REVIEW ARTICLE



Association between dietary carbohydrate intake and risk of type 2 diabetes: a systematic review and meta-analysis of cohort studies

Akinori Yaegashi^{1,2} · Satoshi Sunohara³ · Takashi Kimura⁴ · Wen Hao¹ · Takato Moriguchi³ · Akiko Tamakoshi⁴

Received: 13 April 2022 / Accepted: 22 May 2023 / Published online: 4 July 2023 © The Japan Diabetes Society 2023

Abstract

Background Previous meta-analyses have assessed the relationship between carbohydrate intake and type 2 diabetes (T2D) risk; however, they included few studies of Asian populations who have a higher carbohydrate intake and lower insulin secretory capacity than non-Asians. Since the publication of the previous meta-analyses, three further studies of Asian populations have been conducted. Based on this background, the present study aimed to perform an updated systematically examine observational studies concerning the link between dietary carbohydrate intake and T2D risk.

Methods We conducted a systematic search for cohort studies that investigated the target association. For each analyzed study, parameter-adjusted risk ratios were used to compare the lowest and highest carbohydrate-intake groups in terms of their risk of incident T2D. The risk ratios were calculated using a random-effects model.

Results Ten publications were analyzed. Overall, carbohydrate intake was found not to be associated with increased risk ratios of incident T2D (risk ratio [RR] = 1.07; 95% confidence interval [95% CI] = 0.94, 1.21; P < 0.01, I² = 61.9%). However, studies of Asian populations reported that high carbohydrate intake is significantly associated with this risk (RR = 1.29; 95% CI 1.15, 1.45; P = 0.59, I² = 0.0%).

Conclusions This updated meta-analysis showed that, overall, carbohydrate intake is not associated with the risk of T2D; nevertheless, a significant association exists among Asian populations. To confirm the association between dietary carbohydrate intake and T2D risk observed in this study, further evidence from long-term observational studies of Asian populations is required.

Keywords Carbohydrate · Asia · Diabetes · Meta-analysis · Systematic review

Akinori Yaegashi and Satoshi Sunohara have Co-first authorship.

 □ Takashi Kimura kimura@med.hokudai.ac.jp

 Akinori Yaegashi yaegashi@t.do-bunkyodai.ac.jp

 Satoshi Sunohara

- Graduate School of Medicine, Hokkaido University, North 15, West 7, Kita-ku, Sapporo 060-8638, Japan
- Department of Health and Nutrition, Faculty of Human Science, Hokkaido Bunkyo University, 5-196-1, Kogane-chuo, Eniwa 061-1449, Japan
- School of Medicine, Hokkaido University, Sapporo 060-8638, Japan

sunohara_satoshi@eis.hokudai.ac.jp

Faculty of Medicine, Hokkaido University, North 15, West 7, Kita-ku, Sapporo 060-8638, Japan

Introduction

Type 2 diabetes mellitus (T2D) is a life-threatening health problem. This metabolic disease increases health-care costs and the risk of comorbidities [1]. Lifestyle modifications, such as improved diet, physical activity, and weight loss, have been shown to reduce and even prevent risk of T2D [2, 3]. As dietary carbohydrates affect blood glucose levels [4], there have been suggestions that such intake plays a key role in diabetes management [5]. A previous metaanalysis reported that, overall, higher carbohydrate intake is not associated with a risk of developing diabetes [6], but that a significant association exists when considering Asian populations in isolation. This discrepancy between Asian and non-Asian populations may be attributed to the fact that Asians have a higher carbohydrate intake [7, 8] and lower insulin secretory capacity [9]. However, the abovementioned meta-analysis contained just two studies on



Asian populations [10, 11]; thus, it remains difficult to draw definitive conclusions. Since the publication of the above-mentioned meta-analysis in 2016 [6], three further studies of Asian populations have been conducted [12–14]. Therefore, in the present research we conducted an updated systematic review and meta-analysis with the aim of summarizing the current evidence on the association between carbohydrates and T2D risk.

Materials and methods

To evaluate the association between dietary carbohydrate intake and risk of T2D, we conducted a systematic review and meta-analysis of relevant observational studies. This study was conducted in accordance with the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [15]. We did not register the systematic review and meta-analysis protocol.

Eligibility criteria

The inclusion criteria were cohort studies that (a) investigated the association between dietary carbohydrate intake and T2D; (b) were published in English; (c) assessed and reported risk ratios (RRs), hazard ratios (HRs) or odds ratios (ORs) and the corresponding 95% confidence intervals (95% CIs) for T2D, or included sufficient information to allow their calculation; (d) included at least two groups divided according to dietary carbohydrate intake (e.g. high and low); (e) reported the prevalence of T2D in each group; and (f) reported the prevalence for the total sample. Intervention studies were excluded.

Search strategy and selection criteria

Studies published from May 1, 2015, to November 18, 2021, were retrieved from PubMed and Web of Science by one investigator (AY). For data predating May 1, 2015, we used papers obtained in the previous meta-analysis [6]. Duplicates were removed using EndNote, and the data were exported to Microsoft Excel.

A search strategy was designed using keywords such as "carbohydrates and diabetes" and "cohort study." For PubMed, the following search was performed: (("cohort studies" [MeSH Terms] OR "cohort studies" [Title] OR "Follow-Up Studies" [Title] OR "Longitudinal Studies" [Title] OR "Prospective Studies" [Title]) AND ("diet, carbohydrate restricted" [MeSH Terms] OR "carbohydrate*" [Title/Abstract]) AND ("Diabetes Mellitus" [MeSH Terms] OR "diabetes" [Title/Abstract] OR "diabetic" [Title/Abstract] OR "NIDDM" [Title/Abstract] OR "type 2 DM" [Title/Abstract])). For Web of Science, the following search was

performed: ("cohort studies" OR "cohort studies" OR "Follow-Up Studies" OR "Longitudinal Studies" OR "Prospective Studies") AND ("diet, carbohydrate restricted" OR "carbohydrate*") AND ("Diabetes Mellitus" OR "diabetes" OR "diabetic" OR "NIDDM" OR "type 2 DM"). We did not contact the authors of previous studies.

Data extraction

Two researchers (AY and SS) screened the titles and abstracts, and reviewed the full text independently. Disagreements were resolved through discussion. During the screening and review, the reviewers were blinded to the authors, institutions, and publishing journals. In the case of multiple studies on the same cohort, the study with the longest follow-up period was included. Data extraction was conducted independently by two researchers (AY and SS), and disagreements were resolved through discussion. The coded variables included the characteristics of the studies, including authors, year of publication, country, years of follow-up, sample size (n), proportion of females (%), body mass index (BMI) (kg/m²), number of sample members with incident diabetes (n), diabetes-assessment results, carbohydrate intake category, RRs/HRs/ORs (95% CIs), and adjustment factors. When data were reported separately for men and women, both groups were considered.

Quality assessment

Two researchers (AY and SS) assessed the quality of each study using the Newcastle Ottawa Scale (NOS) [16]. The NOS was applied by focusing on the following three major components: selection of the study group (maximum four stars), quality of adjustment for confounding variables (maximum two stars), and assessment of outcome (maximum three stars). Disagreements were resolved through discussions.

A higher NOS score indicated better methodological quality. The details and results of the quality assessments are presented in Table 1 and Supplemental Table 1.

Statistical analysis

For each study considered eligible for selection, parameter-adjusted RRs were used to compare the lowest and highest carbohydrate-intake groups in regard to the groups' respective risk of incident T2D. The RRs were calculated using a random-effects model because it was difficult to ignore the differences between the studies regarding methods applied and subjects analyzed. Heterogeneity was evaluated by calculating I² values; I² values of 25%, 50%, and 75%, represent low, moderate, and high heterogeneity, respectively. Subgroup analyses were performed in terms of location (Asian



Author, year, Years of Sample country, [refer-follow-up size, n ence]	Sample size, n	Female (%)	$\mathbf{BMI}(\mathrm{kg}/\mathrm{m}^2)^a$	Age, years ^b	IncidentDiabetes diabe- assessme tes, n method	nt	Dietary assess-ment	Dietary Carbohydrate-intake assess-ment category ^{c,d}	Carbohydrate-intake RR/HR/OR (95% CI) category ^{c,d}	Adjustment factors NOS score
Kim et al. 3.96 (2020), Korea [12]	Men 3032 Women 5278	49	Men 23.8±3.(Women 24.4±3.2	1en Men Mer 23.8±3.062.2±9.7 130 Vomen Women Wor 4.4±3.2 60.9±10.0192	l neu	Self-reported Validated and medical FFQ records	Validated	Men T1: 298 g/d (168.9–316) T2: 327.6 g/d (316.1–336.2) T3: 346.2 g/d (336.2–389.6) Women T1: 269.9 g/d (156.4–285.9) T2: 297.0 g/d (286.0–306.3) T3: 314.8 g/d (306.3–351.1)	Men ALL T1: 1.00 (reference) T2: 1.23 (0.81–1.86) T3: 0.89 (0.56– 1.40) BMI < 23.0 kg/m² T1: 1.00 (reference) T2: 0.88 (0.38–2.05) T3: 0.76 (0.35– 1.65) BMI ≥ 23.0 kg/m² T1: 1.00 (reference) T2: 1.36 (0.82–2.26) T3: 0.85 (0.50– 1.47) Women ALL T1: 1.00 (reference) T2: 1.14 (0.76–1.73) T3: 1.48 (0.97– 2.28) BMI < 23.0 kg/m² T1: 1.00 (reference) T2: 0.73 (0.28–1.90) T3: 1.45 (0.54– 3.88) BMI ≥ 23.0 kg/m² T1: 1.00 (reference) T2: 1.25 (0.78–2.00) T3: 1.25 (0.78–2.00) T3: 1.25 (0.78–2.00) T3: 1.25 (0.78–2.00) T3: 1.51 (0.93–2.27)	Men: Age, smoking 6 status, alcohol consumption, BMI, physical activity level, education, cal- cium intake Women: Age, smoking status, physical activity level, education, waist circumfer- ence, calcium intake
Ha et al. 11.5 (2019), Korea [13]	Men 2684 Women 2911	52	Men Q1: 24.4±2.9 Q4: 23.6±2.9 Women Q1: 24.3±3.1 Q4: 24.6±3.2	(40–69) 9 9 1 1	Men 1 533 Women 477	Medical records]	Validated FFQ	Men Q1: 64.7% (46.7– 67.7) Q2: 69.8% (67.7–71.7) Q3: 73.7% (71.7–75.6) Q4: 78.0% (75.6–88.2) Women Q1: 66.3% (37.9– 69.9) Q2: 71.8% (69.6–73.7) Q3: 75.6% (73.7–77.6) Q4: 80.4%	200002000	Age, family history of diabetes, smoking status, alcohol consumption, BMI, physical activity level, education, income level, marital status, residence, protein intake, total energy intake, fasting blood



A. Yaegashi et al.

Author, year, Years of Sample country, [refer- follow-up size, n ence]	Years of follow-up	Sample size, n	Female (%)	BMI $(kg/m^2)^a$	Age, years ^b	Incident diabe- tes, n	IncidentDiabetes diabe- assessment tes, n method	Dietary Carbohydra assess-ment category ^{c,d}	Carbohydrate-intake category ^{c,d}	Carbohydrate-intake RR/HR/OR (95% CI) category ^{c,d}	Adjustment factors NOS score
Sakurai et al. (2016), Japan [14]	01	Men 2006	0	23.4	6.54	232	Medical records	Validated FFQ	Allf Q1: (<50.0%) Q2: (50.0-57.4%) Q2: (50.0-57.4%) Q3: (57.5-65.0%) Q4: (>65.0%) Q4: (>65.0%) Q4: (285.8- 31.3.8 g/d) Q2: (285.8- 341.7 g/d) Q2: (285.8- 341.7 g/d) Q2: (50.0-57.4%) Q3: (313.9- 31.3.8 g/d) Q4: (≥341.8 g/d) Q4: (≥341.8 g/d) Q2: (285.8- 31.3.8 g/d) Q2: (50.0-57.4%) Q2: (285.8- 31.3.8 g/d) Q3: (313.9- 341.7 g/d)	All ^f Q1: 0.88 (0.58–1.31) Q2: 1.00 (reference) Q3: 0.87 (0.61– 1.23) Q4: 1.18 (0.80–1.76) All ^g Q1: 0.95 (0.64–1.41) Q2: 1.00 (reference) Q3: 0.96 (0.65–1.42) Q4: 1.19 (0.80–1.76) BMI < 2.5 0 kg/m ^{2 f} Q1: 1.23 (0.75–2.02) Q2: 1.00 (reference) Q3: 0.87 (0.55–1.38) Q4: 1.19 (0.63–1.90) BMI ≥ 25.0 kg/m ^{2 f} Q1: 0.92 (0.48–1.79) Q2: 1.00 (reference) Q3: 1.19 (0.69–2.04) Q4: 2.01 (1.08–3.71) BMI < 25.0 kg/m ^{2 g} Q1: 0.04 (0.63–1.20) Q2: 1.00 (reference) Q3: 1.19 (0.65–1.88) BMI ≥ 25.0 kg/m ^{2 g} Q1: 0.07 (0.52–1.80) Q2: 1.00 (reference) Q3: 0.88 (0.53–1.46) Q4: 1.10 (0.65–1.88) BMI ≥ 25.0 kg/m ^{2 g} Q1: 0.97 (0.52–1.80) Q2: 1.00 (reference) Q3: 1.14 (0.62–2.10) Q4: 1.76 (0.97–3.21)	Age, family his- tory of diabetes, smoking status, alcohol consump- tion, physical activity level, occupation type, total energy intake, total fiber intake, fasting plasma glucose level



Table 1 (continued)	nued)								
Author, year,	Years of	Sample	Female	Sample Female BMI (kg/ Age,	Age,	IncidentDiabetes	Dietary	Carbohydrate-intake RR/HR/OR (95% CI)	
country, [refer- follow-u]	dn-wolloj ·	size, n	ize, n (%)	$m^2)^a$	years _b	diabe- assessment	assess-ment category ^{c,d}	category ^{c,d}	
encel						tes n method			

Adjustment factors NOS score

	- 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6	io,
	Age, BMI, family 6 history of diabetes, postmenopausal status, smoking status, alcohol intake, physical activity level, multivitamin use, race, total energy intake, red meat consumption, coffee consumption, coffee consumption, tion, magnesium intake, ratio of polyunsaturated fat to saturated fat, trans-fat intake (all dietary variables in quintiles)	Age, total energy intake, BMI, waist-to-hip ratio, education level, pack-years of smoking, alcohol intake, physical activity level
	Q1: 1.00 (reference) Q2: 0.96 (0.89, 1.04) Q3: 0.96 (0.89, 1.04) Q4: 0.99 (0.91, 1.08) Q5: 0.98 (0.89, 1.08)	Q1: 176 g/d (< 192.1)Q1: 1.00 (reference) Q2: 202 g/d (192.1— Q2: 1.05 (0.87–1.26) 210.6) Q3: 218 g/d (210.7— Q4: 0.90 (0.74–1.09) 225.6) Q4: 234 g/d (225.7— 243.8)
	Q1: 159 g/d Q2: 181.0 g/d Q3: 195 g/d Q4: 208.3 g/d Q5: 228.4 g/d	Q1: 176 g/d (< 192.1) Q2: 202 g/d (192.1– 210.6) Q3: 218 g/d (210.7– 225.6) Q4: 234 g/d (225.7– 243.8)
method	Self-reported Validated FFQ	Self-reported Validated FFQ
tes, n	6934	1141
	(30–55)	(55–69)
	Q1: (5 25.1±4.6 Q3: 24.9±4.5 Q5: 24.3±4.3	Q1: 26.9 Q2: 26.8 Q3: 26.8 Q4: 26.6 Q5: 26.8
,	100	100
	Women 100 70,025	Women 35,988
	42	9
ence]	AlEssa et al. (2015), US [19]	Meyer et al. (2000), US [20]



A. Yaegashi et al.

Author, year, Years of Sample country, [refer-follow-up size, n ence]	Years of follow-up	Sample size, n	Female (%)	$\frac{\mathrm{BMI}}{\mathrm{m}^2)^{\mathrm{a}}}$	Age, years ^b	Incident diabe- tes, n	IncidentDiabetes diabe- assessment tes, n method	Dietary Carbohydra assess-ment category ^{c,d}	Carbohydrate-intakı category ^{c,d}	Carbohydrate-intake RR/HR/OR (95% CI) category ^{c.d}	Adjustment factors NOS score
Villegas et al. (2007), China [10]	4.6	Women 64,227	100	I	(40-70)	1608	Self-reported Validated FFQ	Validated FFQ	All Q1: 263.5 g/d° Q2: 269.1 g/d Q3: 276.3 g/d Q4: 287.1 g/d Q5: 337.6 g/d	All Q1: 1.00 (reference) Q2: 0.96 (0.80–1.15) Q3: 0.87 (0.73–1.05) Q4: 1.09 (0.92–1.29) Q5: 1.28 (1.09–1.50) BMI < 25 kg/m² Q1: 1.00 (reference) Q2: 0.86 (0.65–1.13) Q3: 0.80 (0.60–1.06) Q4: 0.73 (0.55–0.97) Q5: 1.22 (0.94–1.58) BMI > 25 kg/m² Q1: 1.00 (reference) Q2: 1.05 (0.82–1.32) Q3: 0.94 (0.74–1.20) Q4: 1.32 (1.06–1.65) Q5: 1.41 (1.14–1.73)	Age, history of 8 hypertension, smoking status, alcohol consump- tion, physical activity level, BMI, waist-hip ratio, education level, occupation type, income, total energy intake
Schulze et al. (2008), Germany [21]	7–11	Men 9702 Women 15,365	61	Men Q1: 27.2 Q2: 26.9 Q3: 26.7 Q4: 26.8 Q5: 26.7 Women Q1: 25.8 Q2: 25.5 Q3: 25.6 Q4: 25.6 Q5: 25.7	(35–65)	44	Self-reported Validated FFQ	Validated FFQ	Men Q1: 30.9% Q2: 35.2% Q3: 38.3% Q4: 41.5% Q5: 46.4% Women Q1: 36.7% Q2: 41.2% Q3: 44.1% Q4: 47.0% Q5: 51.4%	Men Q1: 1.00 (reference) Q2: 0.83 (0.62–1.10) Q3: 0.92 (0.69–1.23) Q4: 0.92 (0.66–1.25) Q5: 0.91 (0.66–1.26) Women Q1: 1.00 (reference) Q2: 0.90 (0.64–1.27) Q3: 0.97 (0.69–1.36) Q4: 0.95 (0.66–1.35) Q5: 0.89 (0.62–1.29)	Age, education 7 level, occupational activity, engagement in sport, smoking, alcohol intake, total energy intake
Similä et al. (2012), Fin- land [22]	12	Men 25,943	0	Median Q1: 26.1 Q2: 26.0 Q3: 25.9 Q4: 25.7 Q5: 25.7	(50–69)	1098	Self-reported Validated FFQ	Validated FFQ	Q1: 33.4% Q2: 37.5% Q3: 40.4% Q4: 43.3% Q5: 47.4%	Q1: 1.00 (reference) Q2: 0.77 (0.65–0.92) Q3: 0.81 (0.68–0.97) Q4: 0.81 (0.68– 0.98) Q5: 0.78 (0.64–0.94)	Age, intervention 7 group, BMI, smoking status, physical activity level, total energy intake, coffee consumption



_	
_	
a)	
_	
_	
$\overline{}$	
_	
~	

(commune)										
Author, year, Years of Sample country, [refer-follow-up size, n ence]	Sample size, n	Female (%)	BMI (kg/ Age, m^2) ^a years ^b	Age, years ^b	Incident diabe- tes, n	IncidentDiabetes diabe- assessment tes, n method	Dietary Carbohydra assess-ment category ^{c,d}	Carbohydrate-intake category ^{c,d}	Carbohydrate-intake RR/HR/OR (95% CI) category ^{c,d}	Adjustment factors NOS score
Alhazmi et al. 6 (2013), Australia [23]	Women 8370	100	ı	(45–50)	311	Self-reported Validated FFQ	Validated FFQ	Q1: 104.38 g/d Q2: 139.28 g/d Q3: 166.76 g/d Q4: 198.65 g/d Q5: 256.91 g/d	Q1: 1.00 (reference) Q2: 1.03 (0.70–1.50) Q3: 1.04 (0.71–1.54) Q4: 0.85 (0.55– 1.30) Q5: 0.97 (0.61–1.55)	Area of residence, 6 education level, current smoking status, physical activity level, good self-rated health, menopau- sal status, BMI, alcohol consump- tion, total energy intake, saturated fatty acid intake, mono-unsaturated fatty acid intake,
Nanri et al. 5 (2015), Japan [11]	Men 27,799 Women 36,875	57	23.6	(40–69)	1191	Self-reported Validated FFQ	Validated FFQ	Men QI: 40.2% (8.9-44.8) QI: 1.00 (reference) Q2: 48.0% (44.8-50.7) Q2: 1.24 (0.93-1.64) Q3: 53.1% (50.7-55.5) (0.84-1.65) Q4: 1. Q4: 58.2% (55.5-61.1) 1.76 Q5: 1.11 (0.6) Q5: 65.3% (61.1-87.6) Women QI: 45.0% (5.5-49.1) Q2: 1.15 (0.80-1.66) Q2: 51.9% (49.1-54.1) Q2: 1.15 (0.80-1.66) Q2: 51.9% (49.1-54.1) (0.78-1.81) Q4: 1. Q3: 56.1% (54.1-58.1) 2.12) Q5: 1.32 (0.70-1.66) Q5: 66.5% (62.9-88.5)	0 Q3: 1.18 18 (0.79– 56–1.86) 0 Q3: 1.19 30 (0.80–	Age, family history 6 of diabetes, his- tory of hyperten- sion, smoking status, alcohol consumption, BMI, physical activity, study area, total energy intake, coffee consumption, magnesium intake, calcium intake, calcium intake, calcium intake, calcium intake, calcium intake, calcium

BMI: body mass index, CI confidence interval, D decile, FFQ food frequency questionnaire, HR hazard ratio, NOS Newcastle-Ottawa scale, OR odds ratio, Q quartile/quintile, RR risk ratio, SD standard deviation, T tertile

Values are presented as means ± standard deviations. If the subjects' full values were not reported in the paper, the values were determined based on dietary carbohydrate intake. Reference no. 20 was determined based on a whole grain intake

 $^{^{\}text{b}}\text{Values}$ are presented as means \pm standard deviations (range). The range is enclosed in parentheses ()

^{*}Units of % indicate a value adjusted for energy using the density method; units of g/d indicate a value adjusted for energy using the residual method. If the energy-adjusted values were obtained using both the density and residue methods, both are shown

¹Values are medians and (ranges). The range is enclosed in parentheses ()

eValues are amounts divided according to the glycemic index

fValues are amounts divided according to energy-adjusted carbohydrates using the density method

^g Values are amounts divided according to energy-adjusted carbohydrates using the residual method

334 A. Yaeqashi et al.

or non-Asian countries), sex (men or women), follow-up period (<7 years or \geq 7 years), and BMI (mean < 25 kg/m² or mean \geq 25 kg/m²). We did not conduct subgroup analyses regarding energy intake because the food frequency questionnaire varies across studies, and their energy intake measurement errors differ. Statistical analyses were performed using the "metafor" [17] (version 3.0.2) package of R [18] (version 3.6.1).

Results

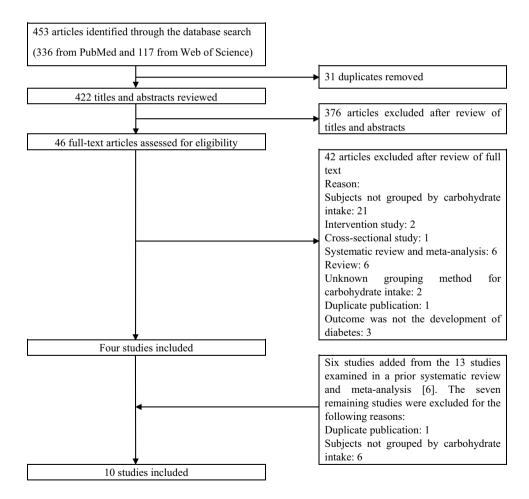
The search strategy yielded 453 articles (336 from PubMed and 117 from Web of Science). After duplicate articles were excluded, 422 titles and abstracts remained; of these, 46 full texts were selected for reading, of which four articles met

all inclusion criteria [12–14, 19]. Additionally, six full-text articles [10, 11, 20–23] were added from a previously published systematic review and meta-analysis [6]. Thus, 10 papers met all inclusion criteria. Figure 1 shows a flowchart of the study-selection process.

Characteristics of the studies

The characteristics of the 10 selected studies are listed in Table 1. The oldest study to meet the inclusion criteria was published in 2000 [20]. The studies were conducted in several different countries: two studies were conducted in Korea, the US, and Japan, respectively, while one study was conducted in China, Finland, Australia, and Germany, respectively. Thus, five studies were conducted in Asian countries and five were conducted in non-Asian countries.

Fig. 1 Flowchart of the study-selection process





The follow-up period was 3.96–11.5 years among the Asia-based studies and 6–24 years among the non-Asia-based studies. The number of participants ranged from 2006 to 64,674 among the Asia-based studies and from 25,067 to 70,025 among the non-Asia-based studies. All studies used validated food frequency questionnaires. For energy adjustment, the residual method and density method were used. T2D was assessed using medical records and self-reported data. All studies had a NOS quality score of 6–8 stars (Supplemental Table 1).

Association between dietary carbohydrate intake and incidence of type 2 diabetes

For each of the 10 articles, the extreme (high and low, respectively) categories of dietary carbohydrate intake were examined in regard to their respective association with diabetes risk. The pooled RR was 1.07 (95% CI 0.94–1.21) with significant heterogeneity (P<0.01, I^2 =61.9%; Fig. 2). When subgroup analysis involving different studies with different geographical regions (the Asia-based studies and the non-Asia-based studies) and BMI (mean <25 kg/m² and mean \geq 25 kg/m²) was conducted, differences were observed (Asian: RR = 1.29, 95% CI 1.15–1.45, P=0.59, I^2 =0.0%; non-Asian: RR=0.92, 95% CI 0.83–1.01, P=0.49, I^2 =21.9%; mean BMI <25 kg/m²: RR=1.17, 95% CI 1.01–1.35, P=0.09, I^2 =39.3%; mean BMI \geq 25 kg/m²: RR=0.97, 95%

Fig. 2 Forest plot indicating the association between carbohydrate intake and type 2 diabetes risk. *CI* confidence interval

Author(s) and Year	Weight for all		Estimate [95% CI]
Asia-based studies			
Kim et al. (2020)-Men	4.9% ⊢		0.89 [0.56, 1.41]
Kim et al. (2020)-Women	5.4%	·	1.48 [0.97, 2.27]
Ha et al. (2019)-Men	5.8%	—	1.54 [1.03, 2.30]
Ha et al. (2019)-Women	5.0%	—	1.69 [1.07, 2.66]
Sakurai et al. (2016)-Men	6.0%	—	1.18 [0.80, 1.75]
Villegas et al. (2007)-Women	11.8%	⊢	1.28 [1.09, 1.50]
Nanri et al. (2015)-Men	4.2%	—	1.11 [0.66, 1.86]
Nanri et al. (2015)-Women	3.1%	-	1.32 [0.70, 2.48]
All Asia-based studies (Q=5.5	7. df=7. p = 0.59: l ² =0.0	% τ ² =0.00)	1.29 [1.15, 1.45]
Other AlEssa et al. (2015)-Women	13.4%	⊢ ■1	0.98 [0.89, 1.08]
` '			
Meyer et al. (2020)-Women Schulze et al. (2008)-Men	10.7%		0.93 [0.76, 1.13] 0.91 [0.66, 1.26]
, ,	7.4%		
Schulze et al. (2008)-Women	6.5% F		0.89 [0.62, 1.28]
Simila et al. (2012)-Men	10.9%		0.78 [0.64, 0.95]
Alhazmi et al. (2013)-Women	4.8% ⊢		0.97 [0.61, 1.55]
All other studies (Q=4.44, df=5	5, p = 0.49; l ⁴ =21.9%, τ ⁴	=0.00)	0.92 [0.83, 1.01]
All (Q=31.13, df=13, p < .01; l ² Subgroup Differences: Q _M = 1	. ,	-	1.07 [0.94, 1.21]
_ ,			
	0.5	1 2	4
	0.0	Observed Outcome	-1

Table 2 Summary of risk ratios for the association between carbohydrate intake and diabetes risk in terms of select study characteristics

		•	
	No. of studies, [reference]	RR	95% CI
All studies	10, [10–14, 19–23]	1.07	0.94, 1.21
Geographical region	of the study		
Asia	5, [10–14]	1.29	1.15, 1.45
Non-Asia	5, [19–23]	0.92	0.83, 1.01
Sex			
Men	6, [11–14, 21, 22]	1.01	0.81, 1.25
Women	8, [10–13, 19–21, 23]	1.11	0.95, 1.29
Follow-up duration			
<7 years	5, [10–12, 20, 23]	1.11	0.95, 1.31
≥7 years	5, [13, 14, 19, 21, 22]	1.05	0.86, 1.27
BMI^{*1}			
$Mean < 25 \text{ kg/m}^2$	7, [10–14, 19, 23]	1.17	1.01, 1.35
$Mean \ge 25 \text{ kg/m}^2$	4, [10, 20–22]	0.97	0.78, 1.20

BMI: body mass index, CI: confidence interval, RR: risk ratio

*¹Reference no. 10 includes results with BMI < 25 kg/m² as "<mean 25 kg/m²" and \geq 25 as " \geq mean 25 kg/m²" because the mean BMI values were not shown

CI 0.78–1.20, P < 0.01, $I^2 = 74.7\%$). These results are shown in Table 2. We also conducted subgroup analyses in terms of sex (men and women) and follow-up period (<7 years and \geq 7 years), but the results did not differ (men: RR = 1.01, 95% CI 0.81–1.25, P=0.05, $I^2 = 54.2\%$; women: RR = 1.11,

95% CI 0.95–1.29, P=0.01, I^2 =61.6%; <7 years: RR=1.11, 95% CI 0.95–1.31, P=0.16, I^2 =38.9%; \geq 7 years: RR=1.05, 95% CI 0.86–1.27, P<0.01, I^2 =73.3%; as shown in Table 2). Figure 3 shows a funnel plot for the data; the plot is symmetrical.

Discussion

The results of our systematic review and meta-analysis suggest that carbohydrate intake was not associated with the risk of T2D overall; however, a significant association existed among Asian populations.

In the present research, we added three more Asia-based studies [12–14] to those included in the above-mentioned meta-analysis [6], and consequently obtained similar results [overall: RR = 1.07 (95% CI 0.94–1.21); Asia-based studies: RR = 1.29 (95% CI 1.15–1.45); non-Asia-based studies: RR = 0.92 (95% CI 0.83–1.01)]. This difference between Asian and non-Asian results may be attributed to the fact that Asians have a higher carbohydrate intake [7, 8] and lower insulin secretory capacity [9]. Furthermore, based on the results of the BMI sub-analysis (as shown in Table 2), the influence of differences in the distribution of BMI between Asia and non-Asia can be considered; however, these cannot be proven.

Thus, the overall findings remain unchanged, but our research has strengthened the evidence by adding three Asiabased studies [12–14]. Additionally, our paper describes the characteristics of the analyzed studies in more detail than the

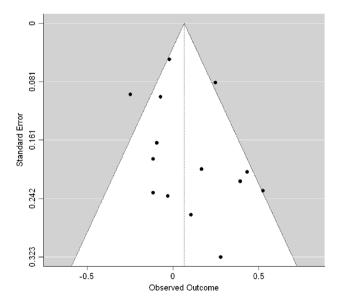


Fig. 3 Funnel plot illustrating the association between carbohydrate intake and type 2 diabetes risk

previous meta-analysis [6], which will help to clarify important target variables for future research. Future research needs are as follows.

Firstly, long-term follow-up studies of Asian samples are warranted. Follow-up periods differed between the Asian and non-Asian samples (Asia-based studies: 3.96–11.5 years; non-Asia-based studies: 6–24 years). Although the difference in results between the Asia-based studies and non-Asia-based studies might be due to differences between Asian and non-Asian individuals regarding insulin secretary capacity [24] and % energy from carbohydrate [7, 8], no conclusions could be drawn because of different follow-up periods.

Secondly, the relationship between the amount of carbohydrates ingested per meal and the risk of diabetes needs to be clarified. All articles analyzed in this study examined the relationship between the amount of carbohydrates per day and the development of diabetes. However, recent studies have suggested that, along with the amount and type of food intake, the circadian timing of food intake should also be considered [25, 26]. For example, a prospective cohort study reported that higher intake of energy at dinner is associated with a higher incidence of obesity, metabolic syndrome, and non-alcoholic fatty liver disease [27].

Finally, studies with objective measures, including formal medical examinations, and fasting blood glucose and HbA1c measurements, are needed. Diabetes assessment of 8 out of 10 studies in this research was self-reported, and it is possible that some studies do not accurately measure risk of T2D.

This study had two limitations. First, publication bias may have existed, given the possibility that studies that obtained negative results were not published. However, we consider that the possibility was low because the funnel plot was symmetrical. Second, this study only reviewed English-language manuscripts, excluding studies in other languages.

Conclusion

This updated meta-analysis showed that, in general, carbohydrate intake is not associated with risk of T2D; however, there is significant association for Asians. Our results indicate that, to prevent the risk of diabetes, Asians need to pay attention to their carbohydrate intake. However, there was a difference between the Asian and non-Asian populations examined in this review in terms of follow-up years. Therefore, further evidence from long-term observational studies of Asian samples is required to confirm the association between dietary carbohydrate intake and T2D risk.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s13340-023-00642-0.



Acknowledgements We would like to thank Editage (www.editage.jp) for the English-language editing.

Author contributions Research conception and design: AY, SS, and KT; statistical analysis: SS and KT; interpretation of data: AY, SS, KT, WH, TM, and AT; writing of the manuscript: AY. All authors have contributed to the final version of this manuscript. All authors have read and approved the final manuscript.

Funding This research was not funded.

Declarations

Conflict of interest The authors declare no conflict of interest.

Human or animal rights This article does not contain any studies with human or animal subjects performed by any of the authors.

References

- Cho NH, Shaw JE, Karuranga S, Huang Y, da Rocha Fernandes JD, Ohlrogge AW, et al. IDF diabetes atlas: global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res Clin Pract. 2018;138:271–81. https://doi.org/10.1016/j.diabr es.2018.02.023.
- Eriksson KF, Lindgärde F. Prevention of type 2 (non-insulindependent) diabetes mellitus by diet and physical exercise. The 6-year Malmo feasibility study. Diabetologia. 1991;34:891–8. https://doi.org/10.1007/BF00400196.
- Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002;346:393–403. https://doi.org/10.1056/NEJMoa012512.
- Lamothe LM, Lê KA, Samra RA, Roger O, Green H, Macé K. The scientific basis for healthful carbohydrate profile. Crit Rev Food Sci Nutr. 2019;59:1058–70. https://doi.org/10.1080/10408 398.2017.1392287.
- Hu FB, Manson JE, Stampfer MJ, Colditz G, Liu S, Solomon CG, et al. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. N Engl J Med. 2001;345:790–7. https://doi.org/10.1056/ NEJMoa010492.
- Noto H, Goto A, Tsujimoto T, Noda M. Long-term low-carbohydrate diets and type 2 diabetes risk: a systematic review and metaanalysis of observational studies. J Gen Fam Med. 2016;17:60–70.
- Dehghan M, Mente A, Zhang X, Swaminathan S, Li W, Mohan V, et al. Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study. Lancet. 2017;390:2050–62. https://doi.org/10.1016/S0140-6736(17)32252-3.
- Zhou BF, Stamler J, Dennis B, Moag-Stahlberg A, Okuda N, Robertson C, et al. Nutrient intakes of middle-aged men and women in China, Japan, United Kingdom, and United States in the late 1990s: the INTERMAP study. J Hum Hypertens. 2003;17:623–30. https://doi.org/10.1038/sj.jhh.1001605.
- Kadowaki T, Miyake Y, Hagura R, Akanuma Y, Kajinuma H, Kuzuya N, et al. Risk factors for worsening to diabetes in subjects with impaired glucose tolerance. Diabetologia. 1984;26:44–9. https://doi.org/10.1007/BF00252262.
- Villegas R, Liu S, Gao YT, Yang G, Li H, Zheng W, et al. Prospective study of dietary carbohydrates, glycemic index, glycemic load, and incidence of type 2 diabetes mellitus in middle-aged Chinese women. Arch Intern Med. 2007;167:2310–6. https://doi.org/10.1001/archinte.167.21.2310.

- Nanri A, Mizoue T, Kurotani K, Goto A, Oba S, Noda M, et al. Low-carbohydrate diet and type 2 diabetes risk in Japanese men and women: the Japan Public Health Center-Based Prospective Study. PLoS One. 2015;10:e0118377. https://doi.org/10.1371/journal.pone.0118377.
- 12. Kim SY, Woo HW, Lee YH, Shin DH, Shin MH, Choi BY, et al. Association of dietary glycaemic index, glycaemic load, and total carbohydrates with incidence of type-2 diabetes in adults aged ≥40 years: the Multi-Rural Communities Cohort (MRCohort). Diabetes Res Clin Pract. 2020;160:108007. https://doi.org/10.1016/j.diabres.2020.108007.
- Ha K, Joung H, Song Y. Inadequate fat or carbohydrate intake was associated with an increased incidence of type 2 diabetes mellitus in Korean adults: a 12-year community-based prospective cohort study. Diabetes Res Clin Pract. 2019;148:254–61. https://doi.org/10.1016/j.diabres.2019.01.024.
- Sakurai M, Nakamura K, Miura K, Takamura T, Yoshita K, Nagasawa SY, et al. Dietary carbohydrate intake, presence of obesity and the incident risk of type 2 diabetes in Japanese men. J Diabetes Investig. 2016;7:343–51. https://doi.org/10.1111/jdi. 12433.
- Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. https://doi.org/10.1136/bmj.n71.
- The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analysis, 2013. http://www.ohri. ca/programs/clinical_epidemiology/oxford.asp. Ottawa Hospital Research Institute [cited 2013]
- Viechtbauer W. Conducting meta-analyses in R with the metafor package. J Stat Soft. 2010;36:1–48. https://doi.org/10.18637/jss. v036.i03.
- 18. R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria, 2019. https://www.R-project.org/.
- AlEssa HB, Bhupathiraju SN, Malik VS, Wedick NM, Campos H, Rosner B, et al. Carbohydrate quality and quantity and risk of type 2 diabetes in US women. Am J Clin Nutr. 2015;102:1543– 53. https://doi.org/10.3945/ajcn.115.116558.
- Meyer KA, Kushi LH, Jacobs DR Jr, Slavin J, Sellers TA, Folsom AR. Carbohydrates, dietary fiber, and incident type 2 diabetes in older women. Am J Clin Nutr. 2000;71:921–30. https://doi.org/10.1093/ajcn/71.4.921.
- Schulze MB, Schulz M, Heidemann C, Schienkiewitz A, Hoffmann K, Boeing H. Carbohydrate intake and incidence of type 2 diabetes in the European Prospective Investigation into Cancer and Nutrition (EPIC)-Potsdam Study. Br J Nutr. 2008;99:1107–16. https://doi.org/10.1017/S0007114507853360.
- Similä ME, Kontto JP, Valsta LM, Männistö S, Albanes D, Virtamo J. Carbohydrate substitution for fat or protein and risk of type 2 diabetes in male smokers. Eur J Clin Nutr. 2012;66:716–21. https://doi.org/10.1038/ejcn.2012.24.
- Alhazmi A, Stojanovski E, McEvoy M, Garg ML. Macronutrient intake and type 2 diabetes risk in middle-aged Australian women. Results from the Australian Longitudinal Study on women's Health. Public Health Nutr. 2014;17:1587–94. https://doi.org/10.1017/S1368980013001870.
- 24. Yoon KH, Lee JH, Kim JW, Cho JH, Choi YH, Ko SH, et al. Epidemic obesity and type 2 diabetes in Asia. Lancet. 2006;368:1681–8. https://doi.org/10.1016/S0140-6736(06) 69703-1.
- Arble DM, Bass J, Laposky AD, Vitaterna MH, Turek FW. Circadian timing of food intake contributes to weight gain. Obesity (Silver Spring). 2009;17:2100–2. https://doi.org/10.1038/oby. 2009.264.



338 A. Yaegashi et al.

26. Garaulet M, Gómez-Abellán P. Timing of food intake and obesity: a novel association. Physiol Behav. 2014;134:44–50. https://doi.org/10.1016/j.physbeh.2014.01.001.

 Bo S, Musso G, Beccuti G, Fadda M, Fedele D, Gambino R, et al. Consuming more of daily caloric intake at dinner predisposes to obesity. A 6-year population-based prospective cohort study. PLoS One. 2014;9:e108467. https://doi.org/10.1371/journal.pone. 0108467. **Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.

