

Higher intake of fruits, vegetables or their fiber reduces the risk of type 2 diabetes: A meta-analysis

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ABSTRACT

Aims/Introduction: Some previous studies reported no significant association of consuming fruit or vegetables, or fruit and vegetables combined, with type 2 diabetes. Others reported that only a greater intake of green leafy vegetables reduced the risk of type 2 diabetes. To further investigate the relationship between them, we carried out a meta-analysis to estimate the independent effects of the intake of fruit, vegetables and fiber on the risk of type 2 diabetes.

Materials and Methods: Searches of MEDLINE and EMBASE for reports of prospective cohort studies published from 1 January 1966 to 21 July 2014 were carried out, checking reference lists, hand-searching journals and contacting experts.

Results: The primary analysis included a total of 23 (11 + 12) articles. The pooled maximum-adjusted relative risk of type 2 diabetes for the highest intake vs the lowest intake were 0.91 (95% confidence interval [CI] 0.87–0.96) for total fruits, 0.75 (95% CI 0.66–0.84) for blueberries, 0.87 (95% CI 0.81–0.93) for green leafy vegetables, 0.72 (95% CI 0.57–0.90) for yellow vegetables, 0.82 (95% CI 0.67–0.99) for cruciferous vegetables and 0.93 (95% CI 0.88–0.99) for fruit fiber in these high-quality studies in which scores were seven or greater, and 0.87 (95% CI 0.80–0.94) for vegetable fiber in studies with a follow-up period of 10 years or more.

Conclusions: A higher intake of fruit, especially berries, and green leafy vegetables, yellow vegetables, cruciferous vegetables or their fiber is associated with a lower risk of type 2 diabetes.

INTRODUCTION

Diabetes has become a serious and increasing global health burden. An estimated 382 million people worldwide were affected by diabetes in 2013, and this number is expected to rise to 592 million by 2035¹. Consequently, diabetes is predicted to become the major cause of death and disability in the world by 2030^{2,3}. Primary prevention of diabetes is clearly a major public health priority. Type 2 diabetes makes up >90% of all diabetes cases. Although the development of type 2 diabetes is complicated, dietary factors could play an important role in its pathogenesis. Dietary modification has been shown to delay or prevent the development of type 2 diabetes^{4,5}.

Intake of sufficient amounts of fruit and vegetables is recommended as a part of a healthy diet, though the individual contribution from different food sources remains largely unknown. Increasing fruit and vegetable consumption could reduce the risk of many chronic diseases, including cardiovascular diseases, cancers, stroke and type 2 diabetes^{6–12}. These foods contain considerable protective constituents, including potassium, folate, vitamins, fiber, anti-oxidant content and phenolic compounds^{13–15}. However, the mechanisms by which fruit and vegetables reduce the risk of type 2 diabetes have not been precisely elucidated. To date, many epidemiological studies have examined the association between type 2 diabetes risk and fruit and vegetable intake^{12,16–28}. Findings from these studies have been surprisingly inconsistent. Some studies suggested a higher

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intake of fruit and vegetables, especially the intake of berries and green leafy vegetables, has the inverse associations with the risk of type 2 diabetes^{12,16–22}. Some studies have not shown such associations with the intake of fruit or vegetables^{23–28}. The discrepancy of these results could arise from the complicity of the disease itself and functional heterogeneity of the biological responses to various foods.

In the present study, we sought to carry out a meta-analysis to investigate the relationship between fruit or vegetable intake, and the incidence of type 2 diabetes. Notably, several previously carried out meta-analyses used relatively limited pooled results around 2008. They primarily focused on the relationship between the intake of fruit or vegetables and type 2 diabetes^{11,16,20,27–30}. They reported no significant association of fruit or vegetables, or fruit and vegetables combined with type 2 diabetes^{11,29,30}. Only a greater intake of green leafy vegetables reduced the risk of type 2 diabetes^{11,29}. Presently, we collected a more up-to-date and large number of prospective cohort relevant studies in the present meta-analysis. Additionally, we included the relationship between the intake of fruit and vegetable fiber, and the risk of type 2 diabetes.

MATERIALS AND METHODS

Search Strategy

Two authors (Ping-Yu Wang and Jun-Chao Fang) carried out the literature search. We systematically searched MEDLINE and EMBASE for studies published from 1 January 1966 to 21 July 2014. To ensure a broad range of relative issues, the search strategy included a combined text and the medical subject headings (type 2 diabetes, diabetes mellitus, prediabetes, impaired glucose tolerance, impaired fasting glucose, fruits, vegetables, fiber, fibre, follow-up, and prospective studies). Furthermore, to search for more studies, we also sought expert opinion and additionally hand-checked the reference lists of original publications and previous meta-analyses or reviews. There were no language restrictions.

Study Selection

To be included, studies had to fulfil the following criteria: (i) prospective cohort studies with healthy participants at baseline; (ii) an individual measure of intake of fruits, vegetables, fruit and vegetables, or fruit and vegetable fiber; (iii) an assessment of the development of type 2 diabetes; (iv) multivariate adjusted relative risk (RR) or hazard ratios (HR) with their corresponding 95% confidence interval (CI). Studies that did not meet the inclusion criteria were excluded during the initial review. When uncertainty existed, we retrieved and assessed the full text article. Two reviewers (Ping-Yu Wang and Zong-Hua Gao) resolved any uncertainty through discussion. If duplicate reports from the same study cohort were identified, only the most recent publication with the most detailed information or the study with the largest population was included.

Data Extraction and Validity Assessment

Data extraction was carried out independently by two authors (Ping-Yu Wang and Jun-Chao Fang), and any differences were resolved through discussion. From each study, the following details were extracted: the first author, publication year, country, number of participants, participants' age, sex, duration of follow up, number of events, methods used to measure exposure, outcome assessment, multivariate adjusted RR or HR of type 2 diabetes and corresponding 95% CI for the highest vs lowest level of intake with the greatest number of adjustments, and confounding factors in the statistical analysis.

For assessing the quality of an observational study, the Newcastle–Ottawa quality assessment Scale (NOS) is recommended³¹. Two authors (Can Zhang and Shu-Yang Xie) independently assessed all studies for quality and validity using the NOS, and any discrepancies were resolved by discussion. For cohort studies, the NOS consisted of three dimensions of quality: selection (4 points), comparability (2 points) and outcome (3 points). It allowed a total score from 0 to 9 points, with a total score of 7 or greater reflecting high-quality studies.

Statistical Analysis

HRs or RRs were used to measure the association between intake of fruit, vegetables or their fiber and risk of type 2 diabetes. We transformed these values by taking their natural logarithms and calculating their standard errors and corresponding 95% CIs. Then we generated pooled estimates to calculate summary hazard ratios and 95% CIs for the highest vs lowest level of intake.

For each outcome, tests of heterogeneity were carried out (using the χ^2 -test of heterogeneity and I^2 statistic). If there was no heterogeneity, a fixed-effect meta-analysis was carried out. If there was substantial heterogeneity (I^2 greater than 50%), the review authors looked for a possible reason for this (e.g., participants). We carried out subgroup analysis based on the quality of the study (high quality vs lower quality), sex (men and women included vs women only), length of follow up (<10 years vs ≥ 10 years) and location (USA and Europe vs China), as these were thought to be possible sources of heterogeneity. If the heterogeneity could not be explained, we used a random-effects model with appropriate cautious interpretation.

We also carried out sensitivity analysis to assess the stability of the results by excluding or including studies at high risk of bias (e.g., those follow-up years <5 years) or using the trim and fill method. The effects of publication bias were assessed using funnel plots and Egger's regression test to measure funnel plot asymmetry^{32,33}. All statistical analyses were analyzed with Stata (version 12.0; StataCorp, College Station, TX, USA).

RESULTS

Search Results

The systematic search identified 2,626 articles (Figure 1), of which 2,589 were excluded on the basis of titles and abstracts.

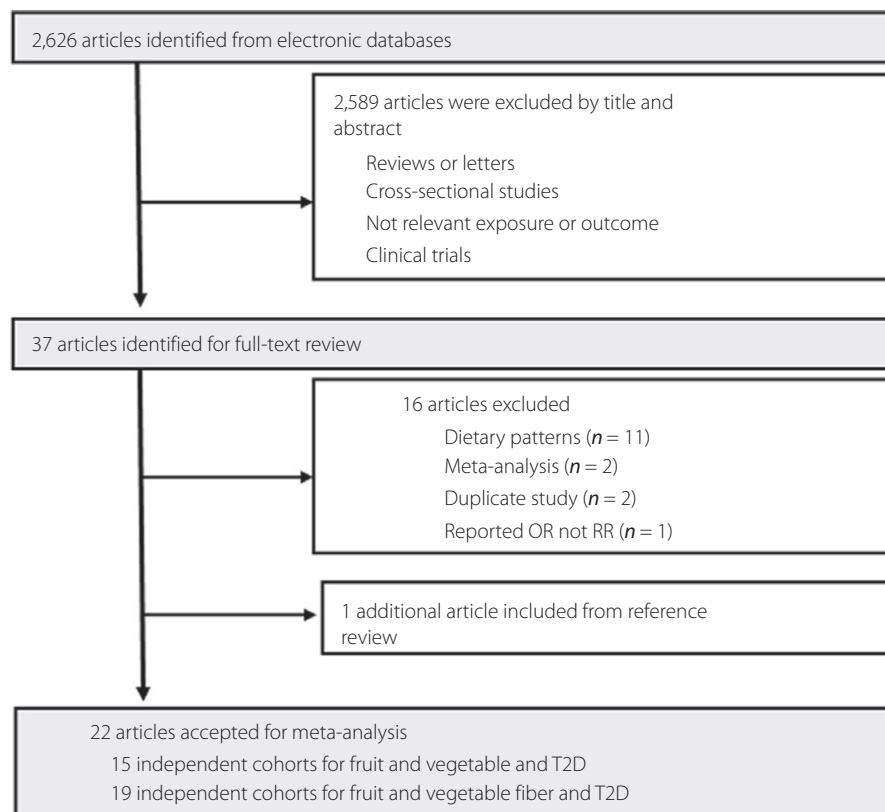


Figure 1 | Process of study selection in the meta-analysis. OR, odds ratio; RR, relative risk; T2D, type 2 diabetes.

We obtained 37 potentially relevant articles for full-text assessment. Of these, several articles, which examined fruit and vegetable intake within dietary patterns only or were meta-analyses, were not included. Two articles reported the same cohort data, so we excluded the article with the smaller population^{16,29}. One study, which examined plasma vitamin C level with the risk of incident of type 2 diabetes, was excluded for data presented as odds ratios²², but we added the data from the study to see if it significantly altered the observed associations in the sensitivity analysis. One additional article was included by checking the reference lists of identified reports²⁴. A total of 22 articles, published between 1992 and 2014, were included in this meta-analysis.

Study Characteristics and Quality Assessment

There were 11 articles including 15 independent cohorts on fruit and vegetable intake and risk of type 2 diabetes (Table 1). In the publications of Muraki *et al.*²⁰, Ford and Mokdad²¹, and Kurotani *et al.*²⁸, the results, reporting for sex or independent cohorts separately, were treated as separate cohorts in the current meta-analysis. The age of participants ranged from 25 to 79 years. Study duration of follow up ranged from 4 to 24 years. In most papers, some adjustments including age, sex, body mass index, energy intake, smoking, alcohol and family

history were made for potential confounding factors. None of the papers met all of the criteria of the quality assessment tool, and the quality scores ranged from 5 to 8.

There were 12 articles including 19 independent cohorts studying on intake of fruit and vegetable fiber and risk of type 2 diabetes (Table 2). In the publications of Sameron, Stevens and Hopping^{34–36}, the results, reporting for independent cohorts separately, were treated as separate cohorts in the current meta-analysis. The age of participants ranged from 26 to 79 years. Study duration of follow-up ranged from 4.6 years to 14 years. All papers made some adjustments for potential confounding factors. The quality scores ranged from 5 to 8.

Fruit Only

The overall maximum-adjusted pooled RR based on all available data for the highest intake of fruit vs the lowest intake with risk of type 2 diabetes was 0.91 (95% CI 0.87–0.96). The I^2 statistic for heterogeneity between studies was 11.2% and $P = 0.33$ for homogeneity, suggesting low between-study heterogeneity. The meta-analysis showed a significant reduction in the risk of type 2 diabetes incidence for consumption of fruits (Figure 2).

Some cohort studies also examined the intake of citrus, strawberries and blueberries with the risk of type 2 diabetes.

Table 1 | Characteristics of included studies on fruit and vegetable intake and risk of type 2 diabetes

Study	Country	Sex	Age (years)	Follow-up (years)	Cases/size	Assessment of T2DM	Measure of intake	Adjustments	Quality score
Meyer (2000) ²⁶	USA	F	55–69	6	1,141/35,988	Self-report	FFQ	Age, BMI, smoking, alcohol, energy, WHR, physical activity, education	6
Ford (2001) ²¹	USA	M	25–74	20	416/3,874	Self-report and HM	24 h recall	Age, BMI, sex, smoking, alcohol, SBP, cholesterol, exercise, education	6
Ford (2001) ²¹	USA	F	25–74	20	602/5,791	Self-report and HM	24 h recall	Age, BMI, sex, smoking, alcohol, SBP, cholesterol, exercise, education	6
Liu (2004) ²³	USA	F	≥45	8.8	1,614/38,018	Self-report	FFQ	Age, BMI, smoking, alcohol, cholesterol, exercise, total calories, history of birth, physical activity, family history of diabetes, alcohol, education, weight change, energy	6
Hodge (2004) ²⁴	Australia	M&F	40–69	4	365/31,641	Self-report	FFQ	Age, sex, BMI, WHR, country of birth, physical activity, family history of diabetes, alcohol, education, weight change, energy	5
Montonen (2005) ¹²	Finland	M&F	40–69	23	383/4,304	HM and via Social Insurance Institution register	DHI (dietary history interview)	Age, sex, BMI, energy intake, smoking, family history of diabetes, and geographic area	7
Bazzano (2008) ²⁵	USA	F	38–63	18	4,529/71,346	Self-report and confirmed if met WHO criteria or ADA criteria	FFQ	BMI, physical activity, family history, postmenopausal hormone, alcohol, smoking, energy	7
Villegas (2008) ¹⁸	China	F	40–70	4.6	1,608/64,191	HM	FFQ	Age, energy, meat, BMI, WHR, smoking, alcohol, physical activity, income, education, occupational status, and hypertension	6
Cooper (2012) ²⁹	Europe	M&F	40–79	11	10,821/24,939	Self-report, linkage to primary-care registers, secondary-care registers, medication use, hospital admissions	FFQ and 24 h recall	Age, sex, education, BMI, physical activity, smoking, energy, alcohol	8
Kurotani (2013) ²⁸	Japan	M	45–75	5	530/12,269	Self-report	FFQ	Age, public health centre area, BMI, smoking, alcohol, leisure-time activity, history of hypertension, family history of diabetes, coffee, Mg, Ca, energy intake	7

Table 1 (Continued)

Study	Country	Sex	Age (years)	Follow-up (years)	Cases/size	Assessment of T2DM	Measure of intake	Adjustments	Quality score
Kurotani (2013) ²⁸	Japan	F	45–75	5	366/27,168	Self-report	FFQ	Age, public health centre area, BMI, smoking, alcohol, leisure-time activity, history of hypertension, family history of diabetes, coffee, Mg, Ca, energy intake	7
Muraki (2013) ²⁰	USA (NHS)	F	38–63	24	6,358/66,105	Self-report and supplementary questionnaires/medical records	FFQ	Age, ethnicity, BMI, smoking, multivitamin use, physical activity, family history of diabetes, energy intake and other factors	6
Muraki (2013) ²⁰	USA (NHS II)	F	26–46	18	3,153/85,104	Self-report and supplementary questionnaires/medical records	FFQ	Age, ethnicity, BMI, smoking, multivitamin use, physical activity, family history of diabetes, energy intake and other factors	6
Muraki (2013) ²⁰	USA (HPFS)	M	40–75	22	2,687/36,173	Self-report and supplementary questionnaires/medical records	FFQ	Age, ethnicity, BMI, smoking, multivitamin use, physical activity, family history of diabetes, energy intake and other factors	7
Mursu (2014) ²⁷	Finland	M	42–60	19.3	432/2,332	A self-administered questions for a physician-set diagnosis	4-d food recording	Age, examination years, BMI, waist-to-hip ratio, smoking, alcohol, education, physical activity, family history of diabetes, and other factors	7

Table 2 | Characteristics of included studies on fruit and vegetable fiber intake and risk of type 2 diabetes

Study	Country	Sex	Age (years)	Follow-up (years)	Cases/size	Assessment of T2DM	Measure of intake	Adjustments	Quality score
Colditz (1992) ³⁷	USA	F	30–55	6	702/84,360	Self-report	FFQ	Age, BMI, alcohol, follow-up period	5
Salmeron (1997) ³⁵	USA	F	40–65	6	915/65,173	Self-report	FFQ	Age, BMI, smoking, alcohol, energy, physical activity, family history of diabetes	8
Salmeron (1997) ³⁵	USA	M	40–75	6	523/42,759	Self-report	FFQ	Age, BMI, smoking, alcohol, energy, physical activity, family history of diabetes	8
Meyer (2000) ²⁶	USA	F	55–69	6	1,141/3,5988	Self-report	FFQ	Age, BMI, smoking, alcohol, energy, WHR, physical activity, education	6
Stevens (2002) ³⁶	USA	M&F	45–64	9	971/9,529	Self-report	FFQ	Age, BMI, sex, smoking, physical activity, education, field center	6
Stevens (2002) ³⁶	USA	M&F	45–64	9	476/2,722	Self-report	FFQ	Age, BMI, sex, smoking, physical activity, education, field center	6
Montonen (2003) ³⁸	Finland	M&F	40–69	10	156/4316	Social insurance institution register	Dietary history interview	Age, BMI, sex, smoking, education, field center	7
Schulze (2004) ³⁹	USA	F	26–46	8	741/91,249	Self-report	FFQ	Age, BMI, smoking, alcohol, physical activity, energy, family history, hormone, magnesium, caffeine	7
Hodge (2004) ²⁴	Australia	M&F	40–69	4	365/31,641	Self-report	FFQ	Age, sex, BMI, WHR, country of birth, physical activity, family history of diabetes, alcohol, education, weight change, energy	5
Schulze (2007) ⁵⁴	Germany	M&F	35–65	7	844/25,067	Self-report	FFQ	Age, sex, BMI, education, sports activity, smoking, alcohol, waist circumference, energy, carbohydrate intake, PUFA-SFA ratio, MUFA-SFA ratio	7
Barclay (2007) ⁴⁰	Australia	M&F	>49	10	138/1,833	Fasting plasma glucose level/self-report	FFQ	Age, sex, family history of diabetes, smoking, triglycerides, HDL cholesterol and other factors	7

Table 2 (Continued)

Study	Country	Sex	Age (years)	Follow-up (years)	Cases/size	Assessment of T2DM	Measure of intake	Adjustments	Quality score
Wannamethee (2009) ⁴¹	British	M	60–79	7	162/3,428	Self-report	FFQ	Age, waist circumference, smoking, physical activity, social class, alcohol, total calorie intake and other factors	6
Hopping (2010) ³⁴	Caucasian	M	45–75	14	1,080/15,116	Self-report/ medical records	FFQ	BMI, physical activity, education, and calories	7
Hopping (2010) ³⁴	Caucasian	F	45–75	14	715/1,4643	Self-report/ medical records	FFQ	BMI, physical activity, education, and calories	7
Hopping (2010) ³⁴	Japanese American	M	45–75	14	2,677/16,572	Self-report/ medical records	FFQ	BMI, physical activity, education, and calories	7
Hopping (2010) ³⁴	Japanese American	F	45–75	14	2,374/18,672	Self-report/ medical records	FFQ	BMI, physical activity, education, and calories	7
Hopping (2010) ³⁴	Native Hawaiian	M	45–75	14	798/4,568	Self-report/ medical records	FFQ	BMI, physical activity, education, and calories	7
Hopping (2010) ³⁴	Native Hawaiian	F	45–75	14	943/5,941	Self-report/ medical records	FFQ	BMI, physical activity, education, and calories	7
Weng (2012) ⁴²	Taiwanese	M&F	≥30	4.6	141/1,604	Fasting plasma glucose concentration/ self-report	FFQ	Age, sex, caloric intake, family history of diabetes, BMI, education, smoking, drinking, hypertension, and other factors	6

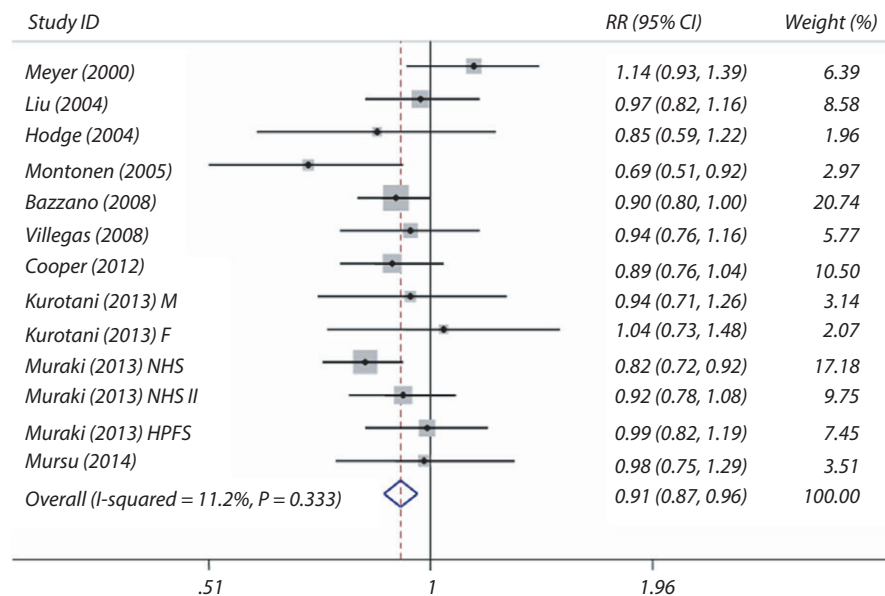


Figure 2 | Maximum-adjusted relative risk (RR) for type 2 diabetes, comparing highest vs lowest intake of fruit. Weights are from fixed effect analysis. CI, confidence interval.

Eight cohort studies investigated the association between citrus intake and the risk of type 2 diabetes, the summary RR was 1.02 (95% CI 0.96–1.09) for the highest intake compared with the lowest intake, with no evidence of between-study heterogeneity ($I^2 = 0.0\%$ and $P = 0.67$ for homogeneity). Five cohort studies investigated the association between strawberry intake and the risk of type 2 diabetes, the summary RR was 0.96 (95% CI 0.78–1.18) for the highest intake compared with the lowest intake. Four cohort studies investigated the association between blueberry intake and the risk of type 2 diabetes, the summary RR was 0.75 (95% CI 0.66–0.84) for the highest intake compared with the lowest intake, with a significant reduction in risk of type 2 diabetes.

Vegetables Only

The overall maximum-adjusted pooled RR based on all available data for highest intake vegetables vs lowest intake with risk of type 2 diabetes incidence was 0.91 (95% CI 0.82–1.01). The I^2 statistic for heterogeneity between studies was 57.2% and $P = 0.01$ for homogeneity, suggesting substantial between-study heterogeneity.

Some cohort studies also examined intake of green leafy vegetables, yellow vegetables and cruciferous vegetables with the risk of type 2 diabetes. Seven cohort studies investigated the association between the intake of green leafy vegetables and the risk of type 2 diabetes, the summary maximum-adjusted RR was 0.87 (95% CI 0.81–0.93) for the highest intake compared with the lowest intake, with no evidence of between-study heterogeneity ($I^2 = 0.0\%$ and $P = 0.50$ for homogeneity; Figure 3). Three cohort studies investigated the association between yellow vegetables intake and the risk of type 2 diabetes,

the summary RR was 0.72 (95% CI 0.57–0.90) for the highest intake compared with the lowest intake. Three cohort studies investigated the association between cruciferous vegetables intake and the risk of type 2 diabetes, the summary RR was 0.82 (95% CI 0.67–0.99) for the highest intake compared with the lowest intake.

Fruit and Vegetables Combined

We identified nine cohort studies on the association between the intake of fruit and vegetables combined and the risk of type 2 diabetes. The summary maximum-adjusted RR was 0.95 (95% CI 0.90–1.02) for the highest intake compared with the lowest intake, with marginal between-study heterogeneity ($I^2 = 34.4\%$ and $P = 0.14$ for homogeneity).

Fruit Fiber

The overall maximum-adjusted pooled RR based on all available data for the highest intake of fruit fiber vs the lowest intake with the risk of type 2 diabetes incidence was 1.00 (95% CI 0.99–1.02). The I^2 statistic for heterogeneity between studies was 1.5% and $P = 0.44$ for homogeneity, suggesting almost no between-study heterogeneity. However, subgroup analysis results showed that a significant reduction in the risk of type 2 diabetes incidence for consumption of fruit fiber in these high-quality studies in which scores were 7 or greater (Figure 4).

Vegetable Fiber

The overall maximum-adjusted pooled RR based on all available data for the highest intake vegetable fiber vs the lowest intake with risk of type 2 diabetes was 0.94 (95% CI 0.86–1.03). The I^2 statistic for heterogeneity between studies was

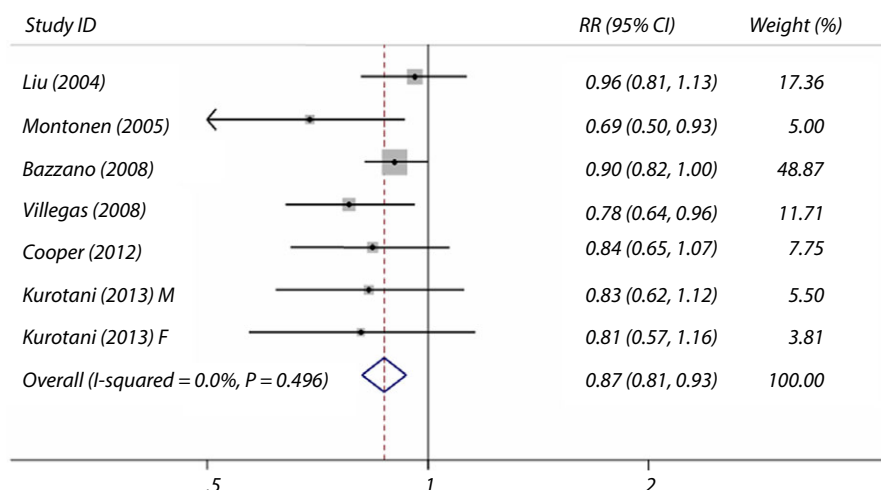


Figure 3 | Maximum-adjusted relative risk (RR) for type 2 diabetes, comparing highest vs lowest intake of green leafy vegetables. Weights are from fixed effect analysis. CI, confidence interval.

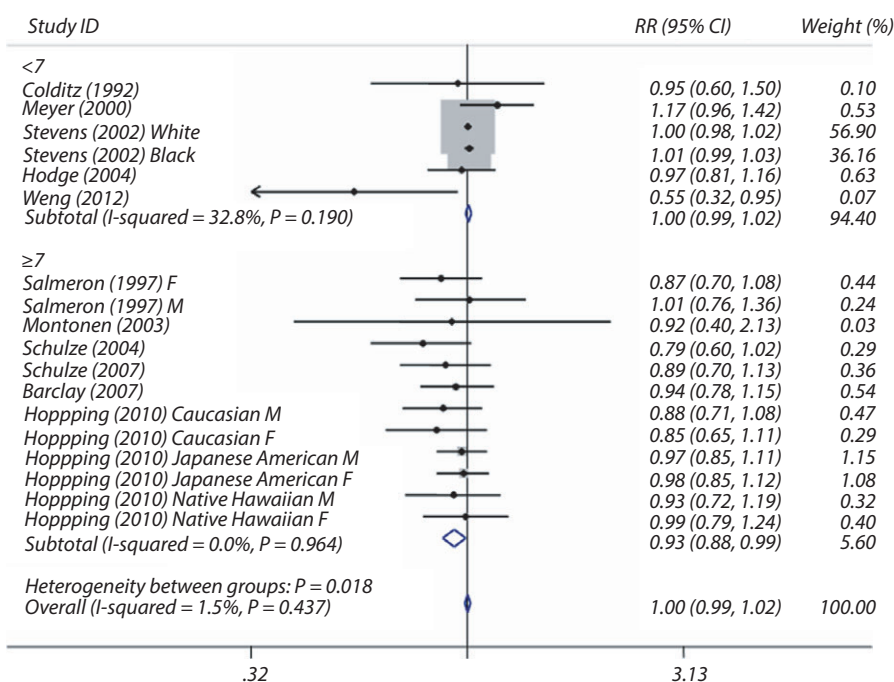


Figure 4 | Maximum-adjusted relative risk (RR) for type 2 diabetes, comparing highest vs lowest intake of fruit fiber. Weights are from fixed effect analysis. CI, confidence interval.

53.4% and $P = 0.005$ for homogeneity, suggesting moderate between-study heterogeneity. We then carried out subgroup analysis to investigate the potential sources of between-study heterogeneity. Sex, quality score of studies, duration of follow up and location, as these were assumed to be potential sources of bias, were analyzed separately. Overall, there were significant associations between the risk of type 2 diabetes and the con-

sumption of vegetables fiber in studies with a follow-up time of 10 years or more (Figure 5).

Subgroup and Sensitivity Analyses

Table 3 shows the subgroup analysis results of intake of fruit, vegetables or their fiber and the risk of type 2 diabetes, comparing highest vs lowest intake. Sex, quality score of studies,

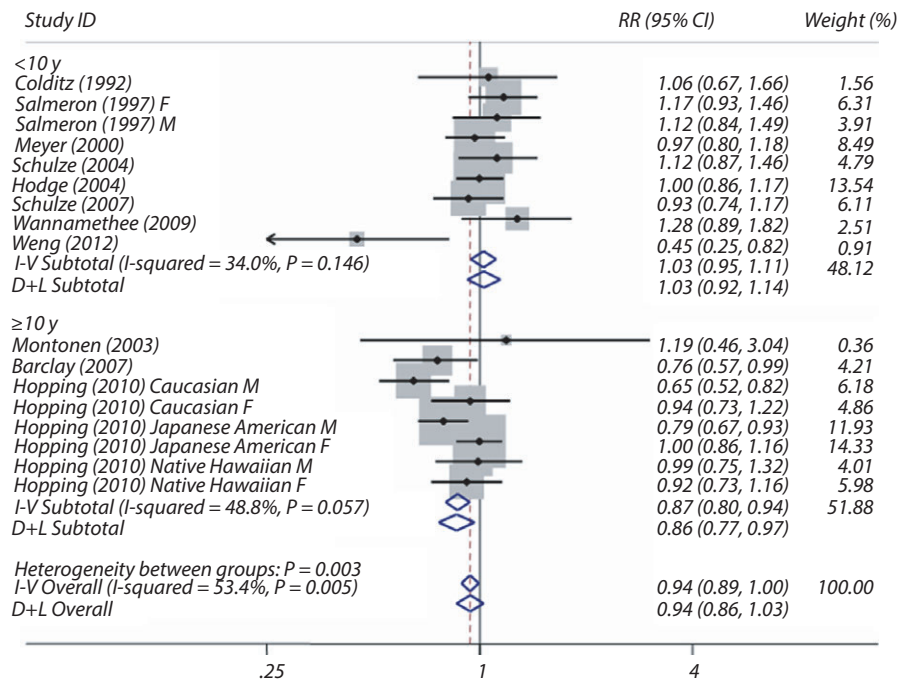


Figure 5 | Maximum-adjusted relative risk (RR) for type 2 diabetes, comparing highest vs lowest intake of vegetable fiber. Weights are from random effect analysis. CI, confidence interval.

duration of follow up and location were separately analyzed. In addition, we made sensitivity analysis by including studies that presented data as odds ratios, or excluding studies with follow-up periods less than 5 years or that used the trim and fill method or both using a fixed and random model. The summary results did not greatly alter the associations.

Publication Bias

There was no evidence of substantial publication bias by using funnel plots and Egger's regression test ($P = 0.50$ fruit, $P = 0.15$ vegetables, respectively; Figure 6).

DISCUSSION

The present meta-analysis has quantitatively assessed the relationship between the intake of fruit, vegetables and their fiber, and the risk of type 2 diabetes. The results show that an increased consumption of fruit, especially berries, is associated with a reduced risk of type 2 diabetes. Increasing intake of green leafy vegetables, yellow leafy vegetables or cruciferous vegetables could help to reduce the risk of type 2 diabetes. In addition, there are significant associations between the risk of type 2 diabetes and the consumption of vegetable fiber in studies with follow-up times of 10 years or more, and also a significant reduction in the risk of type 2 diabetes for the consumption of fruit fiber in these high-quality studies in which the scores are seven or greater. These findings provide strong support for the recommendations encouraging the public to consume more fruit and vegetables. An important point is that different types of fruit and vegetables could have different

effects on the risk of type 2 diabetes. Berries, green leafy vegetables, yellow leafy vegetables or cruciferous vegetables might be good choices for reducing the risk of type 2 diabetes.

Fruit and vegetables are rich sources of fiber, flavonoids and anti-oxidant compounds (carotenoids, vitamin C and E), folate, and potassium, which could explain the protective effects of fruit and vegetables on type 2 diabetes. Dietary fiber was associated with insulin sensitivity, and improved the ability to delay the absorption of carbohydrates and secrete insulin adequately to overcome insulin resistance, resulting in lower postprandial blood glucose and insulin levels^{12,43}. A high intake of dietary fiber can promote the feeling of fullness and reduce the intake of energy-dense foods, resulting in a reduced risk of overweight/obesity, which is an established risk factor for type 2 diabetes^{22,44,45}. The aforementioned studies supported our main finding that consumption of fruit or vegetable fiber decreased the risk of type 2 diabetes.

Fruits and vegetables also contain polyphenols, including flavonoids and anti-oxidant compounds (carotenoids, vitamin C and E) that could also decrease the risk of type 2 diabetes by mitigating the oxidative stress that interferes with the glucose uptake by cells⁴⁶. Intake of anti-oxidants has reportedly improved insulin sensitivity and lowered the risk of incident type 2 diabetes^{30,47}. Berries with high amounts of anthocyanins, thus, could have beneficial effects on glucose metabolism and bodyweight regulation^{19,48,49}. Green leafy vegetables and yellow vegetables also contain polyphenols, such as vitamin C and carotenoids (α -carotene, β -carotene and lutein), and cruciferous vegetables contain substantial amounts of glucocinolates, which

Table 3 | Subgroup analyses of fruit and vegetable and their fiber intake and risk of type 2 diabetes, comparing highest vs lowest intake

	Fruit only			Vegetable only			Fruit and vegetable			Fruit fiber			Vegetable fiber		
	Cohorts, <i>n</i>	RR (95% CI)		Cohorts, <i>n</i>	RR (95% CI)		Cohorts, <i>n</i>	RR (95% CI)		Cohorts, <i>n</i>	RR (95% CI)		Cohorts, <i>n</i>	RR (95% CI)	
All	13	0.91 (0.87,0.96)		10	0.91 (0.82,1.01)		9	0.95 (0.90,1.02)		18	1.00 (0.99,1.02)		17	0.94 (0.86,1.03)	
Sex															
Male	3	0.98 (0.85,1.12)		2	0.81 (0.65,1.00)		3	0.87 (0.71,1.06)		4	0.95 (0.86,1.04)		5	0.91 (0.73,1.14)	
Female	7	0.92 (0.86,0.97)		5	0.95 (0.80,1.13)		5	1.00 (0.92,1.08)		7	0.96 (0.89,1.04)		7	1.01 (0.93,1.10)	
M&F	3	0.84 (0.74,0.96)		3	0.91 (0.83,1.01)		1	0.90 (0.80,1.01)		7	1.00 (0.99,1.02)		5	0.86 (0.70,1.05)	
Duration of follow-up (year)															
<10	6	0.99 (0.90,1.09)		6	0.89 (0.75,1.07)		4	1.03 (0.91,1.16)		11	1.00 (0.99,1.02)		9	1.03 (0.92,1.14)	
≥10	7	0.88 (0.83,0.94)		4	0.94 (0.83,1.06)		5	0.93 (0.86,1.00)		7	0.94 (0.88,1.02)		8	0.86 (0.77,0.97)	
Location															
Asia	3	0.96 (0.82,1.12)		3	0.77 (0.61,0.98)		2	0.97 (0.75,1.25)		1	0.55 (0.32,0.95)		1	0.45 (0.25,0.82)	
Non-Asia	10	0.91 (0.86,0.96)		7	0.97 (0.90,1.05)		7	0.95 (0.89,1.02)		17	1.00 (0.99,1.02)		16	0.95 (0.88,1.04)	
Study quality															
<7	5	0.91 (0.84,0.98)		3	0.85 (0.60,1.19)		4	0.98 (0.87,1.12)		6	1.00 (0.99,1.02)		5	0.97 (0.80,1.18)	
≥7	8	0.92 (0.86,0.98)		7	0.96 (0.88,1.04)		5	0.94 (0.88,1.02)		12	0.93 (0.88,0.99)		12	0.93 (0.84,1.03)	

are known for their anti-oxidant properties, in addition to vitamins A and K, folate, fatty acid, and magnesium content^{50–52}, which further supports the intake of fruits, especially berries, and vegetables, as they are associated with a lower risk of type 2 diabetes in our research.

The previous epidemiological studies, or systematic reviews and meta-analyses have generated somewhat mixed results for the association between the intake of fruit only, vegetables only, fruit and vegetables combined, fruit fiber, vegetable fiber or dietary fiber and the risk of type 2 diabetes. To our knowledge, no other systematic review and meta-analysis involving only prospective studies has been carried out to examine the combined effects of fruit and vegetable intake as well as their fiber with the risk of type 2 diabetes.

Three previous independent meta-analyses investigated the association between fruit and vegetable intake and the risk of incident type 2 diabetes^{11,29,30}. Two meta-analyses investigated the association between fiber intake and the risk of incident type 2 diabetes^{53,54}. However, compared with this current updated meta-analysis, some results limited their superiority.

Our meta-analysis showed that an increased consumption of fruit is associated with a reduced risk of type 2 diabetes. Not similar to the previous independent meta-analyses, which were based on a limited number of studies and significant between-study heterogeneity, the present results were similar to subgroup analysis results according to duration of follow up by Cooper²⁹. In contrast to total fruit consumption, we also analyzed fruit type with the risk of type 2 diabetes, and found that the intake of berries in particular was inversely associated with the risk of type 2 diabetes. Furthermore, using the data from these high-quality studies with scores of 7 or above, we further found that high fruit fiber intake reduced the risk of type 2 diabetes.

Similar to the previous independent meta-analyses, we also found that there was no significant association between total vegetable intake and the risk of type 2 diabetes^{11,29,30}. However, we discovered that increasing the intake of green leafy vegetables, yellow vegetables or cruciferous vegetables could help to reduce the risk of type 2 diabetes. Furthermore, we also found that high vegetable fiber intake reduced the risk of type 2 diabetes using the data from these studies with follow-up period of 10 years or more.

Our meta-analysis had some strengths. The present study included a large number of prospective cohort studies on the intake of fruit, vegetables and their fiber, and the risk of type 2 diabetes, which should eliminate selection bias and recall bias, and allowed for further subgroup analysis. Furthermore, all cohort studies were assessed for quality and validity using NOS, and most studies had high-quality scores, with a large sample size and long duration of follow up, and maximum-adjusted RR for risk of type 2 diabetes.

However, several limitations should also be considered. First, measurement errors were inevitable in the assessment of dietary intake and type 2 diabetes. The potential misclassification of

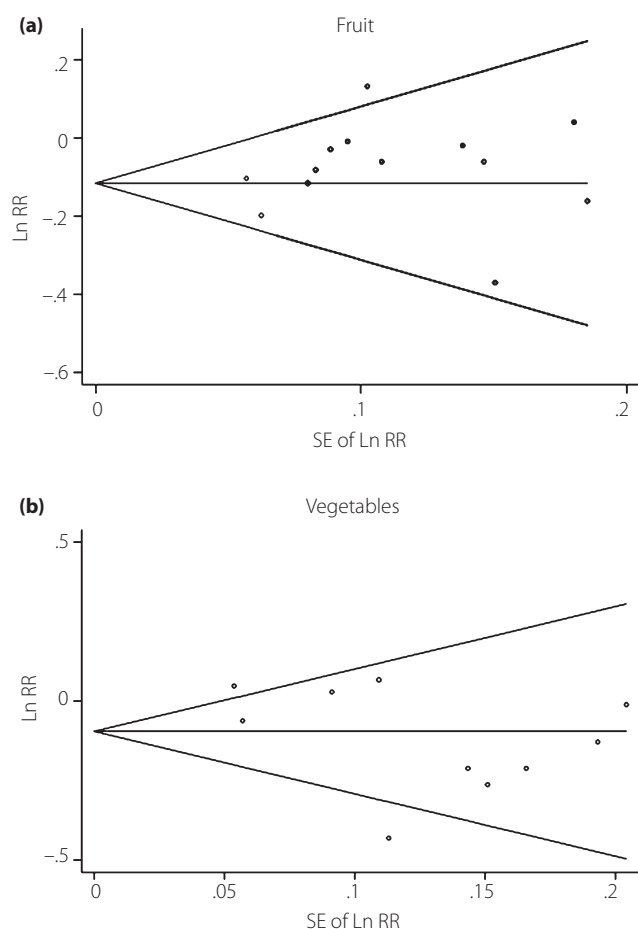


Figure 6 | Publication bias was analyzed using funnel plot. (a) Fruit. (b) Vegetables. SE of Ln RR, standard error or natural logarithm of relative risk.

individuals with undiagnosed type 2 diabetes might also have attenuated the present findings. Different studies used different methods of dietary assessment, such as 24-h recall, dietary assessment interviews or Food Frequency Questionnaire. Different studies split dietary intake into different fractions – either thirds, quarters or fifths. Different studies also used different units of measurement. However, we only collected the data based on the highest vs lowest level of intake, and did not make further dose–response analysis or a standard for dietary measurement in future nutritional studies. Second, although we used the data based on the maximum-adjusted RR for risk of type 2 diabetes, not all authors of the original studies made the same adjustments, in addition, residual or unknown confounding cannot be ruled out. Third, the possibility of publication bias is of a concern. Although there was no evidence of substantial publication bias by using funnel plots and Egger's regression test, it is noteworthy that there were more female cohorts than male cohorts in the original study populations included in our meta-analysis. Further studies in male cohorts are required in future.

In conclusion, findings from the current meta-analysis suggest that a higher intake of fruit, especially berries, as well as green leafy vegetables, yellow vegetables, cruciferous vegetables or their fiber is associated with a lower risk of type 2 diabetes. These results support recommendations on increasing consumption of fruit and vegetables for the primary prevention of many chronic diseases, including type 2 diabetes. However, large randomized controlled trials are required to confirm these findings, and further studies are required to explore potential mechanisms underlying the observed associations.

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DISCLOSURE

The authors declare no conflict of interest.

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