistical software version 5.3.

Results

Study Characteristics

The study characteristics are shown in tables 2-5 (supplementary tables 2-5). In summary, all studies examined the risk of type 2 diabetes among a prospective cohort of participants that were free of the disease at baseline. During the period from two to twenty-two, 24,428 cases of T2DM were identified. Twelve studies were conducted among Western populations (eight studies in the United States, two studies in the United Kingdom, one study in Mexico and one study in Australia), and the other four studies were conducted among Asian populations (two studies in China, one study in Japan and one study in Iran). In each included study, validated food frequency questionnaires were used to assess dietary intake.

Systematic Review:

Refined Carbohydrate Intake and Risk of Type 2 Diabetes

The long-term effects of pure refined carbohydrates on the incidence of type 2 diabetes mellitus (T2DM) were evaluated in eight cohort studies (22-29). Salmeron et al. (22) assessed an association between the risk of non-insulin dependent diabetes mellitus (NIDDM) and dietary patterns featuring a high glycaemic load. A significant positive association was established between a diet characterised by an elevated glycaemic load in conjunction with a low cereal fibre content and the risk of NIDDM in women (relative risk [RR] = 2.50, 95% confidence interval [CI]: 1.14–5.51). It is worth noting that such a diet was also reflective of the consumption of refined dietary carbohydrates and this was stated explicitly by the researchers.

The study by Liu et al. (23) was one of the first in which a relationship between diet and chronic disease was determined. A validated food frequency questionnaire was administered to 75,521 female registered nurses with the objective of conducting a dietary assessment, including that of the consumption of refined grains. A significantly increased incidence of T2DM (according to higher Rutter scores) was reported in relation to the consumption of refined grains (RR = 1.31, 95% CI: 1.12–1.53, $p = 0.000$). The risk was shown to escalate in increasing quintiles of refined grain intake. Conversely, the risk was seen to decrease in those who consumed wholegrains (RR = 0.62, 95% CI: 0.53–0.71, $p = < 0.000$).

Van Dam et al. (24) found that the adoption of Western dietary patterns contributed to the increasing prevalence of T2DM in obese and physically inactive men. The dietary pattern followed was found to be the primary contributing factor to the risk of acquiring T2DM. A healthy dietary pattern, especially one involving the consumption of wholegrains, was found to be inversely associated with the risk of T2DM in extreme quintiles of wholegrain intake (multivariate RR = 0.77, 95% CI: 0.64–0.93, $p = < 0.001$). By contrast, the consumption of a Western-type diet, and refined grains specifically, was found to be positively associated with the risk of T2DM in extreme quintiles of intake (RR = 1.37, 95% CI: 1.13–1.66).

Hodge et al. (25) studied the impact of dietary glycaemic index (GI) on the incidence of T2DM in a mixed-gender cohort and established that starch and refined carbohydrates were connected to an increased incidence of the disease in the highest quartile of starch and carbohydrate intake (white bread: odds ratio [OR] = 1.37, 95% CI: 1.04–1.81, $p = < 0.001$; starch: OR = 1.47, 95% CI: 1.06–2.05). Nevertheless, the authors suggested that effecting a reduction in dietary GI, rather than carbohydrates, by substituting white bread with low-GI bread, might reduce T2DM risk.

Villegas et al. (26) researched the role of a diet that was characterised by a high GI and glycaemic load (GL) in relation to T2DM in their study on 64,227 Chinese women whose diet primarily consisted of staple foods, such as rice, noodles, steamed bread and bread. An association was identified between the consumption of a high-GI and -GL carbohydrate diet, especially rice, and the risk of T2DM (rice: RR = 1.78, 95% CI: 1.48–2.15; refined carbohydrates: RR = 1.28, 95% CI: 1.09–1.50).

Three prospective cohort studies on 39,765 men and 157,463 women in the USA were carried out by Sun et al. (27), who examined the association between the consumption of white and brown rice, and the risk of T2DM. A positive association was established between the intake of white rice in large amounts (≥ 5 servings/week vs. ≤ 1 serving/month) and the increased incidence of T2DM (pooled RR = 1.17, 95% CI: 1.02–1.36). By contrast, brown rice consumption was associated with a lower risk of T2DM (pooled RR = 0.89, 95% CI: 0.81–0.97) when comparing ≥ 2 servings/week vs. ≤ 1 serving/month.

Sun et al. (27) observed a 16% decrease in the risk of T2DM (95% CI: 9.00–21.00%) in all three cohorts when 50 g/day of white rice intake was replaced with an equal quantity of brown rice. Thus, T2DM was linked to the regular consumption of white rice, independent of ethnicity, lifestyle or even dietary risk factors for T2DM, and the recommendation was that carbohydrate intake should be in the form of wholegrains, rather than refined grains. These results are especially meaningful in the context of dietary choices and reducing T2DM risk.

Similarly, in a study set in Japan, Nanri et al. (28) observed a positive correlation between white rice intake and the risk of T2DM in both men and women. In particular, a strong association was identified between the increased consumption of white rice and risk in Japanese women (OR = 1.65, 95% CI: 1.06–2.57, $p = 0.005$) for the highest vs. the lowest quartiles in the multivariate-adjusted model. This association was also found in men, but it was not significant ($p = 0.080$). Thus, the link between dietary patterns and the risk of T2DM, although strong, has not been shown to be absolute. Additional factors may influence risk levels in significant ways.

Lastly, the study by Golozar et al. (29) investigated an association between white rice intake and the incidence of T2DM. The study setting was Iran (Tehran and Golestan) owing to the fact that “Iran is the thirteenth largest white rice consumer worldwide, with an average annual per capita consumption of approximately 34 kg” (29, p.2). Once again, a positive association between white rice intake and the risk of T2DM was identified in Tehran (OR = 1.01, 95% CI: 0.58–1.75) but no such association was observed in Golestan (29). In Tehran, the consumption of 250 g/day was associated with a significant incidence of T2DM which doubled with an intake of ≥ 250 g/day (OR = 2.08, 95% CI: 1.10–3.91). This could be elucidated by the fact that the daily intake of white rice is higher in Tehran compared to that in Golestan (median daily intake of 250 g vs. 120 g in Tehran and Golestan, respectively; $p \leq 0.001$) (25). Thus, a high white rice intake was linked to an increased risk of T2DM. Further research is warranted to explore the lack of a definitive association between lower white rice intake levels and T2DM.

The effect of refined carbohydrates on the incidence of T2DM remained evident, even when refined carbohydrates were consumed with other types of food (30-37).

Fung et al. (30) identified two dietary patterns; “prudent” and “Western”. According to these authors, a prudent diet is characterised by “a higher intake of fruit, vegetables, legumes, fish, poultry and wholegrains, while the Western diet comprises a higher intake of red and processed meats, sweets and desserts, French fries and refined grains”. The authors established a correlation between a Western diet and the risk of T2DM in the highest quintile of overall intake (RR = 1.49, 95% CI: 1.26–1.76, $p \leq 0.001$). Red and processed meats posed a particularly elevated risk. Having made an adjustment to the model by removing the consumption of red and processed meats; major contributors to the Western diet, the association between T2DM and the Western diet remained for the highest quintile of overall intake (RR = 1.28, 95% CI: 1.05-1.57, $p \leq 0.001$) (30).

A relationship between T2DM risk and a Western diet was also observed by Schulze et al. (31). They described similar dietary patterns and focused on the relationship between food types and chronic inflammation. The study found that dietary pattern that was high in “sugar-sweetened soft drinks, refined grains, soft diet drinks and processed meat, but low in wine, coffee, and cruciferous and yellow vegetables” was strongly associated with inflammatory markers and subsequently with an increased risk of T2DM (OR = 3.09, 95% CI: 1.99–4.79) for extreme (very high and very low) quintiles of intake in the multivariate-adjusted model (31, p.678). The authors concluded that this dietary pattern elevated the risk of T2DM through an increase in chronic inflammation.

Similarly, McNaughton et al. (32) sought to determine the relationship between T2DM risk and the consumption of a Western diet by assessing the relationship between food types and insulin resistance, and subsequently T2DM. The authors identified diets that were positively correlated with insulin resistance using a reduced-rank regression method. The identified dietary patterns were characterised by the “high consumption of low-calorie soft diet drinks, onions, sugar-sweetened beverages, burgers, sausages, crisps, snacks, white bread”; and by the consumption, to a lesser extent, of “whole meal bread, French dressing or vinaigrette, jam, and medium- to high-fibre breakfast cereals” (32, p.1345). A positive association was found between the diet and T2DM in the high quintile intake (HR = 2.95, 95% CI: 2.19–3.97) (32). Thus, following this dietary pattern was considered to be a substantial risk for the development of T2DM.

Nettleton et al. (33) explored the association between dietary patterns and type 2 diabetes incidence in 5,011 multi-ethnic study subjects (African, Caucasian, Chinese and Hispanic adults). The diets characterized by high consumption of “beans, tomatoes and refined grains” found to be linked to the increased incidence of type 2 diabetes among study groups (HR = 1.23, 95% CI :0.85–1.78, $p = 0.004$) (33). The incidence of T2DM was 11.3% among Hispanics, 9.5% in Africans, 7.5% in Chinese and 6.3% among Caucasian individuals (33). In contrast, a wholegrain and fruit-containing diet was associated with a low risk of T2DM (HR = 0.66, 95% CI :0.47–0.93, $p = 0.005$) (33). This supports the authors’ theory that a combination of foods or specific food groups contribute to T2DM risk, rather than the individual foods themselves (33). The findings of Nettleton’s study suggest that particular groups may be at greater risk of T2DM based on their dietary patterns. Such risks may be cultural rather than regional, especially as diversity and migration patterns have begun to reshape the geographical relationship between region and culture. Additionally, while the researchers found a correlation between diet type and T2DM risk, as well that between race or ethnicity and diet type, they did not find an independent relationship between race or ethnicity and T2DM, suggestive that such risk is a function of dietary choice, which may be influenced by culture, but not by a biological factor.

Brunner et al. (34) found that dietary patterns have a direct bearing on many diseases, including T2DM. The researchers used a Cluster analysis method to determine the frequent dietary patterns consumed by healthy adults, including diets characterised by “high consumption of fruit and vegetables, polyunsaturated oils, high-fibre bread and breakfast cereals, and by a low intake of red meats, saturated fats and refined carbohydrate foods” (34, p.1415). The authors found that the incidence of T2DM was lower in those engaged in healthy eating (HR = 0.69, 95% CI: 0.52–0.92). Thus, healthy eating can reduce the risk of T2DM.

Denova-Gutierrez et al. (35) examined three dietary patterns; prudent, Western, and high protein or fat, in an urban Mexican population in relation to metabolic syndrome (MetS), an important indicator of T2DM risk. It was reported that the Mexican population are at increased risk of MetS and T2DM (35). The authors described the Western diet as comprising the high consumption of pastries, refined cereal, corn tortillas and soft drinks, thereby associated with a higher prevalence of high fasting glucose (OR = 1.67, 95% CI: 1.36–2.06) for the highest tertile (35). The authors conclude that following a Western diet can lead to MetS and subsequently to T2DM (35).

Similarly, Yu et al. (36, p.1137) found that a Western diet, typified by the “high consumption of red and processed meat, fried food, high-fat dairy products, refined grains, sweets and desserts” was associated with an increased risk of T2DM (OR = 1.39, 95% CI: 1.04–1.84). Potential contributing factors, such as age, activity levels and other demographic elements, were taken into account in this study set in Hong Kong. It is suggested in this work that T2DM risk is independent of race and ethnicity (36). Most studies to date have focused on Caucasians and a similar relationship between dietary patterns and the risk of acquiring T2DM has been established (36).

Malik et al (37) investigated the association between dietary patterns in the period of adolescence and the risk of T2DM later in life. In this study, the Western pattern of eating involving “a high intake of desserts, snacks, processed meat, red meat, French fries and refined grains; and a low consumption of vegetables, fruit and fish was positively associated with a 29% higher risk of type 2 diabetes developing in women (RR = 1.29, 95% CI: 1.00–1.66; $p = 0.040$) (37, p.12). The authors also demonstrated a link between weight gain and subsequent T2DM risk beginning in adolescence (37). The authors reported that unhealthy eating patterns tend to continue into adulthood and pose health risks associated with weight gain (37).

Quantitative Synthesis

In the meta-analysis, data were used from 8 prospective cohort studies, including 13 datasets, containing a total sample of 487,719 male and female participants aged 20 years and above. In the systematic review, the random effects model used for the included studies indicated a positive link between refined carbohydrate consumption and the increased incidence of T2DM (pooled relative risk [RR] = 1.33; 95% confidence interval [CI] = 1.18–1.48), with moderate heterogeneity ($I^2 = 57\%$) of a non-practical type (supplementary Fig. 2). Asian populations were found to be at a higher risk of T2DM than those in the West.

After conducting a subgroup analysis, there was a relatively stronger association amongst Asians (RR = 1.51; 95% CI = 1.22–1.86) compared to Western populations (RR = 1.22; 95% CI = 1.10–1.37; see supplementary Fig. 3). Studies with a lower sample size may have biased this association; therefore, secondary analyses were conducted that excluded such studies (Golozar et al’s and Salmeron et al’s studies; see supplementary Fig. 4). There was slight decrease in the relative risk (pooled RR = 1.29; 95% CI = 1.16–1.44), but the association between the consumption of refined carbohydrates and incidence of T2DM was still significant, which confirmed that the results of those two studies did not drive the pooled effect size.

Publication Bias

A gross asymmetry can be seen in the *Doi* and funnel plots with a paucity of higher effect studies (supplementary Fig. 5). This asymmetry is likely due to the effects of small studies or to the heterogeneity across the studies included.

Discussion

The findings from this systematic review and meta-analysis study showed a significant association between the consumption of diets high in refined carbohydrates and an increased incidence of T2DM. However, Asians were found to be at a higher risk of T2DM compared with the Western population. The relatively higher risk among Asians could be due to the fact that refined carbohydrates, particularly white rice, are dietary staples among the Asian population [35]. For each serving of refined carbohydrates per day, the risk of T2DM increased by 33% in the overall population.

This study's findings are based on prospective cohort studies and a more rigorous methodology that involved the full adjustment of all confounders. After bias adjustment, the strong association between the high consumption of refined carbohydrates and the risk of T2DM remained. This study's results also concur with the Hu et al's systematic review and meta-analysis that examined the association of refined carbohydrates, more specifically white rice, with the incidence of T2DM (20).

However, the present study found an even stronger association than that previous study (RR:1.11, 95% CI: 1.08–1.14). Furthermore, the inclusion of 8 studies in the meta-analysis compare to 4 studies by Hu et al which make it more strength and reliable.

Results in Relation to Other Studies

Several potential mechanisms could explain the relationship between the consumption of refined carbohydrates and the risk of T2DM. Refined carbohydrates, mainly white rice, are the major contributor of the glycaemic load (26, 38). Several studies support the hypothesis of the association between glycaemic load and T2DM development. For example, in Western populations, a meta-analysis of cohort studies confirmed the association between a diet with a high glycaemic load and the increased incidence of T2DM (39). Similarly, several studies conducted among the Asian population found a positive association between dietary glycaemic load and T2DM incidence (26, 28, 38). Nonetheless, the association between refined carbohydrate intake and the risk of developing T2DM may occur through other mechanisms, including chronic inflammation.

Schulze et al. (31) confirmed this hypothesis and found a strong association between refined carbohydrate dietary patterns and inflammatory markers and the subsequent increased risk of T2DM. The authors concluded that this dietary pattern elevated the risk of T2DM through increased chronic inflammation (31). Additionally, the association between the consumption of refined carbohydrates and the risk of T2DM could be due to insulin resistance. McNaughton et al. (32) confirmed this hypothesis, finding that refined carbohydrate diets were positively correlated with insulin resistance and, subsequently, T2DM.

In refined carbohydrates, fibre and valuable nutrients, such as vitamins and magnesium, are extracted during the refining process (13). These nutrients are found to be associated with a reduced risk of T2DM in many studies (22,40-41). Thus, the consumption of refined carbohydrates could lead to the increased incidence of T2DM due to the low intake of these beneficial nutrients.

Strengths and limitations

Among the studies examined, a common limitation was the self-reporting of food intake. While it is not expected that participants who voluntarily take part in a study will deliberately provide inaccurate results, it is possible for participants to inadvertently record and provide inaccurate information, thus compromising the results of the study. Another common limitation was the subjective nature of food groupings. Although many studies had similar definitions of a Western diet and a healthy or "prudent" diet, there existed some differences, and some studies devised additional dietary patterns against which these groups were compared.

Although there was a significant positive association among the included studies in the meta-analysis (pooled RR = 1.32, 95% CI [1.18, 1.48]), a significant heterogeneity was detected ($I^2 = 59\%$; $p < 0.05$), a heterogeneity that can be explained by many factors, firstly, differences in the types and doses of exposure among the studies, and the difference in other factors, such as diet, body condition, age and sample size; secondly, the included studies performed in a different country and setting; and thirdly, the difference in the method of outcome measurement.

This study has many strengths, which includes being the first study to examine the effect of refined carbohydrate intake on the incidence of T2DM through a systematic review and meta-analysis design using fully adjusted models. Furthermore, the included studies have large sample sizes and long follow-up periods and involve populations from Western and Asian countries.

Conclusion

From the systematic review and meta-analysis of the prospective cohort studies suggest that the high consumption of refined carbohydrate predict the development of T2DM. The variety of studies considered, and their various contexts means that this finding is conclusive. Furthermore, as dietary guidelines strive to reflect optimal dietary health information, this finding should be further incorporated into guidelines.

Additional primary research and review of studies is necessary to better understand this correlation. Particularly, the intersection between food groups and dietary patterns, as opposed to individual foods, must further be explored in order to thoroughly comprehend the significance of refined carbohydrates in a variety of dietary contexts.

With the influence of globalization, the spread of Western eating patterns and resulting increased T2DM risk is expected to grow worldwide. However, T2DM risk is also observed in many nations where the primary cultural diet contains refined carbohydrates as a primary energy source, particularly white rice. Therefore, while the Western diet has been found to influence this disease risk, improved information about their risk and access to this information is needed worldwide.

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Acknowledgements I would like to thank Dr Abdullah Al Mamun for his time, and would like to thank my wife Arwa Aldali, my parents and Mr. Mohammad Ali Hamzi for their ongoing assistance and supports.

Tables

Table 1 shows the results of the risk of bias of included studies using ROBINS-I assessment tool for cohort-type studies:

Study	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported results	Overall judgment
Salmeron et al1997	MROB	MROB	LROB	LROB	LROB	LROB	MROB	7
Liu et al2000	MROB	LROB	LROB	LROB	LROB	LROB	MROB	7
Van Dam et al2002	MROB	LROB	LROB	LROB	LROB	LROB	MROB	7
Hodge et al2004	MROB	LROB	LROB	LROB	LROB	LROB	MROB	7
Villegas et al2007	MROB	LROB	LROB	LROB	LROB	LROB	MROB	7
Nanrietet al2010	MROB	LROB	LROB	LROB	LROB	LROB	MROB	7
Sun et al2010	MROB	LROB	LROB	LROB	LROB	LROB	MROB	7
Golozaretet al2017	MROB	LROB	LROB	LROB	LROB	LROB	MROB	7
Fung et al2004	MROB	LROB	LROB	LROB	LROB	LROB	MROB	7
Schulze et al2005	MROB	LROB	LROB	LROB	LROB	SROB	MROB	6
McNaughton et al2008	MROB	LROB	LROB	LROB	LROB	LROB	MROB	7
Nettleton et al2008	MROB	LROB	LROB	NI	NI	LROB	MROB	5
Brunner et al2008	MROB	LROB	LROB	MROB	LROB	LROB	MROB	7
Denova-Gutiérrez et al2010	MROB	LROB	LROB	NI	NI	LROB	MROB	5
Yu et al2011	MROB	LROB	LROB	MROB	LROB	LROB	MROB	7
Maliket al2012	MROB	LROB	LROB	MROB	LROB	LROB	MROB	7

LROB: LOW RISK OF BIAS

MROB: MODERATE RISK OF BIAS;

SROB: SERIOUS RISK OF BIAS

NI: NO INFORMATION

Table 2| Characteristics of prospective studies of pure refined carbohydrate intake in relation to incident type 2 diabetes: participants, follow-up, and exposures

Author	Study participants	Follow-up period and person time	Exposure and assessment method
Salmeron et al1997	Total no. of participants: 65,173 Gender: females No. of Cases:915 cases Age: 40-65years Country: United States	Follow-up:6 years person-years: NA	Exposure: Refined carbohydrate diets “high glycemic load and low cereal fibre”. Assessment method: FFQ consisting of 134 food items.
Liu et al2000	Totalno. of participants: 75,521 Gender: females No. of cases: 1879 cases Age: 38-63 years Country: United States	Follow-up: 10 years Person-years: 722,419 person-years	Exposure: Refined grain Assessment method: FFQ consisting of 126 food items.
Van Dam et al2002	Totalno. of participants:42,504 Gender: males No. of cases:1,321 cases Age: 40 -75 years Country: US	Follow-up: 12 years Person years: 466,508 person-years	Exposure: Consumptionof refined grains. Assessment method: FFQ consisting of 131 food items.
Hodge et al2004	Total no. of participants: 31,641 No. of cases: 365 cases Gender: males and females Age:40-69 years Country: Australia	Follow-up: 4 years Person years:129,190 person-years	Exposure: White bread intake Assessment method: FFQ consisting of 121 food items.
Hodge et al2004	Same as above	Same as above	Exposure: Intake of starch Assessment method: FFQ consisting of 121 food items.
Villegas et al2007 (I)	Total no. of participants:64,191 Gender: female No. of cases=1,608 cases Age: 40-70 years Country: China	Follow-up: 5 years Person years: 297,755 person-years	Exposure: White rice. Assessment method: FFQ consisting of 77 food items.
Villegas et al2007 (II)	Same as above	Same as above	Exposure: Refinedcarbohydrates Assessment method: Same as above
Nanri et al2010	Total no. of participants: 25,666 Gender: males No. of cases:625 cases Age 45-75 years Country: Japan	Follow-up: 5 years Personyears:128,330 person-years	Exposure: White rice Assessment method: FFQ consisting of 147 food items.
Nanri et al2010	Total no. of participants: 33,622 Gender: females No. of cases: 478 cases Age: 45-75 years Country: Japan	Follow-up: 5 years Person years:168,110 person-years	Same as above
Sun et al2010 (HPFS)	Total no. of participants: 39,765 Gender: males No. of cases: 2,648 cases Age:32-87years Country: United States	Follow-up: 20 years Person years:702,920 person-years	Exposure: Cooked white rice Assessment method: FFQ consisting of 116-131 food items.
Sun et al2010 (NHS I)	No. of participants:69,120 Gender: females No. of cases: 5,500 cases Age:37-65years Country: United States	Follow-up: 22 years Person years: 1,404,373 person-years	Same as above

Sun et al2010 (NHS II)	Total no. of participants: 88,343 Gender: females No. of cases: 2,359 cases Age: 26-45 years Country: United States	Follow-up 14 years Person years: 1,210,903 person-years	Same as above
Golozaret al2017	Total no. of participants: 2,173 Gender: male and female; No. of cases= 81 cases Age: 20 years and above Country: Iran	Follow-up: 3 yearsperson years: NA	Exposure: Cooked white rice.Assessment method: FFQ consisting of 121 food items.

FFQ: food frequency questionnaire

NA: not available

Table 3 | Characteristics of prospective studies of pure refined carbohydrates intake in relation to incident type 2 diabetes: outcomes, relative risks, and covariates

Author	Study outcome and ascertainment	Comparison categories and corresponding Covariates in fully adjusted model relative risk (95% CI)	Covariates in fully adjusted model
Salmeron et al1997	Type2diabetes identified through self-reports and confirmed by validatedsupplementary questionnaire; National Diabetes Data Group (before 1998) and American Diabetes Association 1997 (after 1998) diagnostic criteria	2.50(1.14-5.51)	Age; ethnicity (white, African American, Hispanic, and Asian); body mass index; smoking status; alcohol intake; multivitamin use; physical activity; family history of diabetes; total energy; intakes of red meat, fruits and vegetables, whole grains, and coffee
Liu et al2000	Type 2 diabetes identified through self-reports and confirmed by validated supplementary questionnaire; National Diabetes Data Group (before 1997) and American Diabetes Association 1997 (after 1997) diagnostic criteria	Q1: 1.0 (referent) Q2: 1.09 (0.94, 1.26) Q3: 1.01 (0.86, 1.17) Q4: 1.09 (0.92, 1.27) Q5: 1.11 (0.94, 1.30)	Adjustment for age, BMI, cigarette smoking, alcohol intake, history of diabetes in first-degree relative, use of multivitamins, use of vitamin E supplements, physical activity, and total energy intake.
Van Dam et al2002	Type 2 diabetes identified through a validated supplementary questionnaire and confirm by World Health Organization criteria 1985	1.32 (1.09 ,1.60)	Adjusted for age, body mass index ,total energy intake (quintiles), and time period , physical activity), cigarette smoking, alcohol consumption, ancestry (Northern European, Southern European, or other), hypercholesterolemia, hypertension, and family history of type 2 diabetes mellitus.

Hodge et al2004	Type 2 diabetes identified through self-reports; 83% (303/365) cases confirmed by medical practitioners	Q1: 1.0 (referent) Q2:0.66 (0.44–0.99) Q3: 0.95 (0.67–1.35) Q4: 1.13 (0.86–1.50)	Age, sex, country of birth, physical activity, family history of diabetes, alcohol, total energy intake, education, 5 year weight change, body mass index, and waist: hip ratio
	Same as above	1.52 (1.09–2.11)	Same as above
Villegas et al2007 (I)	Type 2 diabetes identified through self-reports; American Diabetes Association 1997 diagnostic criteria	Q1:1.0 (referent) Q2: 1.04 (0.86 to 1.25) Q3: 1.29 (1.08 to 1.54) Q4: 1.78 (1.48 to 2.15)	Age, body mass index, waist: hip ratio, smoking status, alcohol consumption, physical activity, income level, education level, occupation, diagnosis of hypertension, and total energy
Villegas et al2007) II	Same as above	1.28(1.09-1.50)	Same as above
Nanri et al2010 (males)	Type 2 diabetes identified through self-reports and confirmed by medical records; Japan Diabetes Society 1982 diagnostic criteria	Q1: 1.00 (referent) Q2: 1.24 (1.00 to 1.55) Q3: 1.25 (0.93 to 1.67) Q4: 1.19 (0.85 to 1.68)	Age; study area; smoking status; alcohol consumption; family history of diabetes mellitus; total physical activity; history of hypertension; occupation; total energy intake; intakes of calcium, magnesium, fibre, fruit, vegetables, fish, coffee, bread, and noodles; and body mass index
Nanri et al2010 (females)	Same as above	Q1: 1.00 (referent) Q2: 1.15 (0.85 to 1.55) Q3: 1.48 (1.08 to 2.02) Q4: 1.65 (1.06 to 2.57)	Same as above
Sun et al2010 (HPFS)	Type 2 diabetes identified through self-reports and confirmed by validated supplementary questionnaire; National Diabetes Data Group (before 1998) and American Diabetes Association 1997 (after 1998) diagnostic criteria	Q1: 1.0 (referent); Q2: 1.09 (0.96 to 1.24) Q3: 1.07 (0.93 to 1.23) Q4: 1.30 (1.12 to 1.50) Q5: 1.02 (0.77 to 1.34)	Age; ethnicity (white, African American, Hispanic, and Asian); body mass index; smoking status; alcohol intake; multivitamin use; physical activity; family history of diabetes; total energy; intakes of red meat, fruits and vegetables, whole grains, and coffee
Sun et al. (2010) NHSI	Same as above	Q1: 1.0 (referent) Q2: 1.00 (0.90 to 1.11) Q3: 1.07 (0.96 to 1.20) Q4: 1.09 (0.97 to 1.23) Q5: 1.11 (0.87 to 1.43)	Same as above, plus further adjustments for postmenopausal status, hormone use, and oral contraceptive use
Sun et al2010 (NHS II)	Same as above	Q1: 1.0 (referent) Q2: 0.93 (0.81 to 1.07) Q3: 0.94 (0.81 to 1.10) Q4: 0.95 (0.81 to 1.11) Q5: 1.40 (1.09 to 1.80)	Same as above

Golozaret al2017	Type 2 diabetes identified through self-reports; American Diabetes Association 1997 diagnostic criteria	Q1: 1.0 (referent) Q2: 1.08 (0.61, 1.92) Q3: 2.28 (1.19, 4.37)	Age, sex, race/ethnicity, wealth score, education, marital status, employment status, opium, alcohol, occupational, physical activity, smoking, daily meat intake and daily calorie intake and body mass index.
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Table 4: Characteristics of prospective studies of refined carbohydrate intake with other types of food in relation to incident type 2 diabetes: participants, follow-up, and exposures

Author	Study participants	Follow-up period and person time	Exposure and assessment method
Fung et al2004	Total no. of participants:121,700 Gender: females No. of cases:2,699 cases Age: 30-55 years Country: United States	Follow-up:14 years person years: NA	Exposure: refined carbohydrates in form of sweets, desserts and refined grains as apart from Western pattern included higher intakes of red and processed meats, sweets and desserts, French fries, and refined grains Assessment method: FFQ consisting of 116 food items.
Schulze et al2005 (NHS)	Total no. of cases: 35,340 Gender: females No. of cases:1,517 cases Age:30 –55 years Country: US	Follow-up: 10years person years: 458,991 person-years	Exposure: The pattern represented a diet relatively high in sugar-sweetened soft drinks, refined grains, diet soft drinks, processed meat, and “other vegetables” (other than yellow, cruciferous, and green leafy vegetables, tomatoes, and legumes) but low in wine, coffee, cruciferous vegetables, and yellow vegetables Assessment method: FFQ consisting of 39 food items.
Schulze et al2005 (NHS-II)	Total no. of participants: 89,311 No. of cases:724 cases Gender: female Age: 24 – 44 years Country: US	Follow-up: 6 years person years: 701,155 person-years	Same as above
McNaughton et al2008	Total no. of participants: 7,339 Gender: Males and females No. of cases:264 cases Age: 39–63 years Country: United Kingdom	Follow-up: 11 years person years: NA	Exposure: a dietary pattern characterized by high consumption of low- calorie/diet soft drinks, onions, sugar-sweetened beverages, burgers and sausages, crisps and other snacks, and white bread and low consumption of medium-/high-fiber breakfast cereals, jam, Frenchdressing/vinaigrette, and whole meal bread Assessment method: FFQ consisting of 127 food items.
Nettleton et al2008	Total No. of participants: 5,011 Gender: males and females No. of cases:411 cases Age: 45–84 years Country: US	Follow-up: 5 years person years: NA	Exposure: “Beans, tomatoes, and refined grains” Assessment method: FFQ consisting of 121 food items.

Brunner et al2008	Total no. of participants: 7,731 Gender: males and females No. of cases:410 cases Age: mean age of 50 years Country: United Kingdom	Follow-up: 15 years Person years: 106,633 person-years	Exposure: consumption of Sweet (high consumption of biscuits, cakes, meat, sausages and savory pies, white bread, full-cream milk, butter, and wine and beer) Assessment method: FFQ consisting of 127 food items.
Denova-Gutiérrez et al 2010	Total no. of participants:5,240 Gender: males and females No. of cases: NA Age:20–70 years Country: Mexico	Follow-up: 2 years person years: NA	Exposure: Intake of Western dietary pattern (pastries, refined cereals, corn tortillas, and soft drinks) Assessment method: FFQ consisting of 116 food items.
Yu et al2011	Total no. of participants: 1,010 No. of cases: 74 cases Gender: males and females Age: 25–74 years Country: China	Follow-up:9-14 years person years: NA	Exposure: Diet rich in refined grains Assessment method: FFQ consisting of 266 food items.
Malik et al2012	Total no. of participants: 37,038 Gender: females No. of cases:550 cases Age: 24–44 years Country: US	Follow-up: 7 years person years: 290,703 person-years	Exposure: The Western pattern characterized by desserts, processed meats, and refined grains. Assessment method: HSFFQ consisting of 124 food items.

Table 5 | Characteristics of prospective studies of refined carbohydrate intake with other types of food intake in relation to incident type 2 diabetes: outcomes, relative risks, and covariates

Author	Study outcome and ascertainment	Comparison categories and corresponding Covariates in fully adjusted model relative risk (95% CI)	Covariates in fully adjusted model
Fung et al2004	Type 2 diabetes identified through self-reports and confirmed by validated supplementary questionnaire; National Diabetes Data Group and medical record	Q1: 1.0 (referent) Q2: 1.21 (1.05, 1.38) Q3: 1.35 (1.17-1.56) Q4:1.33 (1.14-1.55) Q5: 1.49 (1.26-1.76)	Adjusted for age, family history of diabetes, history of hypercholesterolemia, smoking, menopausal status, calories, history of hypertension, physical activity, alcohol intake, BMI (continuous and quadratic), and missing food frequency questionnaire.
Schulze et al2005 (NHS)	Type 2 diabetes identified through self-reports and confirmed by validated supplementary questionnaire; medical record,National Diabetes Data Group(before 1998) and American Diabetes Association (after 1998) diagnostic criteria	Q1: 1.0 (referent) Q2: 1.50 (1.21, 1.86) Q3: 1.61 (1.31,1.99) Q4: 1.96 (1.61, 2.40) Q5: 2.56 (2.10, 3.12)	Adjusted for age, BMI, physical activity, family history of diabetes, smoking, postmenopausal hormone use, energy intake.

Schulze et al2005 (NHSII)	Same as above	Q1: 1.0 (referent) Q2: 1.92 (1.39, 2.64) Q3: 1.64 (1.18, 2.26) Q4: 2.10 (1.55, 2.86) Q5: 2.93 (2.18, 3.92)	Same as above
McNaughton et al2008	Type 2 diabetes identified through self-report and confirmed by WHO1999 diagnostic criteria	Q1: 1.0 (referent) Q2: 1.24 (0.90–1.73) Q3: 1.48 (1.08–2.02) Q4: 1.51 (1.10–2)	Adjusted for age, sex, and energy misreporting, ethnicity, employment grade, health behaviors (smoking, alcohol use, and physical activity), blood pressure and BMI
Nettleton et al2008	Type 2 diabetes identified through self-reported, fasting glucose >or =126g/dl, or use of antidiabetic medication.	Q1: 1.0 (referent) Q2: 0.99 (0.71–1.38) Q3: 1.09 (0.78–1.51) Q4: 1.09 (0.78–1.52) Q5: 1.28 (0.88–1.84)	Adjusted for energy intake study center (California, Minnesota, Maryland, New York, Illinois, or NorthCarolina), age, sex, and race/ethnicity (white, black, Chinese, or Hispanic), education, physical activity, smoking and waist circumference
Brunner et al2008	Incident cases of diabetes were identified by self-report of doctor's diagnosis and diabetic medication and 2-h 75-g oral- glucose-tolerance test at phases 3, 5, and 7 according to the 1999 World Health Organization classification.	1.16 (0.83, 1.61)	Adjusted for employment grade, smoking, physical activity, obesity, waist circumference, and biomedical risk factors
Denova-Gutiérrezetal2010	Plasma glucose measured with the enzymatic colorimetric method by using glucose oxidize,	T1: 1.0 T2: 1.21 (0.98–1.49) T3: 1.71 (1.40–2.10)	Adjusted for age, gender, cigarette smoking , physical activity , weight change within last year (, place of residence (Mexico State or Morelos State), estrogen use , menopausal status , and energy intake (kJ/d).
Yu et al2011	Type 2 diabetes identified through The WHO Study Group (1998) criteria for glucose intolerance and diabetes.	1.02(0.80, 1.29)	Adjusted for sex, age, BMI, WHR, current smoking status, alcohol intake, participation inexercise/sports and family history of diabetes.
Malik et al2012	Type 2 diabetes identified through self-reports and confirmed by validated supplementaryquestionnaire; American Diabetes Association 1997 diagnostic criteria and medical record.	Q1: 1.0 (referent) Q2: 1.13 (0.85–1.49) Q3: 1.12 (0.85–1.47) Q4: 1.30 (1.00–1.68) Q5: 1.39 (1.08–1.78)	Adjusted for age, BMI at age 18 years, and high school total calories. high school smoking and physical activity, adult risk factors: physical activity, family history of diabetes, smoking status, postmenopausal hormone use, oral contraceptive use, total energy intake, and alcohol.

Figures

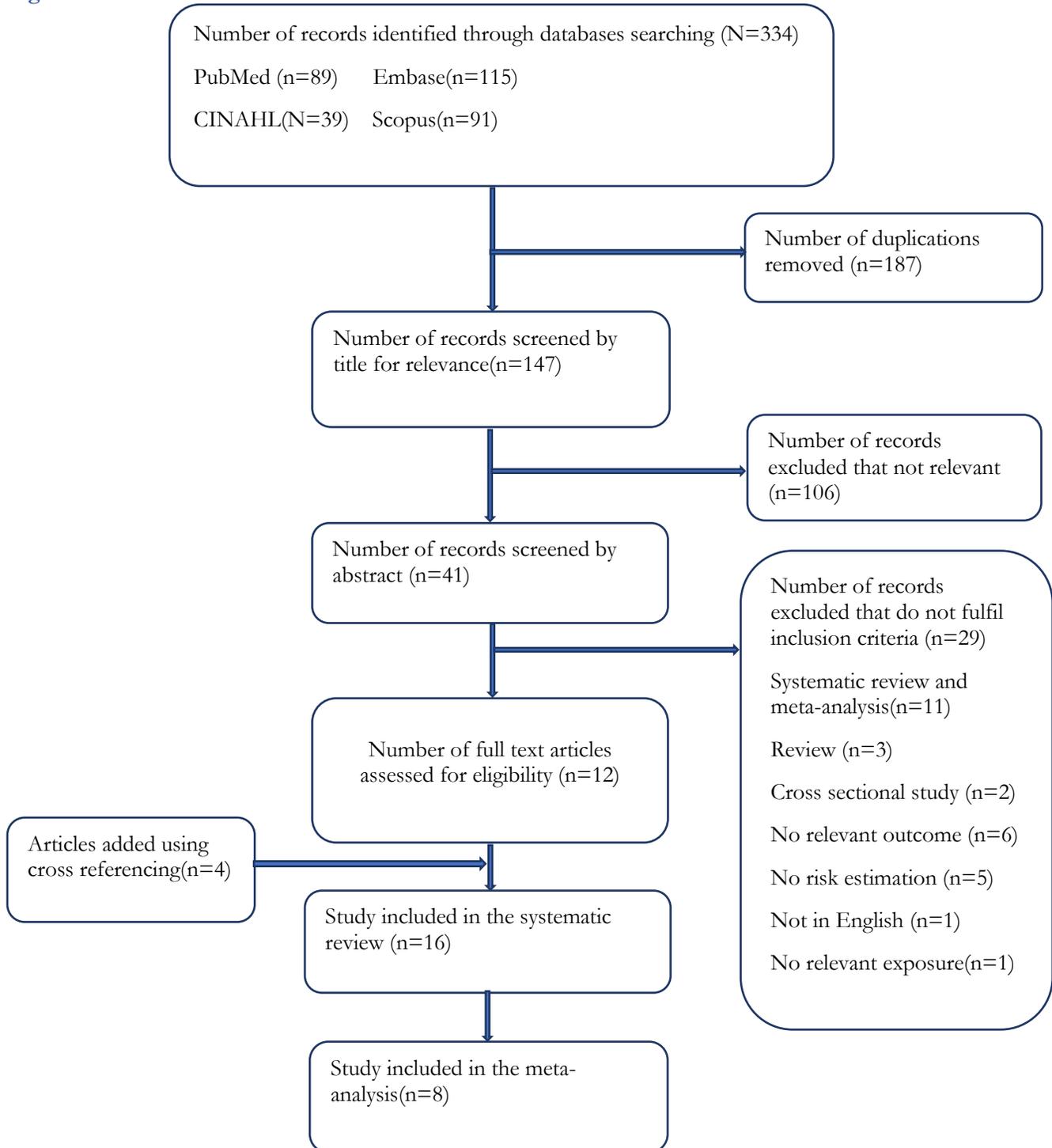


Figure 1: Literature search and study selection (based on PRISMA reporting)

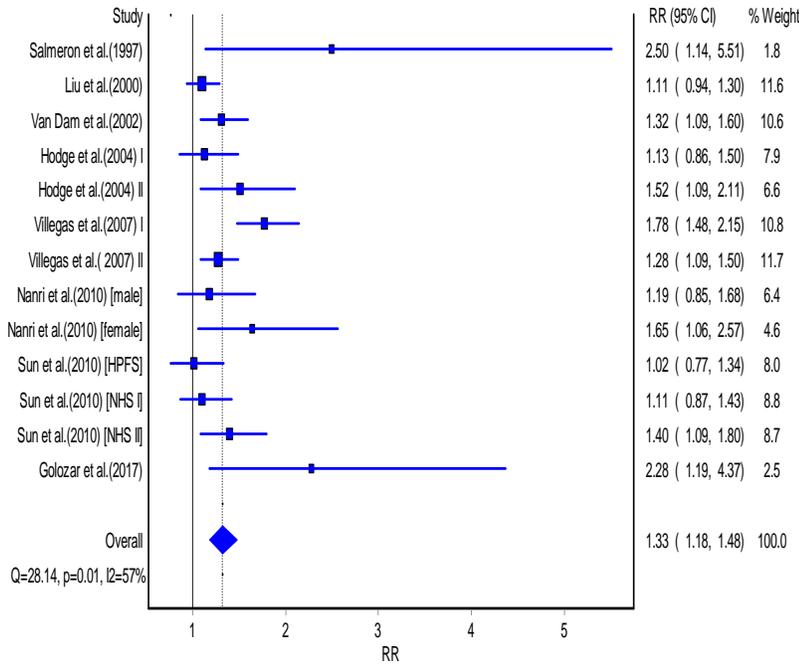


Figure 2: forest plot of random effect model examines the effect of refined carbohydrates intake on incidence of T2DM

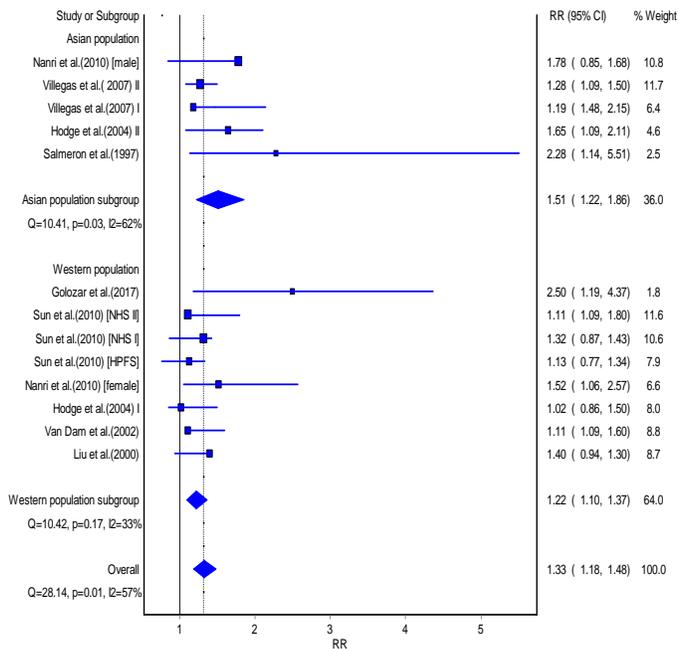


Figure 3: forest plot of random effect model examines the effect of refined carbohydrates intake on incidence of T2DM using subgroups analysis

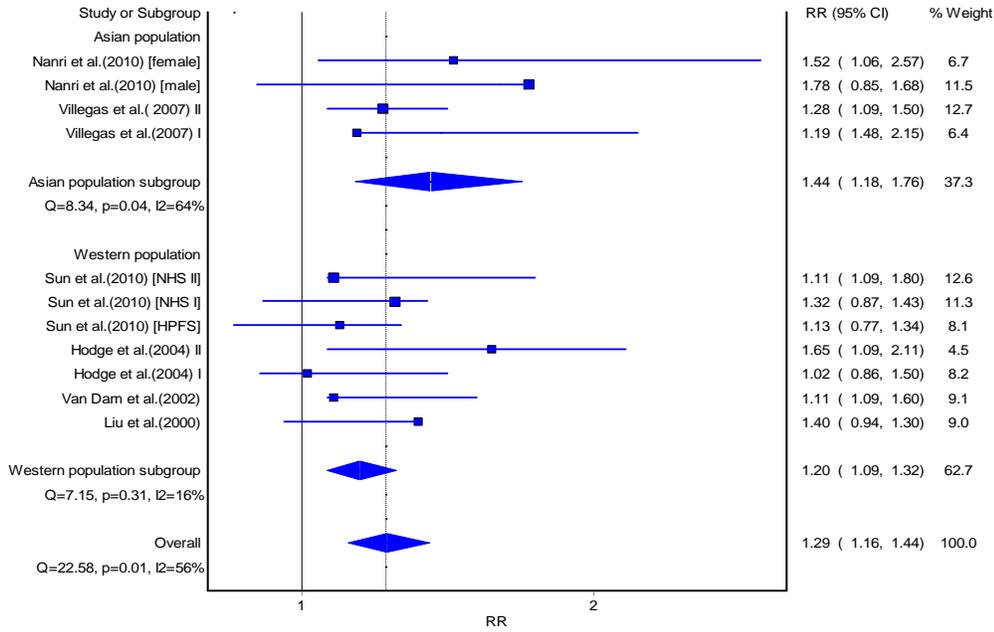


Figure 4: Forest plot of random effect model after exclusion of Salmeron et al’s 1997 and Golozaret al’s 2017 studies

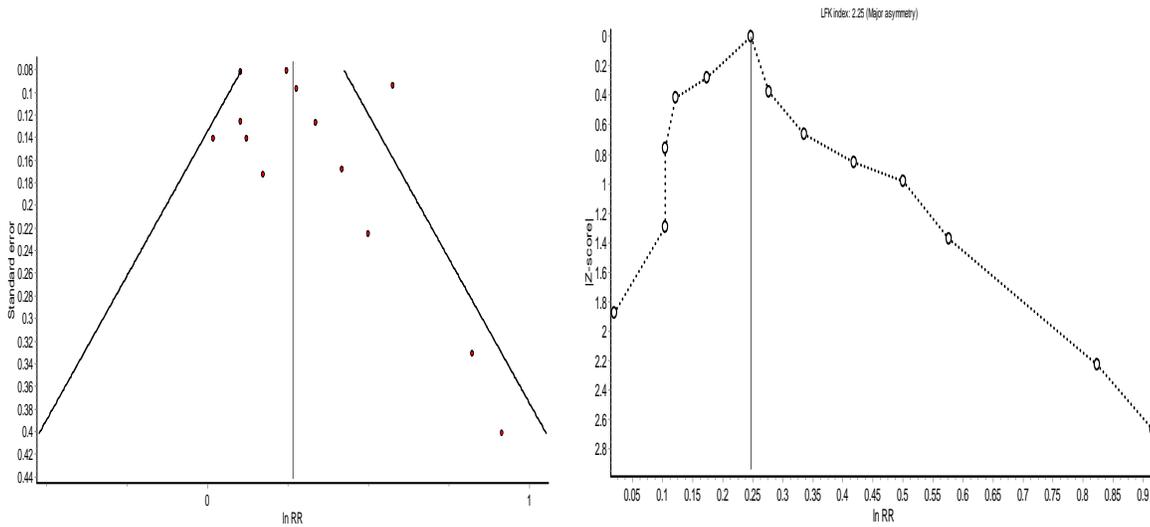


Figure 5: Funnel plot(left) and Doi plot (right)suggest gross publication bias favoring positive effects.