



Effects of resistant starch on glycaemic control: a systematic review and meta-analysis

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(Submitted 5 June 2020 – Final revision received 8 September 2020 – Accepted 13 September 2020 – First published online 22 September 2020)

Abstract

The effects of resistant starch on glycaemic control are controversial. In this study, a systematic review and meta-analysis of results from nineteen randomised controlled trials (RCT) was performed to illustrate the effects of resistant starch on glycaemic control. A literature search was conducted on PubMed, Scopus and Cochrane electronic databases for related publications from inception to 6 April 2020. Key inclusion criteria were: RCT; resistant starch as intervention substances and reporting glucose- and insulin-related endpoints. Exclusion criteria were: using type I resistant starch or a mixture of resistant starch and other functional food ingredients as intervention; using substances other than digestible starch as controls. The effect of resistant starch on fasting plasma glucose was significant (effect size (ES) -0.09 (95 % CI -0.13 , -0.04) mmol/l, $P = 0.001$) compared with digestible starch. Subgroup analyses revealed that the ES was larger when the dosage of resistant starch was more than 28 g/d (ES -0.16 (95 % CI -0.24 , -0.08) mmol/l, $P < 0.001$) or the intervention period was more than 8 weeks (ES -0.12 (95 % CI -0.18 , -0.06) mmol/l, $P < 0.001$). The effect on homeostatic model assessment (HOMA)-insulin resistance (IR) was significant (ES -0.33 (95 % CI -0.51 , -0.14), $P = 0.001$). However, the effects on other insulin-related endpoints were not significant, including fasting plasma insulin, four endpoints from the frequently sampled intravenous glucose tolerance test (insulin sensitivity index, acute insulin response, disposition index and glucose effectiveness) and HOMA- β . The current study indicated moderate effects of resistant starch on improving glycaemic control.

Key words: Resistant starch; Glycaemic control; Fasting plasma glucose; Insulin sensitivity; Meta-analyses

The morbidity of diabetes has reached an epidemic level. In 2019, about 463 million adults between 20 and 79 years old had diabetes worldwide⁽¹⁾. By 2014, the estimated annual cost of diabetes-related health care has reached 825 billion international dollars⁽²⁾. Patients with diabetes have a higher risk of developing CVD, which is ranked as the number one cause of death globally⁽¹⁾. Diabetes is also associated with a higher risk of developing other complications including kidney complications, nerve damage, eye complications, foot complications, etc.⁽³⁾. Diabetics are often treated with hypoglycaemic drugs such as sulphonylureas and metformin. However, these hypoglycaemic drugs have various side effects^(4,5). Adjunctive therapy which can improve glycaemic control may be beneficial. The intake of functional foods can improve the glycaemic control for patients with type 2 diabetes mellitus (T2DM)^(6,7). Certain functional foods may also mitigate the risk of developing T2DM⁽⁸⁾.

Resistant starch, defined as the starch portion which is not digestible by human enzymes, has shown potential for improving glycaemic control⁽⁹⁾. Resistant starch is classified into five

types: I, II, III, IV and V according to the different mechanisms of being resistant to human enzymes^(10,11). Resistant starch will enter the colon and be fermented by the residing microbiota. The majority of fermentation products are SCFA, including acetate, propionate and butyrate⁽¹²⁾. These SCFA can stimulate the production of two insulin-related hormones, the glucagon-like peptide-1 and the peptide YY^(13,14), which were shown to promote insulin secretion^(15,16). In addition, the consumption of resistant starch has been proposed to increase insulin sensitivity by reducing ectopic body fat and regulating adipogenesis⁽¹⁷⁾, possibly through the action of SCFA⁽¹²⁾.

Previous randomised controlled trials reported both positive^(18–27) and negative effects^(28–31) of resistant starch on glycaemic control. In addition, the sample size of the reported randomised controlled trials was small, most of which ranged from nine to thirty subjects^(18,20–24,28,30,32). A meta-analysis would be helpful to provide convincing results by pooling the effects of the published randomised controlled trials results.

Abbreviations: AIR, acute insulin response; DI, disposition index; ES, effect size; HOMA, homeostatic model assessment; IR, insulin resistance; RS II, type II resistant starch; S_G, glucose effectiveness; S_I, insulin sensitivity index.

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In the present study, we conduct a systematic review and meta-analysis including results of all populations from nineteen clinical trials in fifteen publications^(18–33). The effects of resistant starch on all common glucose and insulin endpoints related to glycaemic control are analysed. We exclude the studies on type I resistant starch because it overlaps with studies on whole grains whose effects on glycaemic control were summarised previously^(34,35). Subgroup meta-analyses are performed for pre-defined covariates including dosage of resistant starch, intervention duration, age, health status and study design. The included relevant endpoints for glycaemic control are: fasting plasma glucose, glycated Hb (HbA1c) percentage, fasting plasma insulin, four endpoints from the frequently sampled intravenous glucose tolerance test (insulin sensitivity index (S_I), acute insulin response (AIR), disposition index (DI) and glucose effectiveness (S_G)) and two endpoints from the homeostatic model assessment (HOMA), HOMA- β and HOMA-insulin resistance (IR).

Methods

Search strategies

A systematic search of the studies published from inception to 6 April 2020 was performed on PubMed, Scopus and Cochrane electronic databases. The search process used the following terms: ('diabetes' OR 'insulin resistance' OR 'insulin sensitivity' OR 'insulin' OR 'euglycemic clamp' OR 'glucose clamp techniques' OR 'intravenous glucose tolerance test' OR 'FSIVGTT' OR 'homeostasis model assessment' OR 'HOMA' OR 'metabolic syndrome' OR 'glycated hemoglobin A' OR 'HbA1c' OR 'glycosylated hemoglobin A' OR 'blood glucose' OR 'blood sugar' OR 'glucose tolerance test' OR 'OGTT' OR 'glucose intolerance' OR 'impaired glucose tolerance') AND ('resistant starch' OR 'amylose'). The search was restricted to studies published in English.

Inclusion and exclusion criteria

Inclusion criteria include: (1) randomised controlled trials; (2) resistant starch supplementation by itself or incorporated into food and beverage; (3) reporting blood glucose or insulin endpoints. Exclusion criteria include: (1) supplementing type I resistant starch or whole grains; (2) supplementing a mixture of resistant starch and other functional foods (e.g. fibre and polyphenol etc.) and (3) using substances other than digestible starch as controls. Two investigators (K. X. and J. W.) independently evaluated the studies based on inclusion and exclusion criteria. Any disagreement was resolved by discussion.

Quality assessment

The Jadad scale was used to assess the quality of the included human trials for the meta-analysis. The range of possible scores is 0 (bad) to 5 (good)⁽³⁶⁾.

Data extraction

The extracted basic information includes: the first author's name, the publication year, the location of the study, the study design, the number of participants, the mean age, the health status of the participants, the duration of the interventions and the dosage of

resistant starch. The extracted results include both the baseline and post-treatment values of the fasting plasma glucose concentration, HbA1c, the fasting plasma insulin concentration, S_I , AIR, DI, S_G , HOMA- β and HOMA-IR.

Statistical analysis

Weighted mean difference between change-from-baseline values (test *v.* control) was used as the effect size (ES). If baseline values were not reported, weighted mean difference between post-treatment measurements were used as the ES instead. When insufficient data are available, the effect variance was calculated using methods described by Follmann *et al.*⁽³⁷⁾. For a crossover design, within-study comparisons were based on paired *t* tests. Correlations between two measures on the same subject were estimated from *P* values when possible. If a correlation coefficient needs to be used, it was assumed to be 0.5 between the two measures on the same subject⁽³⁸⁾. For a parallel design, correlations between change-from-baseline measures were assumed to be zero.

An I^2 test was used to evaluate the heterogeneity. A random effects model was used to pool the effects considering the different characteristics of the included trials (e.g. different dosages, different sexes, different health status etc.) Meta-regression and subgroup analyses were used to explore the potential source of heterogeneity including the intervention duration, the dosage of resistant starch, the mean age of subjects, the health status and the study design. In the subgroup analyses, for intervention duration, 8 weeks was used as the division point according to a methodology proposed by Chinese Nutrition Society for evidence rating⁽³⁹⁾. Dietary Guidelines for Americans 2015–2020 (8th edition)⁽⁴⁰⁾ recommended a dietary fibre intake of 14 g/4184 kJ (1000 kcal). Assuming a daily energy intake of 8369 kJ (2000 kcal), we used 28 g/d as the division point for the subgroup analysis by dosage. For the subgroup analysis by age, 50 years old was used as the division point because 50 years old is generally considered middle-aged.

Publication bias was evaluated using the Begg's rank correlation test and the Egger's regression test. Sensitivity analysis was performed by removing one trial at a time and recalculating. All statistical analyses were performed using STATA 15 software (StataCorp). The results were considered statistically significant when the *P* value was <0.05 unless it was noted otherwise.

Results

A total of 2441 papers were found through PubMed, Scopus and Cochrane library databases (Fig. 1). After title and abstract screening, 2407 papers were excluded and the rest thirty-four papers were subjected to full-text screening. After full-text examination, nineteen papers were excluded due to missing relevant outcome (*n* 7), inappropriate control (*n* 8) or missing detailed results (*n* 4). Fifteen papers were included in this study. The study by Gower *et al.*⁽¹⁸⁾ consisted of four subgroups, in which two dosages (2.5 and 7.6 g/d) of resistant starch were used for each of the two groups of subjects (insulin-resistant and insulin-sensitive groups). Since the control group (0 g/d resistant



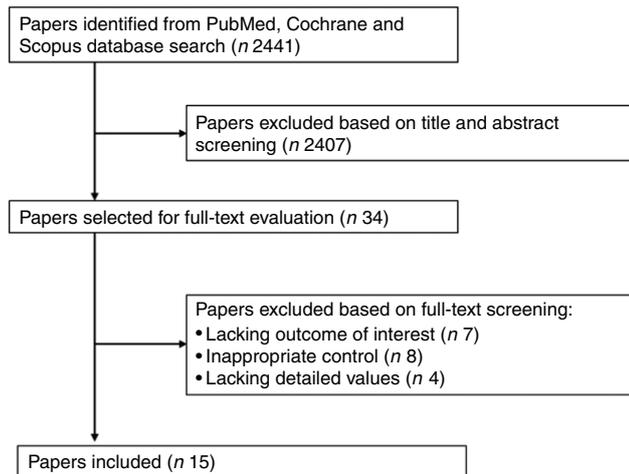


Fig. 1. Flow diagram of the study selection process.

starch) was shared, the two intervention subgroups for the same type of subjects were combined. The study by Bergeron *et al.*⁽³²⁾ was composed of two subgroups. The subjects consumed either a high-carbohydrate (51–53% of the energy intake) or a low-carbohydrate (39–40% of the energy intake) diet, in which a 66 and a 48 g/d dosage of resistant starch were included, respectively. The results of the low-carbohydrate group were not included because of possible confounding effects between low-carbohydrate consumption and resistant starch intake. The study by Alfa *et al.*⁽²⁶⁾ consisted of two subgroups, in which the effects of resistant starch on subjects with a middle age (an age of 37–47 years) and an old age (an age of 73–82 years) were evaluated separately. The results of these two subgroups were treated as two trials in this work. The study by Maki *et al.* was composed of four subgroups. Two different dosages (9 and 18 g/d) of resistant starch were consumed by each of the two groups of subjects (male and female groups)⁽²⁷⁾. Since the control group (0 g/d resistant starch) was shared, the two intervention subgroups for the same type of subjects were combined before the meta-analysis. The study by Nichenametla *et al.*⁽³¹⁾ included two subgroups (with or without metabolic syndrome), which were treated as two trials. Therefore, nineteen trials from fifteen papers were included in this study.

Characterisations of the studies

The characterisations of the included studies are summarised in Table 1. The nineteen trials consisted of 503 subjects. Five trials used a parallel design and fourteen trials used a crossover design. The dosage of resistant starch ranged from 5 to 66 g/d. The intervention duration ranged from 2 to 12 weeks. Eight trials were performed on healthy subjects, ten trials on overweight subjects or subjects with a high risk of developing diabetes and one trial on individuals with diabetes. The Jadad scale was used to evaluate the quality of the included studies. The Jadad score of the included trials ranged from 2 to 5 as summarised in Table 1.

Effects on fasting plasma glucose

The effect of resistant starch on fasting plasma glucose was examined in sixteen trials. The results from a meta-analysis using a random effects model indicated that resistant starch had significant lowering effects on fasting plasma glucose (ES -0.09 (95% CI $-0.13, -0.04$) mmol/l, $P=0.001$) compared with the control (Fig. 2). There was a moderate heterogeneity among the ES of the included studies (I^2 52.7%, $P=0.007$). A subgroup meta-analysis was conducted for pre-defined covariates (intervention duration, dosage of resistant starch, mean age of subjects, health status and study design) to investigate the source of heterogeneity (shown in Table 2). Resistant starch had significant lowering effects (ES -0.12 (95% CI $-0.18, -0.06$) mmol/l, $P<0.001$) on fasting plasma glucose in the subgroup with more than 8 weeks of intervention, which included eight trials. The effects of resistant starch were significant when the dosage was higher than 28 g/d (ES -0.16 (95% CI $-0.24, -0.08$) mmol/l, $P<0.001$), which included five trials. The effects were significant for both the subgroups with a mean age of more than 50 and lower than 50. The effects were significant for the subgroup of overweight or high risk of having diabetes (ES -0.09 (95% CI $-0.16, -0.03$) mmol/l, $P=0.005$), which included eight trials. The effects were significant when a crossover study design was used (ES -0.09 (95% CI $-0.15, -0.04$) mmol/l, $P=0.001$), which included thirteen trials. No significant publication bias was detected (Begg's test $P=1.00$ and Egger's test $P=0.30$).

Effects on HbA1c

The effect of resistant starch on HbA1c was examined in four trials. The meta-analysis using a random effects model showed no significant effect of resistant starch on HbA1c (ES -0.03 (95% CI $-0.08, 0.03$)%, $P=0.39$) and a high heterogeneity (I^2 77.9%, $P=0.004$) (online Supplementary Fig. A1). The limited number of trials prevented a subgroup meta-analysis. No significant publication bias was detected (Begg's test $P=1.00$ and Egger's test $P=0.48$).

Effects on fasting plasma insulin

The effect of resistant starch on fasting plasma insulin was examined in fifteen trials. The meta-analysis using a random effects model showed that the effect of resistant starch on fasting plasma insulin was not significant compared with control (ES -0.87 (95% CI $-4.03, 2.28$) pmol/l, $P=0.59$) (Fig. 3). A moderate heterogeneity was observed (I^2 55.0%, $P=0.005$). A subgroup meta-analysis was performed for pre-defined covariates to illustrate the potential source of the heterogeneity (shown in online Supplementary Table A1). The effect was significant when the intervention duration was more than 8 weeks (ES -8.64 (95% CI $-15.83, -1.44$) pmol/l, $P=0.02$), though the heterogeneity was high (I^2 70.8%). No significant publication bias was detected (Begg's test $P=1.00$ and Egger's test $P=0.28$).

Table 1. Characteristics of the included trials

First author	Publication year and region	Number of participants	Sex	Mean age (years)	Health status	Interventions	Dosage of resistant starch (g/d)	Duration (weeks)	Study design	Jadad score
Penn-Marshall ⁽²⁸⁾	2010, USA	15	Eight males, seven females	36.6	Overweight or high risk of developing diabetes	HI-MAIZE® 260 added to bread v. control bread	7.4	6	Double-blinded randomised crossover study, 2 weeks washout	4
Gower ⁽¹⁸⁾	2016, USA	14	All females	48.3	Healthy	HI-MAIZE® 260 v. AMIOCA® added to crackers and cookies	5.1	4	Double-blinded, randomised crossover study, 4 weeks washout	4
Gower ⁽¹⁸⁾	2016, USA	9	All females	48.3	Healthy	HI-MAIZE® 260 v. AMIOCA® added to crackers and cookies	5.1	4	Double-blinded randomised crossover study, 4 weeks washout	4
Bodinham ⁽²⁰⁾	2012, UK	12	Eight males and four females	37.0	Overweight or high risk of developing diabetes	HI-MAIZE® 260 v. AMIOCA® in ready-to-use sachets	40.0	4	Subject-blinded randomised crossover study	2
Kwak ⁽¹⁹⁾	2012, South Korea	85	Forty-seven males, thirty-eight females	51.0	Overweight or high risk of developing diabetes	Maize resistant starch added to refined rice v. refined rice	6.5	4	Subject-blinded randomised parallel study	2
Bergeron ⁽³²⁾	2016, USA	26	Ten males, sixteen females	45.7	Healthy	HI-MAIZE® 260 v. MELOJEL® starch added to food	66.0	2	Triple-blinded randomised crossover study, 2 weeks washout	5
Peterson ⁽²⁹⁾	2018, USA	59	Twenty males, thirty-nine females	55.0	Overweight or high risk of developing diabetes	HI-MAIZE® 260 v. AMIOCA® added to yogurt	27.0	12	Double-blinded randomised parallel study	4
Noakes ⁽²¹⁾	1996, Australia	23	Thirteen males, ten females	51.0	Overweight or high risk of developing diabetes	High-amylose maize starch v. low-amylose maize starch diet (in bread, cereal and pasta)	21.5	4	Randomised crossover study, no washout period	2
Bodinham ⁽²²⁾	2014, UK	17	Twelve males, five females	55.0	Type 2 diabetes mellitus	HI-MAIZE® 260 v. AMIOCA® in sachet mixed into beverage	40.2	12	Single-blinded randomised crossover study, 12 weeks wash out	2
Robertson ⁽²³⁾	2005, France	10	Four males, six females	48.5	Healthy	HI-MAIZE® 260 v. AMIOCA® in sachet incorporated into daily food	30.0	4	Single-blinded randomised crossover study, 4 weeks wash out	2
Robertson ⁽²⁴⁾	2012, UK	16	Eight males, eight females	48.9	Overweight or high risk of developing diabetes	HI-MAIZE® 260 v. AMIOCA® in sachet mixed in food or drink	40.0	8	Single-blinded randomised crossover study, 8 weeks washout	2
Dainty ⁽²⁵⁾	2016, Canada	24	Sixteen males, eight females	55.3	Overweight or high risk of developing diabetes	Resistant starch bagel (60% flour replaced with HI-MAIZE® 260) v. control bagel	25.4	8	Double-blinded randomised crossover study, 4 weeks washout	5

Resistant starch and glycaemic control

Table 1. (Continued)

First author	Publication year and region	Number of participants	Sex	Mean age (years)	Health status	Interventions	Dosage of resistant starch (g/d)	Duration (weeks)	Study design	Jadad score
Alfa ⁽²⁶⁾	2018, Canada	42	Eighteen males, twenty-four females	42.0	Healthy	MSPrebiotic® (70 % resistant starch, unmodified potato starch) v. AMIOCA® TF in pouch mixed with other unheated fluid or food	21.0	12	Triple-blinded randomised parallel study	5
Alfa ⁽²⁶⁾	2018, Canada	42	Seventeen males, twenty-five females	75.0	Healthy	MSPrebiotic® v. AMIOCA® TF in pouch mixed with other unheated fluid or food	21.0	12	Triple-blinded randomised parallel study	5
Maki ⁽²⁷⁾	2012, USA	22	All females	49.5	Healthy	HI-MAIZE® 260 v. AMIOCA® in sachet mixed into beverage or food	13.5	4	Double-blinded randomised crossover study, 3 weeks washout	4
Maki ⁽²⁷⁾	2012, USA	11	All males	49.5	Healthy	HI-MAIZE® 260 v. AMIOCA® in sachet mixed into beverage or food	13.5	4	Double-blinded randomised crossover study, 3 weeks washout	4
Johnston ⁽³³⁾	2010, UK	20	Twelve males, eight females	47.7	Overweight or high risk of developing diabetes	HI-MAIZE® 260 v. AMIOCA® in sachet mixed into daily foods	40.0	12	Single-blinded randomised parallel study	2
Nichenametla ⁽³¹⁾	2014, USA	26	Twenty-seven males, fifty-nine females	51.7	Overweight or high risk of developing diabetes	RS4 flour (30 % RS4) v. control flour made into bread, dumpling, etc.	–	12	Double-blinded crossover study, 2 weeks washout	3
Nichenametla ⁽³¹⁾	2014, USA	30	Twenty-seven males, fifty-nine females	51.7	Healthy	RS4 flour (30 % RS4) v. control flour made into bread, dumpling, etc.	–	12	Double-blinded crossover study, 2 weeks washout	3

RS4, type IV resistant starch.

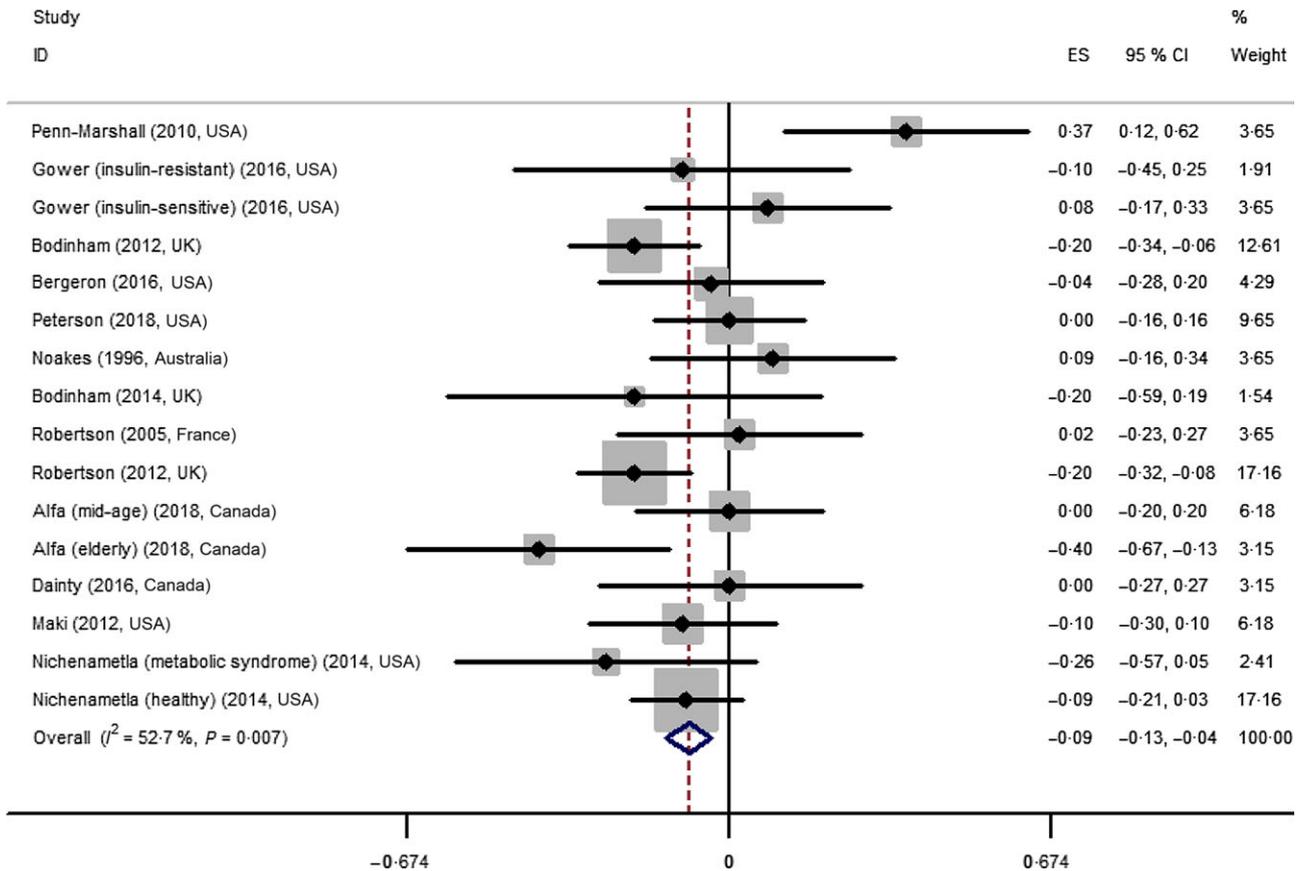


Fig. 2. Forest plot of the effect of resistant starch supplementation on fasting plasma glucose by a random effects model. The P value for the overall effect was 0.001. The diamond denotes the overall estimated effect, and the horizontal lines denote the 95% CI. The grey bar denotes the weight percentage. ES, effect size.

Effects on insulin sensitivity index, acute insulin response and disposition index

The effect of resistant starch on S_I was examined in four trials. A meta-analysis using a random effects model revealed that the effect was not significant (ES 0.30 (95% CI -0.15, 0.75) mU/(l × min), $P = 0.186$) and a low heterogeneity (I^2 16.9%, $P = 0.31$) (online Supplementary Fig. A2). In addition, the effect of resistant starch on AIR was investigated in five trials. A meta-analysis using a random effects model indicated that the effect was not significant (ES 91.31 (95% CI -255.35, 437.98) pmol × min/l, $P = 0.61$) (online Supplementary Fig. A3). A high heterogeneity (I^2 79.4%, $P = 0.001$) was observed. The publication bias was not significant (Begg's test $P = 0.22$ and Egger's test $P = 0.71$). The effect of resistant starch on DI was evaluated in four trials. A meta-analysis using a random effects model showed no significant effect (ES 329.51, 95% CI -80.79, 739.82, $P = 0.12$) (online Supplementary Fig. A4). No heterogeneity was observed (I^2 0%, $P = 0.85$).

Effects on glucose effectiveness

The effect of resistant starch on S_G was examined in five trials. A meta-analysis using a random effects model showed no significant effect (ES 0.002 (95% CI -0.003, 0.006)/min, $P = 0.43$) and a high heterogeneity (I^2 67.5%, $P = 0.02$) (online Supplementary

Fig. A5). The publication bias was not significant (Begg's test $P = 0.79$ and Egger's test $P = 0.51$).

Effects on homeostatic model assessment-β and homeostatic model assessment-insulin resistance

The effect of resistant starch on HOMA-β and HOMA-IR was evaluated in six trials and three trials, respectively. The HOMA-IR values by Alfa *et al.*⁽²⁶⁾ were unusually large, and these trials were excluded from the meta-analysis of HOMA-IR. A meta-analysis using a random effects model showed that the effect on HOMA-β was not significant (ES -0.06, 95% CI -6.51, 6.40, $P = 0.99$) and no heterogeneity (I^2 0%, $P = 0.66$) (online Supplementary Fig. A6). A meta-analysis using a random effects model revealed that the effect on HOMA-IR was significant (ES -0.33, 95% CI -0.51, -0.14, $P = 0.001$) and a high heterogeneity (I^2 69.8%, $P = 0.04$) (online Supplementary Fig. A7). No significant publication bias was detected for HOMA-β (Begg's test $P = 0.71$ and Egger's test $P = 0.83$) and HOMA-IR (Begg's test $P = 0.30$ and Egger's test $P = 0.31$). The limited number of trials prevented a subgroup meta-analysis to investigate the impact of covariates.

Sensitivity analysis

A sensitivity analysis was performed for the meta-analysis of the effect of resistant starch on the indices above including fasting

Table 2. Subgroup analysis to assess the effects of resistant starch supplementation on fasting plasma glucose

	No. of trials	I^2 (%)	Effect size	95 % CI	<i>P</i>
Intervention duration (weeks)					
<8	8	60.5	-0.04	-0.11, 0.04	0.35
≥8	8	38.5	-0.12	-0.18, -0.06	<0.001
Dosage of resistant starch (g/d)					
<28	9	56.6	-0.002	-0.08, 0.07	0.95
≥28	5	0	-0.16	-0.24, -0.08	<0.001
Mean age of subjects					
<50	9	63.3	-0.09	-0.15, -0.03	0.006
≥50	7	39.4	-0.08	-0.16, -0.01	0.03
Health status					
Healthy	7	26.1	-0.07	-0.15, 0	0.05
Overweight or high risk of having diabetes	8	69.7	-0.09	-0.16, -0.03	0.005
Diabetics	1	-	-0.20	-0.59, 0.19	0.32
Study design					
Crossover design	13	51.5	-0.09	-0.15, -0.04	0.001
Parallel design	3	70.6	-0.07	-0.18, 0.05	0.24

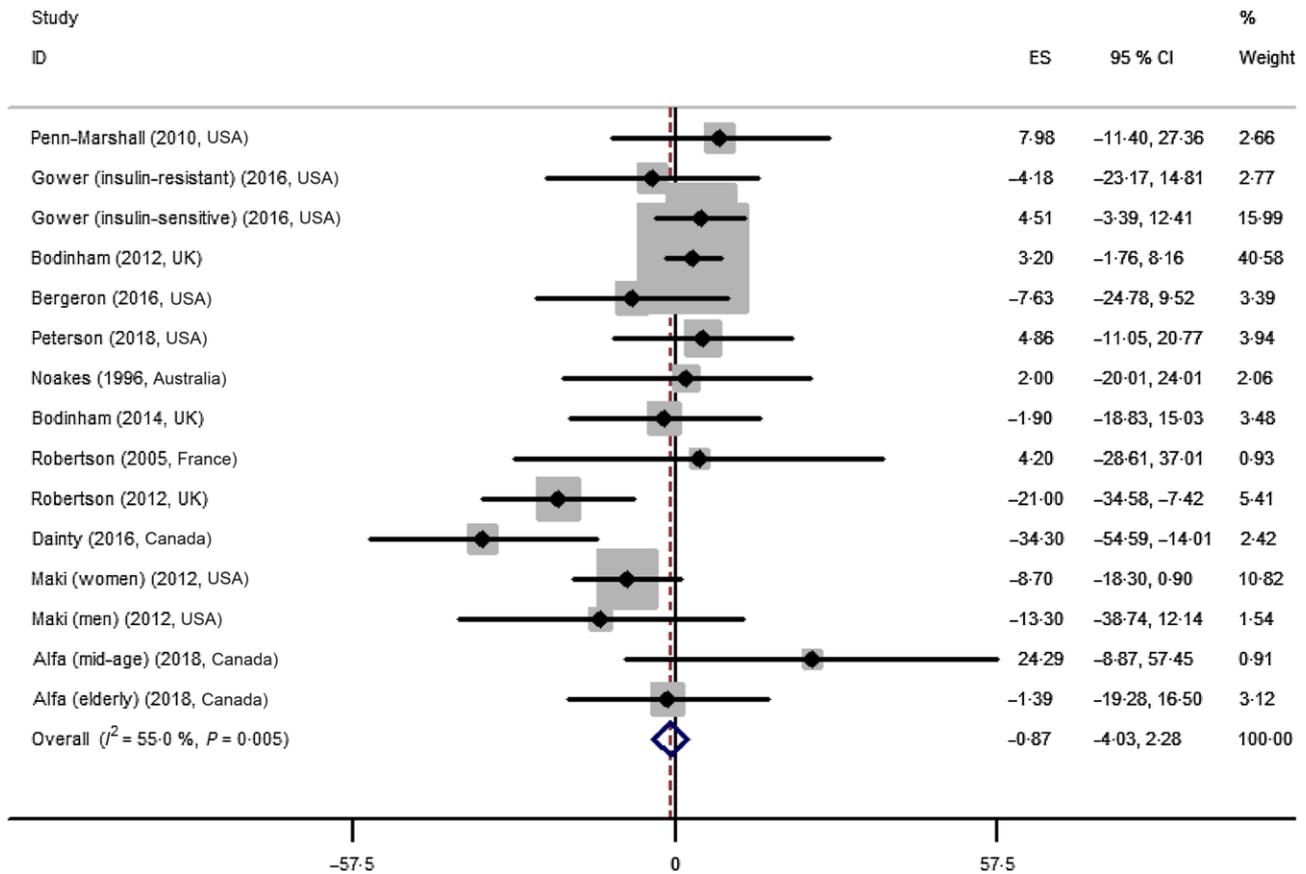


Fig. 3. Forest plot of the effect of resistant starch supplementation on fasting plasma insulin by a random effects model. The *P* value for the overall effect was 0.59. The diamond denotes the overall estimated effect, and the horizontal lines denote the 95 % CI. The grey bar denotes the weight percentage. ES, effect size.

plasma glucose, HbA1c, fasting plasma insulin, S_I , AIR, DI, S_G , HOMA- β and HOMA-IR (data not shown). The results indicated that all the meta-analyses were stable and omitting any one trial did not change the results, except for HOMA-IR. The removal of the trial by Robertson *et al.*⁽²⁴⁾ would make the effect on HOMA-IR insignificant.

Discussion

A meta-analysis including 503 subjects from nineteen human trials in the current literature was performed to resolve the controversy of the effects of resistant starch on glycaemic control. To our knowledge, the current meta-analysis investigated additional outcomes related to insulin resistance/sensitivity

compared with previous meta-analyses and studied the impact of resistant starch dosage on the results. Our results indicated that the consumption of resistant starch could significantly reduce the fasting plasma glucose concentration and HOMA-IR, compared with the consumption of digestible starch. The ES was larger when the dosage of resistant starch was more than 28 g/d. In contrast, the effects of resistant starch were not significant for other insulin-related endpoints including fasting plasma insulin, S_I, AIR, DI, S_G and HOMA- β .

The consumption of resistant starch may reduce fasting plasma glucose by increasing insulin secretion and insulin sensitivity, possibly through the action of SCFA, as demonstrated by previous animal studies^(12,17,41). Consistently, the current meta-analysis showed that resistant starch significantly reduced fasting plasma glucose. Our meta-analysis included results of 357 subjects from sixteen clinical trials, which should be robust. Furthermore, the subgroup meta-analyses indicated that the effect was larger when the intervention duration was more than 8 weeks or the dosage of resistant starch was more than 28 g/d. A short intervention period or small dosage may explain why some previous literature did not observe any significant effects of resistant starch on fasting plasma glucose. The consumption of resistant starch had a significant reducing effect for the fasting plasma glucose in the subgroup of overweight subjects or high risk of developing diabetes. It is possible that these subjects have higher baseline fasting plasma glucose and thus more room for improvement.

Similarly, Halajzadeh *et al.*⁽⁴²⁾ reported a significant reduction in fasting plasma glucose among patients with the metabolic syndrome by the supplementation of resistant starch (ES -0.24 (95% CI -0.39, -0.09) mmol/l) in a meta-analysis, although their meta-analysis included two studies which used resistant dextrin as the intervention substance^(43,44), and two studies which used a mixture of resistant starch and other functional ingredients as the intervention substance^(45,46). Conversely, Snelson *et al.*⁽⁴⁷⁾ focused the effects of type II resistant starch (RS II) and reported a null effect of RS II on fasting plasma glucose (ES -0.03 (95% CI 0.11, 0.05) mmol/l) in a meta-analysis. However, their meta-analysis used endpoint instead of change-from-baseline values to calculate the mean differences between the intervention and control group. After removing two type IV resistant starch studies, our meta-analysis indicated a significant reducing effect of RS II on fasting plasma glucose (ES -0.08 (95% CI -0.14, -0.03) mmol/l) (data not shown).

The effects of resistant starch on HbA1c were not significant based on our meta-analysis. However, the results should be interpreted with caution. First, the meta-analysis only included four trials which showed a high heterogeneity (I^2 70.9%, $P=0.008$). Second, two of the four trials used an intervention period <3 months^(30,31). Since HbA1c represents a 3-month average blood glucose level⁽⁴⁸⁾, the effects of resistant starch cannot be fully reflected with intervention duration shorter than 3 months. The meta-analysis by Halajzadeh *et al.*⁽⁴²⁾ reported a significant reduction in HbA1c in patients with the metabolic syndrome by supplementing resistant starch (ES -0.60 (95% CI -0.95, -0.24) %). However, their meta-analysis included studies which used resistant dextrin

or a mixture of resistant starch and other functional ingredients as intervention substances⁽⁴³⁻⁴⁶⁾.

The meta-analysis did not show any significant effects of consuming resistant starch *v.* digestible starch on insulin-related indices except for HOMA-IR. However, these results should be carefully interpreted because of the limited number of trials (4-6 trials) included in the meta-analysis. In addition, the heterogeneity of the meta-analysis was high (I^2 67.5-79.4%) for a few of these endpoints (fasting plasma insulin, AIR, S_G and HOMA-IR). Future studies should continue investigating the potential effects of resistant starch on insulin secretion and sensitivity.

The present study has the following advantages. First, we strictly focused on studying the effects of resistant starch as a single intervention substance. Second, we found that the dosage of resistant starch was an important covariate in determining the effects of resistant starch. Third, in addition to HOMA endpoints, frequently sampled intravenous glucose tolerance test endpoints were also included in the present study to evaluate the effects of resistant starch on insulin sensitivity and secretion.

Limitations of the study are included below. First, many indices related to insulin secretion and insulin sensitivity were derived from models including the HOMA and the minimal model. Both models have limitations⁽⁴⁹⁻⁵¹⁾. More precise results can be obtained from the sophisticated hyperglycaemic and euglycaemic clamp method. However, the clamp method is time-consuming, requires considerable efforts from the patients and is rarely reported in human intervention trials. Second, the number of available human trials investigating the effects of resistant starch on the insulin-related endpoints was much smaller. The heterogeneity of the studies for many endpoints was high. These reduce the reliability of the meta-analysis.

The overall quality of the included trials was moderate. The median Jadad score was 4. A few trials had a low Jadad score of 2, which was mainly due to the lack of description about the randomisation method, blinding method and dropout. Future trials should include the information. The majority of the available trials included the effects of RS II on glycaemic control. With increasing research and development in resistant starch, the effects of other resistant starch types, particularly type III, IV and V resistant starch, should be more widely investigated in well-controlled human trials. In addition, the subgroup analysis revealed a greater ES by an intervention period of more than 8 weeks and a dosage of more than 28 g/d of resistant starch. Future trials should focus on investigating the effects of resistant starch under these conditions.

In summary, the current meta-analysis showed that the effects of resistant starch on fasting plasma glucose were significant with an ES of -0.09 mmol/l ($P=0.001$) compared with the control. A subgroup analysis revealed that the effect was larger when the dosage of resistant starch was more than 28 g/d or the intervention period was more than 8 weeks. No significant effect was observed for insulin-related endpoints except for HOMA-IR. The current work indicates that the consumption of resistant starch is beneficial for glycaemic control. Future efforts should be put into the investigations of the effects of resistant starch types other than RS II on glycaemic control with appropriate dosage and intervention duration.



Acknowledgements

This work was funded by Qingdao University ((K. X., grant number DC1900009730) and (J. W., grant number DC1900009731)). The funder had no role in the design, analysis or writing of this article.

K. X.: conceptualisation, methodology, formal analysis, writing-original draft preparation and funding acquisition. J. W.: methodology, formal analysis, funding acquisition and writing-review and editing. T. K.: investigation. F. X.: investigation. A. M.: conceptualisation, methodology, writing-review and editing, and project administration.

The authors declare that there are no conflicts of interest.

Supplementary material

For supplementary material referred to in this article, please visit <https://doi.org/10.1017/S0007114520003700>

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