FOOD STANDARDS Australia New Zealand
Te Mana Kounga Kai – Ahitereiria me Aotearoa

Systematic review of the evidence for a relationship between resistant starch and peak postprandial blood glucose concentration

19 December 2017

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Executive Summary

This report addresses two separate but related relationships for foods or properties of foods which might affect peak blood glucose concentration after consuming a food: (i) replacement of digestible starch with resistant starch; and (ii) addition of resistant starch.

Does dietary replacement of digestible starch with resistant starch reduce peak postprandial blood glucose concentration?	
Food-health relationship	Replacement of digestible starch with resistant starch in a food reduces peak postprandial blood glucose concentration
Degree of certainty (GRADE rating)	⊕⊕⊕⊕ High
Component	***Notes***
Body of evidence	Nineteen randomised controlled trials (RCTs) were included in this new systematic review. Thirteen trial arms measuring peak blood glucose concentrations were included in the meta-analysis. Resistant starch doses ranged from 5.8 to 15 g, however some studies did not quantify dose of resistant starch in test foods, instead referring to high amylose starch or commercially prepared resistant starch products. A significant decrease in peak postprandial blood glucose concentration was noted in subjects that consumed foods in which digestible starch was replaced with resistant starch compared to control foods (-1.06 mmol/L, P<0.00001). A greater reduction in peak postprandial blood glucose was observed as the dose of resistant starch was increased. At doses of less than 7.1 g the decrease was 0.78 mmol/L; in the dose range of 7.1–14 g the decrease was 1.05 mmol/L, and at doses greater than 14 g the decrease was 1.71 mmol/L.
Consistency	All of the RCTs showed that replacement of digestible starch with resistant starch in food decreased peak postprandial blood glucose. The overall level of heterogeneity was high (I^2= 95%). Studies were then grouped based on the dose of resistant starch in the test food compared to control (<7.1 g, 7.1–14 g and >14 g). Heterogeneity was not observed at the lower dose range and could not be assessed in the high dose range. The level of heterogeneity decreased in the 7.1–14 g range (I^2= 58%). This could be associated with different food types varying in macronutrient content, different resistant starch types and varying pre-testing dietary instructions.
Causality	RCTs are a strong study design for causality. The meta-analysis showed an effect at every dose tested with the effect increasing with dose. Therefore a causal link was established between replacement of digestible starch with resistant starch in food and decreased peak postprandial blood glucose.
Plausibility	It is plausible that resistant starch, when replacing digestible starch could reduce peak postprandial blood glucose. The physicochemical nature of resistant starch makes it inaccessible to digestive enzymes. Furthermore, there is evidence that resistant starch delays gastric emptying and decreases absorption of macronutrients.
Generalisability	The systematic review included RCTs from Europe, US, Canada, and Asia published between 1992 and 2015. Most studies tested healthy adult subjects and measured acute postprandial glucose measurements only, so results should not be influenced by usual dietary patterns and therefore should be generally applicable to Australia and New Zealand. The effect was also evident in type 2 diabetic participants.

FSANZ has conducted a new systematic review of the evidence for the relationship between replacement of digestible starch with resistant starch in a food and peak postprandial blood glucose. FSANZ followed the required elements of a systematic review given in the

mandatory information requirements in Part 3 of the FSANZ *Application Handbook* and Schedule 6 – Required elements of a systematic review in the *Australia New Zealand Food Standards Code.*

Nineteen replacement trials met the inclusion criteria and were included in the analysis. However not all trials could be included in the quantitative meta-analysis as six studies did not report standard deviations or standard errors and these could not be extracted from the trial details. Thus thirteen trials were included in the replacement review meta-analysis.

Overall the risk of bias was low. Most studies did not report the method of randomisation, whether or how the allocation was concealed and whether participants and/or outcome assessors were blinded. Seven out of thirteen trials included in the meta-analysis were not blinded, providing an opportunity for performance bias. However, given the acute and objective nature of the outcome it is unlikely that performance bias would occur.

Of the thirteen trials included in the meta-analysis all demonstrated a reduction in the peak blood glucose concentration of between 0.4 and 2.5 mmol/L. The overall effect size for diabetic subjects was a decrease of 1.45 mmol/L (95% CI [-1.85, -1.05]) and a decrease of 0.99 mmol/L (95% CI [-1.43, -0.50]) for normoglycaemic subjects.

Although many trials reported small numbers of participants, the total number of participants from the thirteen trials included in the meta-analysis was 225. The six trials that were included but not subject to meta-analysis involved 84 subjects, and each trial resulted in a significant decrease in peak postprandial blood glucose. These results taken together strongly support a causal relationship. There was a high degree of heterogeneity among these studies (I^2=95% overall); heterogeneity is typically higher in intervention studies with food compared to those with pharmaceuticals.

FSANZ considers that there is a ‘high’ degree of certainty that replacing digestible starch with resistant starch in a food reduces peak postprandial blood glucose concentration. Therefore the food-health relationship is substantiated.

Does addition of resistant starch to a food reduce peak postprandial blood glucose concentration?	
Food-health relationship	Addition of resistant starch to a food decreases peak postprandial blood glucose concentration
Degree of certainty (GRADE rating)	⊕⊕⊕ Moderate (no effect)
Component	**Notes**
Body of evidence	Seven randomised controlled trials (RCTs) were included in this new systematic review. Five trial arms measuring peak blood glucose concentrations were included in the meta-analysis. Resistant starch dose ranged from 2.5 to 30.4 g. Evidence was downgraded for imprecision due to low numbers of participants in included studies.
Consistency	None of the RCTs showed that addition of resistant starch in a food caused a significant decrease in postprandial peak blood glucose concentration. Due to the small number of studies in the meta-analysis, heterogeneity could only be assessed in the >14.4 g dose subgroup (I^2=19%). Overall the level of heterogeneity was assessed as moderate (I^2= 43%).
Causality	RCTs were included because they are a strong design for determining causality of a relationship. The meta-analysis in normoglycaemic populations did not show a significant effect on peak postprandial blood glucose concentration from the addition of resistant starch at any dose level. Therefore a causal relationship between addition of resistant starch and a decrease in peak postprandial blood glucose concentration was not established.
Plausibility	It is plausible that addition of resistant starch to food could reduce peak postprandial blood glucose. The physicochemical nature of resistant starch makes it inaccessible to digestive enzymes. There is also evidence that resistant starch delays gastric emptying and decreases absorption of macronutrients.
Generalisability	The systematic review included RCTs from the US, Canada, Europe, South America and Asia published between 1998 and 2017. All studies tested healthy adult subjects and measured acute postprandial glucose measurements only, so results should not be influenced by usual dietary patterns and therefore should be generally applicable to Australia and New Zealand.

FSANZ has conducted a new systematic review of the evidence for a relationship between addition of resistant starch and peak postprandial blood glucose. FSANZ conducted this systematic review concurrently with that examining the effect of replacement of digestible starch with resistant starch but a separate meta-analysis was conducted.

Seven trials met the inclusion criteria and were included in the analysis. However, two trials could not be included in the meta-analysis as they did not report standard deviations or standard errors, and these could also not be extracted from the report. Therefore five trials were included in the meta-analysis.

Overall the risk of bias was low. Although most studies did not outline the method of randomisation, allocation concealment or blinding of participants or outcome assessors, due to the short term nature and objective outcome measurements these were not considered to result in a high risk of bias.

Of the five studies in the meta-analysis, none demonstrated a significant reduction in the peak postprandial blood glucose concentration. The overall effect size was a non-significant decrease of 0.05 mmol/L (95% CI [-0.52, 0.41]), P=0.13. Of the studies included in the analysis but excluded from the meta-analysis, one showed a small reduction in peak blood glucose (0.17 mmol/L with addition of 25 g resistant starch, P value not provided).

There were 68 participants from the five meta-analysed studies. Two further studies with 34 participants were not included in the meta-analysis. No study showed a significant decrease in peak postprandial blood glucose when resistant starch was added to a food indicating that there is not a causal relationship. A small number of studies were included in the meta-analysis. There was a moderate degree of heterogeneity among these studies (I^2=43% overall); heterogeneity is typically higher in intervention studies with food compared to those with pharmaceuticals.

FSANZ considers that there is a ‘moderate’ degree of certainty that a relationship does not exist between the addition of resistant starch to a food and the reduction of peak postprandial blood glucose concentration. Therefore the food-health relationship is not substantiated.

1 Introduction

In 2012, the European Union authorised the health claim 'Replacing digestible starches with resistant starch in a meal contributes to a reduction in the blood glucose rise after that meal' (European Commission regulation (EU) no. 432/2012 of 16/05/2012). FSANZ notes that "the claim may be used only for food in which digestible starch has been replaced by resistant starch so that the final content of resistant starch is at least 14% of total starch". The EFSA conclusions were drawn from the scientific literature, however a systematic review of the literature was not performed (EFSA 2011).

In this report FSANZ considers two food-health relationships related to resistant starch and peak postprandial blood glucose concentration. First, FSANZ is considering whether a relationship between replacement of digestible starch with resistant starch in a food reduces peak postprandial blood glucose after consuming the food can be incorporated into Schedule 4 of Standard 1.2.7 Nutrition, Health and Related Claims in the Australia New Zealand Food Standards Code (the Code). The EU claim states that 'replacing digestible starch with resistant starch in a meal contributes to a reduction in the blood glucose rise after that meal'. FSANZ considered that a food in which digestible starch was replaced with resistant starch but was not eaten as part of a meal could have the same effect. Therefore the first relationship investigated by FSANZ (referred to in this document as relationship A) is that replacement of digestible starch with resistant starch in a food reduces the peak postprandial blood glucose concentration after consuming the food. The second relationship that FSANZ is considering (referred to as relationship B) is that the addition of resistant starch to a food, without removing any existing digestible starch, reduces peak postprandial blood glucose concentration after consuming the food.

Studies were categorised as addition or replacement studies based on macronutrient information provided in the publications. Studies where digestible starch content decreased by a similar number of grams to the increase in resistant starch in the test food were considered to be replacement studies. Addition studies were those in which digestible starch was constant in both control and test food but resistant starch was higher in the test food. The literature search for both relationships was carried out concurrently, and where necessary, the relationships are presented (tables, plots, diagrams, GRADE) separately.

Investigators used a number of different measures of postprandial blood concentration. These included rate of rise, peak, time to peak, incremental peak, area under the curve (over differing time points), incremental area under the curve, 2-hour glucose, mean glucose, incremental glucose and others. After consultation with FSANZ's Health Claims Scientific Advisory Group, peak glucose concentration was chosen as the most appropriate measure of postprandial blood glucose rise.

No relevant systematic reviews were identified which could be updated.

The purpose of this paper is to systematically review the evidence for two relationships:

A: replacement of digestible starch with resistant starch in a food reduces peak postprandial blood glucose concentration and

B: addition of resistant starch to a food reduces peak postprandial blood glucose concentration

1.1 Property of food

Starch is one of the main forms of carbohydrate in the diet. It is composed of two major polysaccharides: amylose, which has a mainly linear structure of glucose units linked by α(1–4) bonds and amylopectin which has a highly branched structure of glucose units linked by α(1– 4) and α(1– 6) bonds. Starch typically contains 15 – 20% amylose and 80 – 85% amylopectin. Starch generally occurs in plants as granules that can vary in size, shape and physicochemical properties (Stark and Lynn 1992).

Resistant starch is the fraction of starch that is not digested when it passes through the small intestine (Raigond et al. 2015). The undigested portion is then available for fermentation by bacteria in the large intestine. Bacterial fermentation of resistant starch results in a number of by-products, including short-chain fatty acids and gases.

Starch with high amylose content is resistant to digestion while high amylopectin content starch is highly digestible. Resistant starch is found in many common foods including vegetables (especially potatoes), grains, cereals, legumes, seeds and nuts. Starch digestibility is also influenced by non-starch components in the diet and processing methods, as well as the structure of the starch. Five resistant starch (RS) sub-types have been defined (Englyst et al. 1992; Gelders et al. 2005).

Type 1 resistant starch (RS1) is physically inaccessible to digestion and is found in whole or partially milled grains, seeds and legumes.

Type 2 resistant starch (RS2) is granular native starch that is protected from digestion due to the conformational structure of the granule. It can be found in green bananas, raw potatoes and in high-amylose starch. Several naturally-occurring mutations in corn and rice have led to varieties much higher in amylose (and thus resistant starch) than others.

Type 3 resistant starch (RS3) refers to non-granular starch that is formed during retrogradation in food processing. Retrogradation occurs when starch granules are disrupted by cooking above their gelatinization temperature. Upon cooling, the starch granules re-associate into crystalline structures that resist hydrolysis by amylase. RS3 can be found in cooked and cooled pasta, potatoes, high-amylose cornstarch, legumes and rice.

Type 4 resistant starch (RS4) is chemically modified starch (i.e. semi-synthetic) that resists digestion (Brown 2004). Several RS4s have been created synthetically for use in food (Lattimer and Haub, 2010).

Amylose can also form helical complexes with lipids in native and processed starches, thereby enhancing resistance to digestion. These complexes are referred to as RS5 (Gelders et al. 2005). RS5 is not considered in this review due to difficulties in quantification (FSANZ 2017).

The average daily intake of dietary fibre including some resistant starch in Australia in 2011-2012 among men and women aged 19 and over was 24.8 g and 21.1 g respectively (Australian Bureau of Statistics, 2014). A study using 1995 data from the Australian health survey estimated that the Australian intake of resistant starch was 10.7 g/day for adult males over 19 years and 8.2 g/day for females (Roberts et al. 2004). Resistant starch intake in New Zealand was estimated to be 6.5 g and 4.8 g for males and females age 10 and over (Baghurst and Baghurst 1996). However, in the context of the present systematic review the amount of resistant starch per serving of food is the relevant quantity.

1.2 Health effect

Blood glucose rise after a meal is a normal physiological response as glucose is liberated from food and then absorbed or generated from the carbohydrate contained in the food (Green and Venn 2007). This rise in blood glucose promotes insulin release from the islet cells into the bloodstream which in turn facilitates uptake into muscle and fat cells. When blood glucose concentrations fall too low, the peptide hormone glucagon is released from alpha cells in the pancreas, telling the liver to convert stored glycogen into glucose. Thus the interplay between insulin and glucagon keeps blood glucose concentrations tightly controlled.

However, in the case of insulin insensitivity, the glucose present in the blood is inefficiently transported into cells, most likely due to a lipid-induced breakdown in insulin-initiated signal transduction (Samuel and Shulman, 2012). Therefore it is relevant to examine whether ingestion of resistant starch is associated with unexpected changes in insulin concentrations.

There are a number of ways of measuring changes in blood glucose concentration after a meal. Researchers report fasting serum values and then, following an intervention, typically every 5, 10, 15 or 30 minutes for anywhere between 120 minutes to 5 hours. Serial blood samples are taken using an indwelling catheter under laboratory conditions. In the literature, commonly reported measures of glucose response include glucose concentrations at various times after ingestion, time to peak, rate of rise, peak, incremental peak, mean, incremental mean, 2-hour glucose concentration, area under the blood glucose curve (AUC)(which may be over differing time points), and incremental area under the blood glucose curve (iAUC).

The highest value measured is often referred to as ‘peak glucose’ even though most studies measure glucose intermittently and so cannot determine the actual peak. In addition, the true peak might occur at different times in people consuming different types of food. There is no agreement among researchers as to which of these methods is the most relevant for assessing the biological usefulness of changes in post-prandial glucose concentrations.

After consultation with FSANZ’s Health Claims Scientific Advisory Group, peak blood glucose concentration was chosen as the most appropriate measure of postprandial blood glucose response because this is the most uniformly reported measurement and also measures immediate postprandial effect. FSANZ has selected the highest reported blood glucose concentration measurement after ingestion of a food as the parameter to quantitatively evaluate in the meta-analysis. This will hereafter be referred to as the peak. FSANZ notes that the true peak may not have been measured or reported.

Normal fasting blood glucose concentration was defined as < 6.1 mmol/L, impaired glucose tolerance was defined as 6.1 to <7 mmol/L and diabetic was defined as ≥7.0 mmol/L (World Health Organization, 2006).

1.3 Proposed relationship

The food-health relationships being assessed in this report are:

- replacement of digestible starch with resistant starch in a food reduces peak blood glucose concentration after consuming the food
- addition of resistant starch to a food reduces peak blood glucose concentration after consuming the food

2 Evaluation of evidence

A systematic review of the literature was performed to assess the proposed food-health relationships. The same systematic review of the literature was used for both food-health relationships. The effect of resistant starch on blood insulin concentrations was also

assessed because an increase in postprandial blood insulin concentration that occurred with a decrease in peak blood glucose concentration would be considered an adverse effect.

2.1 Methods

2.1.1 Search strategy

A search was conducted in PubMed and Cochrane Central on 25th February 2016 and repeated in EMBASE on the 29th February 2016. Search terms included those that related to resistant starch as the property of the food, and blood glucose levels as the health effect. The search strategies are provided in Appendix 1.

2.1.2 Inclusion and exclusion criteria

The eligibility criteria are summarised in Table 1.

Population
Study participants could be adults or children (2 years of age or older), and could include individuals with chronic non-communicable diseases such as diabetes, hyperlipidaemia or hypertension. Trials whose subjects had glycogen storage disease were excluded. Trials in acutely ill populations were also excluded.

Intervention and Comparator
Papers were included if the test material was described as resistant starch, high amylose starch or where starches with varying levels of amylose content were studied. Papers in which only starch was mentioned were excluded, for example, when test substances were described as corn starch, uncooked corn starch, wheat starch or potato starch. Test materials that were described as dextrins (e.g. maltodextrin or cyclodextrins) or inulin were excluded. Studies that tested resistant starch types 1–4 but not RS5 were included.

The food used in resistant starch interventions could be in different forms as long as an appropriate control was also tested. Examples of interventions include: resistant starch-rich food versus equivalent food without resistant starch, resistant starch made into food or resistant starch powder consumed with food (e.g. sprinkled on breakfast cereal) versus food with no added powder, resistant starch supplements given as capsules versus placebo capsules. Consequently, not all the studies were blinded.

In order for studies to be included macronutrients must have been closely matched in comparison foods. Matching content within 10% for protein, fat, carbohydrate and dietary fibre (excluding resistant starch) was considered a minimum requirement. Studies were excluded in cases where macronutrient content was not provided or could not be sourced elsewhere e.g. commercial product website.

Studies in which the test and control foods contained an ingredient from different sources were permitted, e.g. wheat flour versus corn flour. Studies in which the test and control foods were in different forms (e.g. biscuit vs bread) were permitted as long as the macronutrient compositions were closely matched.

Trials were included if they could be categorised as either addition or replacement studies based on macronutrient information. Replacement studies were identified as those in which digestible starch decreased by a similar amount (±10%) of added resistant starch compared to control food. For example, a study which had a control food containing 10 g digestible starch would be considered a replacement study if the test food contained 5 g resistant starch and 5 g digestible starch but would be considered an addition study if the test food contained 10 g digestible starch and 5 g resistant starch. Addition studies were those in which digestible starch levels were the same in both the control and test food but resistant

starch was higher in the test food. Studies which did not fall into either category were excluded.

Outcome and Time
The required outcome for each study is peak postprandial blood glucose. All included trials tested blood glucose at intervals between 10 and 30 minutes. The peak was determined to be the highest blood glucose concentration during the observed period, even if this occurred at a different time point between the intervention and the control. Papers were excluded if they did not include multiple measurements of blood glucose concentration in the 90 minutes following consumption of test food. Papers that only provided area under the curve results were also excluded.

The minimum period of time between trials with the same group of subjects was 4 hours which is considered sufficient for blood glucose concentrations to stabilise (Harris et al. 1993).

Study Design
Only human controlled trials were included in the systematic review. In order to be included trials must also have stated that they were randomised or have described an allocation method that suggested randomisation (such as Williams Latin Square) and have an appropriate control group. Trials with a concomitant intervention were excluded also, unless the intervention did not differ between control and test groups. Parallel and cross-over designs were acceptable but sequential designs were excluded. The absence of double-blinding was not treated as an exclusion criterion because the outcome (postprandial blood glucose concentrations) is measured within two to three hours following a meal by standard laboratory methods and there is no opportunity for non-compliance or other participant factors to affect the results. Multi-meal studies in which subjects consumed several test foods over several days, before blood glucose was measured were excluded from the review. When data were missing from a paper the authors were contacted.

Table 1 PICOTS criteria for study selection

Population	Non-acutely ill adults or children ≥ 2 years
Intervention	Consumption of food where digestible starch has been replaced by resistant starch or resistant starch has been added to food.
Comparator	The same food without the replacement or addition of resistant starch.
Outcome	Peak postprandial blood glucose concentration.
Time	At least 90 minutes of postprandial assessment reported.
Study design	Randomised controlled trials.

2.1.3 Additional material

The WHO International Clinical Trials Registry Platform was also searched using the search terms resistant starch, RS1, RS2, RS3, RS4 and amylose individually to identify potential unreported or impending clinical trials. No trials were identified.

A search was performed on the retracted publication website (retractionwatch.com) using the search terms resistant starch, RS1, RS2, RS3, RS4 and amylose individually to identify any relevant retracted papers. None were identified. Twenty six additional papers were identified by hand-searching the reference lists of the publications that were full-text reviewed.

2.1.4 Study selection, data extraction and quality assessment

Records identified during the search process were imported into EPPI-Reviewer 4 (http://eppi.ioe.ac.uk/cms/er4). Following removal of duplicates, records were screened on title and abstract. Candidate full-text articles were retrieved and assessed against the inclusion/exclusion criteria. Screening was conducted by one investigator and cross-checked by a second investigator.

Peak postprandial blood glucose data were extracted by one investigator and cross-checked by a second investigator. Numerical data were extracted when available. If the data were present only in graphs, the means and standard deviations or standard errors were extracted using the online program WebPlotDigitizer Version 3.12[1]. All included studies tested blood glucose concentration at intervals of 15 or 30 minutes (from fasting until a final postprandial time point of either 120, 180, or in one case, 300 minutes) and so the peak was defined as the highest blood glucose concentration measured during the observed period. If some data (e.g. means) were presented numerically and other data only available in a graph, then the numerical value was extracted, even when this meant that a reported mean was used with a standard error extracted from a graph. Where error bars for several arms overlapped and it was not clear which mean the bar related to, the widest error was selected for extraction. Data were extracted from trials presenting absolute values at each time point as well as those presenting incremental increases in blood glucose concentrations from baseline. Blood glucose concentrations reported in mg/dL were converted to mmol/L by multiplying by 0.0555.

All data concerning insulin were examined to ensure glucose lowering was not affected through increased insulin secretion. Increased insulin secretion would be an important adverse effect. All other adverse effects mentioned by study authors were also extracted.

Some studies had several intervention arms. For example, studies may have measured different types or amounts of resistant starch. To prevent double counting of the control group by using it to calculate more than one difference (Higgins and Green 2011), only one intervention group was chosen from multi-arm studies using the following criteria:

- If there was a difference in macronutrient content between arms, then the arm in which macronutrient levels most closely matched between test and control was selected.
- If different quantities of resistant starch were tested, and macronutrient content was equal, then the arm with the highest dose of resistant starch was chosen, owing to the focus of this review.
- If the same form of resistant starch was tested in different meals then the arm most closely resembling a true meal was chosen (e.g. orange juice + glucose ± resistant starch; beef + juice ± resistant starch – the latter would be chosen), providing the control was appropriate.

Intervention arms that were used in meta-analysis are described in Table 2.

Some papers reported studies in more than one group of subjects. These papers were regarded as having more than one stratum.

Trials were assessed for risk of bias according to the Cochrane Handbook (Higgins and Green, 2011), and were collated using Review Manager Version 5.3, the systematic review software developed by The Cochrane Collaboration (The Nordic Cochrane Centre 2014).

[1] http://arohatgi.info/WebPlotDigitizer/index.html

FSANZ used the Grading of Recommendations Assessment, Development and Evaluation system (GRADE) to assess the quality of the body of evidence to determine the degree of certainty in the food-health relationship (Guyatt et al. 2011a; Guyatt et al. 2011b; Guyatt et al. 2011c; Guyatt et al. 2011d; Guyatt et al. 2011e; Guyatt et al. 2008) (Section 3.1 and Appendix 4).

2.1.5 Statistical analyses

Review Manager Version 5.3, the systematic review software developed by The Cochrane Collaboration (The Nordic Cochrane Centre 2014) was used to calculate standard error only where variance data were presented as confidence intervals or as a p-value. Following data extraction, changes in glucose concentration were calculated if values were not stated by study authors.

For cross-over studies differences in blood glucose concentrations were calculated as:

$$\text{Difference} = \text{Glucose}_{(\text{peak in intervention})} - \text{Glucose}_{(\text{peak in control})}$$

and its standard error of the mean (SEM) as:

$$\text{SEM} = \sqrt{[(\text{SEM}_{(\text{peak in intervention})}^2 + \text{SEM}_{(\text{peak in control})}^2) - 2r(\text{SEM}_{(\text{peak in intervention})})(\text{SEM}_{(\text{peak in control})})]}$$

For parallel studies reporting the change in each group the difference between the groups was calculated as:

$$\text{Difference} = \text{Glucose}_{(\text{change in intervention group})} - \text{Glucose}_{(\text{change in control group})}$$

and its standard error as:

$$\text{SEM} = \sqrt{[(\text{SEM}_{(\text{change in intervention group})}^2 + \text{SEM}_{(\text{change in control group})}^2)]}$$

For parallel studies, which did not report change values and their standard error, the difference in blood glucose between groups was calculated as:

$$\text{Difference} = (\text{Blood glucose}_{(\text{end, intervention})} - \text{Blood glucose}_{(\text{baseline, intervention})}) - (\text{Blood glucose}_{(\text{end, control})} - \text{Blood glucose}_{(\text{baseline, control})})$$

And its standard error as:

$$\text{SEM} = \sqrt{(\text{SEM1}^2 + \text{SEM2}^2)}, \text{ where}$$

$$\text{SEM1} = \sqrt{[(\text{SEM}_{(\text{end, intervention})}^2 + \text{SEM}_{(\text{baseline, intervention})}^2) - 2r(\text{SEM}_{(\text{end, intervention})})(\text{SEM}_{(\text{baseline, intervention})}]}$$

$$\text{SEM2} = \sqrt{(\text{SEM}_{(\text{end, control})}^2 + \text{SEM}_{(\text{baseline, control})}^2) - 2r(\text{SEM}_{(\text{end, control})})(\text{SEM}_{(\text{baseline, control})})}$$

The correlation coefficient (r) was imputed as 0.6 based on the intra-class correlation coefficient obtained from a linear mixed model fitted on 150 people with between one and 12 replicate measurements of capillary blood glucose concentration taken at baseline and after 30 minutes after consuming 50 g glucose in a fasting state (data supplied by Sydney University's Glycaemic Index Research Service, personal communication, 2015).

Meta-analysis was performed using a random effects model and generic inverse variance method to allow combination of the varied data reporting methods, and to ensure cross-over studies were not given less weight compared to parallel studies. Review Manager was used for meta-analysis.

I^2 was used to assess heterogeneity among the strata. It describes the "percentage of total variation across studies that is due to heterogeneity rather than chance" and 0%, 25%, 50% and 75% could be interpreted as indicating no, low, medium and high heterogeneity respectively (Higgins et al. 2003).

2.1.6 Subgroup analyses

Ten subgroup analyses were identified *a priori* to explore differences in effect size in both addition and replacement studies:

- Dose of resistant starch
- Type of resistant starch
- Presentation of food (food vs drink)
- Populations with normal fasting blood glucose vs type 2 diabetic subjects
- Blood extraction method (venous vs capillary)
- Gender
- Funding source
- High vs low quality studies
- Study design (parallel vs cross-over design)
- Adults vs children

The following subgroup analyses were not carried out as the number of studies fulfilling these criteria was too small:

- Type of resistant starch (addition studies)
- Populations with normal fasting blood glucose vs type 2 diabetic subjects (addition studies)
- Study design (replacement studies)
- Adults vs children (addition and replacement studies)

2.2 Results

2.2.1 Search results

The screening of articles retrieved from the search strategies is detailed in Figure 1. Of the 837 articles that were screened (after 484 duplicates were removed), 672 articles were excluded on title/abstract and another 140 after reading the full text (Figure 1). Studies excluded after full text examination are listed in Appendix 2. FSANZ reported only one reason for the exclusion of each study although studies may have been able to satisfy more than one exclusion criterion. A total of 25 articles describing 26 trials were included in the review.

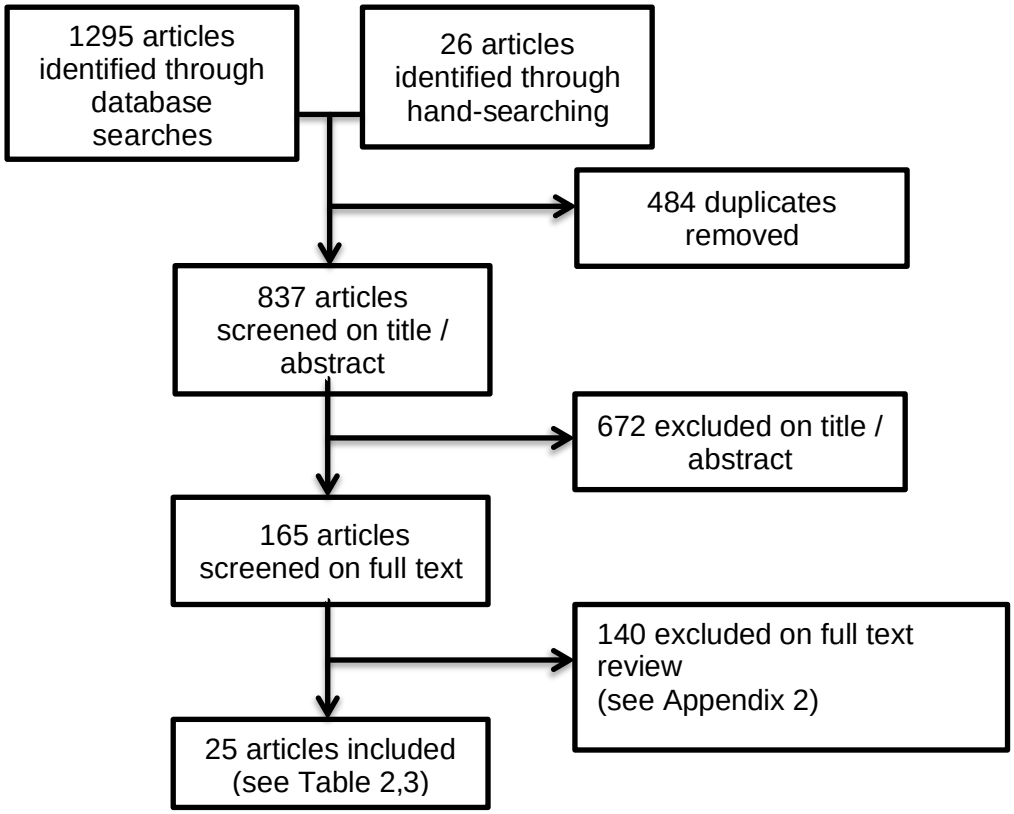

Figure 1 PRISMA diagram of study identification process

2.2.2 Included studies

Twenty five publications were included in the systematic review. These publications described twenty six trials (Achour et al. 1997; Åkerberg et al. 1998; Behall et al. 2002; Behall et al. 2006; Bodinham et al. 2010; Brighenti et al. 2006; Giacco et al. 1998; Goddard et al. 1984; Hallstrom et al. 2011; Haub et al. 2012; Hospers et al. 1994; Kinnear et al. 2011; Klosterbuer et al. 2012; Krezowski et al. 1987; Li et al. 2010; Lin et al. 2015; Luhovyy et al. 2014; Marchini et al. 1998; Maziarz et al. 2017; Seal et al. 2003 (two trials); Seewi et al. 1999; Shimotoyodome et al. 2011; Tachibe et al. 2010; Tachibe et al. 2011; van Amelsvoort et al. 1992).

The twenty five studies described results from 411 adult subjects, 32 of whom were type 2 diabetic and 379 who were normoglycaemic.

Data were extracted from 18 trials with 18 intervention arms included in the meta-analyses; 13 of which were replacement trials and 5 were addition trials. The remainder were not included in the meta-analysis as the standard error or standard deviation was not provided and could not be calculated from quoted P values.

2.2.3 Quality assessment of individual studies

FSANZ assessed the quality of each included study based on the following considerations

- a clearly stated hypothesis

- minimisation of bias
- the study participants' background diets and other relevant lifestyle factors
- adequate control for confounding
- study duration and follow-up adequate to demonstrate the health effect
- the statistical power to test the hypothesis.

Adequate hypothesis
All of the included studies had a clearly stated hypothesis and purpose for testing the effect of resistant starch on postprandial blood glucose. Studies were categorised as replacement or addition studies based on nutrient composition of test and control foods. Replacement studies were identified as those in which digestible starch decreased by a similar amount of added resistant starch compared to control food. Addition studies were those in which digestible starch was constant between test and control foods. All included studies reported peak glucose concentrations for each of the treatments.

Minimisation of bias
The risk of bias analysis was used to assess the quality of the evidence and found there was a low degree of variability in the quality of included trials (Figure 2A - 2D, Appendix 3).

Random sequence generation (selection bias)
Trials were only included in the review if they stated that they were randomised. Only six studies (Behall et al. 2002; Behall et al. 2006; Haub et al. 2012; Hospers et al. 1994; Maziarz et al. 2017; Seewi et al.1999) provided details of the method of randomisation however FSANZ considered that the risk of bias was low for selection bias (random sequence generation) as there was no subject choice in the quantity consumed in any included study as well as the short timeframe of the test phases.

Allocation concealment (selection bias) and blinding of participants and personnel (performance bias)
Most studies used a cross-over design in which the same individuals received both intervention and control substances. FSANZ concluded that the overall risk of bias in the body of evidence was low for selection bias (allocation concealment) and performance bias (blinding of participants and personnel) due to the use of cross-over design.

Approximately 35% of trials described blinding participants and/or study personnel, however, the difficulty of blinding in dietary trials is acknowledged. Approximately 19% of trials reported blinding outcome assessors to the intervention (laboratory staff or statisticians; detection bias). Blinding is important when participants have to comply with their allocated treatment over time. This is less important in the current set of trials in which blood glucose was measured in the hours that immediately follow consumption of foods and subjects do not have a choice in quantity consumed.

The risk of performance bias was rated low despite lack of blinding of the subjects and personnel relating to the subjects because the studies were very short term (several hours), did not require compliance to a longterm dietary or other protocol prior to the test and the vehicle was given in a pre-specified quantity.

Blinding of outcome assessment (detection bias)
Trials were only included if blood glucose was measured several times in the 2 hours following consumption of foods therefore limiting bias due to differences in subject compliance or other lifestyle factors that might arise in longer term studies.

The risk of outcome assessment bias was rated low if venous blood was drawn but high if a finger-prick sample was taken and blinding of the operator was not described because variations in technique can alter the glucose concentration of a sample collected by finger-

prick (Colagiuri et al. 2003). Eight studies described collection of blood using finger-prick technique. Variation in results was assessed for these studies using subgroup analysis.

Incomplete outcome data (attrition bias) and selective reporting (reporting bias)
The risk of attrition and selective reporting was considered to be low in the body of evidence. Attrition rates were very low in all studies. Seventy seven percent of trials either indicated that all participants completed the study or provided details of loss to follow up that did not relate to study participation (Achour et al. 1997; Akerberg et al. 1998; Giacco et al. 1998; Goddard et al. 1984; Marchini et al. 1998; Seewi et al. 1999). Studies that were not correctly reported were not included in the review.

Participants' background diets and relevant lifestyle factors
All studies except for one (Lin et al. 2015) indicated that subjects fasted overnight (10-12 hr) prior to testing. Seventeen of the included studies (68 %) either provided instructions to participants relating to background diets (e.g. low fibre diet, no alcohol) or provided standardised meals prior to testing. Standardised meals were either provided as the final meal prior to fasting (Achour et al.1997; Bodinham et al. 2010; Luhovvy et al. 2014; Shimotoyodome et al. 2011; Tachibe et al. 2010; Tachibe et al. 2011), or for two days (Behall et al. 2002; Behall et al. 2006; Brighenti et al. 2006; Giacco et al. 1998) prior to testing. Most single standardised meals were consumed in the evening prior to testing except for one study (Luhovvy et al. 2014) in which participants consumed a standardised breakfast following an overnight fast and 4 hours prior to testing.

Most studies that provided background dietary information also provided instructions regarding minimisation of excessive exercise in the day or days before testing (Achour et al. 1997; Bodinham et al. 2010; Brighenti et al. 2006; Hallstrom et al. 2011; Li et al. 2010; Marchini et al. 1998; Seal et al. 2003; Shimotoyodome et al. 2011; Tachibe et al. 2010; Tachibe et al. 2011; van Amelsvoort et al. 1992). Instructions relating to background diet and physical activity are important as the food consumed shortly before a carbohydrate test as well as physical exertion can have an impact on outcomes.

Studies that provided neither standardised meals prior to testing or dietary guidance to participants were considered to be of lower quality (Åkerberg et al. 1998; Haub et al. 2012; Kinnear et al. 2011; Lin et al. 2015; Maziarz et al. 2017; Seal et al. 2003; Seewi et al. 1999), with the remaining studies considered to be of high quality (Achour et al. 1997; Behall et al. 2006; Bodinham et al. 2010; Brighenti et al. 2006; Giacco et al. 1998; Goddard et al. 1984; Hallstrom et al. 2011; Hospers et al. 1994; Klosterbuer et al. 2012; Krezowski et al. 1987; Li et al. 2010; Luhovyy et al. 2014; Marchini et al. 1998; Shimotoyodome et al. 2011; Tachibe et al. 2010; Tachibe et al. 2011; van Amelsvoort et al. 1992).

Control for confounding
Randomisation in trials is used to control for confounding. FSANZ included studies where authors stated that the trial had been randomised. Furthermore, most included studies were designed as crossover RCTs that further control for confounders. One included study used a parallel design (Maziarz et al. 2017). In this study a range of baseline anthropometric and body composition characteristics for participants in the test and control arms were measured. The authors noted non-significant differences between groups and therefore confounders were also controlled for in this study.

Most included studies provided details of washout period between consumption of test foods which usually ranged from 1 day to 1 week, although some studies had more than one week between test periods (Goddard et al. 1984, 1-2 weeks; Klosterbuer et al. 2012, 3+ weeks). Two studies provided sufficient detail in study design to indicate that foods were tested on different days (Behall et al. 2006; Haub et al. 2012). Testing the effects of postprandial blood glucose only requires a washout period of a few hours after which time blood glucose

concentrations return to baseline following intervention. Therefore all washout periods described in included studies was sufficient to eliminate the effects of the previous treatment.

FSANZ noted that the level of detail regarding macronutrient composition varied among publications, with older studies often containing less detailed information. FSANZ only included studies in which sufficient macronutrient composition was provided to indicate a close match (±10%) between test and control foods. In studies that contained several strata the stratum with the most closely matched macronutrient composition to control foods was selected.

Study duration and follow-up adequate to demonstrate the health effect
Due to the short term nature of the study design required to assess postprandial blood glucose levels following consumption of test foods all studies which tested postprandial blood glucose several times for 2 hours were included in the review.

Statistical power to test the hypothesis
Studies that were included were considered to be significantly powered for meta-analysis.

FSANZ concluded that the overall risk of bias in the body of evidence was low (Figure 2A - D). To determine whether the relationship is present in high quality studies, studies were classified as high quality if study participants were provided with standardised meals prior to testing or were provided with instructions regarding background diets.

Table 2 Properties of the studies included in the **replacement** of digestible starch by resistant starch review analysis

Reference and study location	Study design*	Objectives	Participant Characteristics & sample size ǂ	Interventions	Methods **	Results	Arm used for review
Achour 1997 (France)	Cross-over	Determine the metabolic effect of digestible and partially indigestible cornstarch	8 healthy adults (2 female, 6 male)	Morning and evening test meals containing 50 g retrograded or pre-gelatinsed cornstarch (RS3)	**Glucose**: hourly for 8 hr pp (capillary); hexokinase method **RS**: Not measured	**Peak glucose**: 1.3 mmol/L lower than control ($P < 0.05$) **Insulin:** lower than control at 60 min and 120 min ($P < 0.05$)	Partially indigestible vs digestible cornstarch porridge meal
Akerberg 1998 (Sweden)	Cross-over	Determine the metabolic effect of amylose/amylopectin ratios and baking conditions	9 healthy adults (6 female, 3 male)	Breakfast meal including bread with 70% high amylose flour providing 50 g total starch (RS2/3)	**Glucose**: 0, 30, 45, 70, 95, 120,180 min pp; oxidase-peroxidase **RS**: Akerberg method (Akerberg et al. 1998)	**Peak glucose**: 1.4 mmol/L lower than control ($P < 0.05$) **Insulin:** Non-significantly lower than control at 30, 50 min. Lower than control at 90 min ($P < 0.05$)	Long-time low temperature baked high-amylose barley bread vs white wheat bread
Behall 2002 (USA)	Cross-over	Study the effect of consumption of breads with varying amylose content on glucose and insulin	25 healthy adults (13 male and 12 female) One additional subject was recruited but withdrew due to the large number of blood samples required	Bread with varying amylose content	**Glucose**: 0, 30 60,120,180 min pp **RS:** Akerberg method (AOAC 991.43 data can underestimate resistant starch (FSANZ, 2017)	**Peak glucose:** 0.84 mmol/L lower than control (P value not provided) **Insulin:** lower than control 60 min (P value not provided)	50% amylose vs 40% amylose Concern was raised by the author regarding the quantification of 30% amylose bread therefore this was not used
Behall 2006 (USA)	Cross-over	Determine the acute metabolic effect of resistant starch and beta glucan	20 women (10 normal and 10 overweight) One subject withdrew with reason provided that was unrelated to study	Glucose solution or breakfast muffin with varying amounts RS and/or beta glucan (RS2)	**Glucose**: 0, 30 min, 1, 2, 3 hr pp; automated spectrophotometric method **RS**: AOAC 991.43	**Peak glucose**: 0.88 mmol/L lower than control ($P < 0.05$). **Insulin**: Non-significantly lower than control at 30 min, 1 hr, 3hr, 4hr.	Low beta glucan with high vs low RS

						Lower than control at 2 hr (P < .05)	
Brighenti 2006 (Italy)	Cross-over	Study the second meal effect of high and low GI carbohydrates eaten during the previous meal	10 healthy adults (2 female, 8 male)	Breakfast test meals differing in RS content (RS2)	**Glucose**: 0, 30, 60, 90,120 min pp; YSI 2300 **RS**: method not provided	**Peak glucose:** 0.94 mmol/L lower than control P<0.05 **Insulin:** Significantly lower than control at 1 hr (P < 0.02), 2hr (P < 0.03)	Low glycaemic index (LGI) vs high glycaemic index(HGI)
Giacco 1998 (Italy)	Cross-over	Evaluate the metabolic response to high RS meal and the SME in subjects with type 2 DM	10 adults with T2DM (4 female, 6 male)	Two meals differing only is RS content	**Glucose**: 0, 30 min, 1, 2, 3, 4 hr pp; standard enzymatic / colorimetric methods **RS**: provided by manufacturer	**Peak glucose:** 1.71 mmol/L lower than control P<0.03 **Insulin:** Non-significantly lower increments compared to control (P = 0.16). Details not provided	No additional arms in experiment
Goddard 1984 (USA)	Cross-over	Evaluate the effects of amylose and amylopectin content on glucose response to rice	33 healthy adults (17 female, 16 male)	Three types of rice differing in relative amounts of amylose and amylopectin	**Glucose**: 0,30, 60, 120, 180 min pp; Beckman glucose analyser **RS**: quantification not provided. % amylose method not provided	**Peak glucose:** 0.54 mmol/L lower than control P<0.05 **Insulin:** lower than control at 30 min and 60 min (P = 0.5)	23-25% amylose vs 0% amylose
Hospers 1994 (Netherlands)	Cross-over	Study the postprandial effects of changing the amylose to amylopectin ratio in the starch fraction of pastas.	16 healthy male adults	Test meals consisting of normal levels of amylose or high levels of amylose	**Glucose**: 0, 30, 60, 120, 180 pp; Gluco quant kit Boehringer Mannheim 1989 **RS**: quantification not provided. % amylose quantification provided from manufacturer	**Peak glucose:** 0.32 mmol/L lower than control (P < 0.05) at 30 min. **Insulin:** lower than control at 1hr (P < 0.006); 2hr (P = 0.0005); 3 hr (P = 0.004). No significant difference at 30 min (P = 0.052)	High (70-75%) vs low (24-26%) amylose pasta- stored samples

Krezowski 1987 (USA)	Cross-over	Investigate the insulinemic and glycaemic responses to various starch containing foods in Type II diabetic subjects	9 male adults with untreated T2DM	Cornstarch muffins – with high or low amylose content	**Glucose**: 0, 30, 60, 120, 180, 240, 300 min pp; Beckman glucose analyser **RS**: quantification not provided. % amylose quantification provided from manufacturer	**Peak glucose:** 3.33 mmol/L lower than control (P value not provided). **Insulin:** lower than control at 30, 60, 90, 120, 240, 300 min (P value not provided)	High amylose vs low amylose muffin
Li 2010 (China)	Cross-over	Determine the glycaemic and insulinemic responses and fermentation products of resistant starch enriched rice in healthy adults	16 healthy adults (7 female and 9 male)	Test meals consisting of either resistant starch enriched or wild type rice	**Glucose:** 15, 30, 45, 60, 90, 120, 180, 240 min pp; glucose oxidase method **RS**: AOAC 2002.02	**Peak glucose:** 0.4 mmol/L lower than control, $P < 0.05$. **Insulin:** significantly lower than control at 45, 60, 90, 120 ($P < 0.05$).	RS rice vs wild type rice
Lin 2015 (Taiwan)	Cross-over	Study the effect of RS based diet on blood glucose regulation and safety in healthy and normal subjects	40 healthy adults	Type 3 RS substituting starch in test meals in which other macronutrients were controlled	**Glucose:** 0, 15, 30, 45, 60, 90, 120, 180 min pp; information not provided **RS**: not measured	**Peak glucose:** 0.56 mmol/L lower than control, $P<0.05$; **Insulin:** non-significantly lower at 15 min and significantly lower at 30, 45, 60, 90 min ($P< 0.05$) compared to control	PPB-R-203 vs macronutrient matched control food
Luhovyy 2014 (Canada)	Single blinded cross-over	Determine the effect of RS from high amylose flour on blood glucose, satiety and food intake in young men	30 healthy male adults	Cookie with high maize starch replacing all-purpose flour	**Glucose:** 15, 30, 45, 60, 90, 120min pp; glucose meter Accu-check compact plus (finger prick, second droplet) **RS**: information from manufacturer	**Glucose:** 0.71 mmol/L lower than control $P < 0.05$; **Insulin:** not tested	High dose vs low dose treatment

Seal 2003 (UK) **Study 1**	Double blinded cross-over	Evaluate the effect of different starches on carbohydrate metabolism in healthy subjects	4 male,4 female healthy adults	Starch suspensions containing differing levels of RS as well as SDS and RDS	**Glucose:** 10 min intervals for 3hr pp; Daly et al. 1998 **RS**: Englyst 1992	**Peak glucose:** 1.14 mmol/L lower than control (P < 0.05) **Insulin:** lower at all time points between 15 - 150 min (P value not provided)	R starch (50 g) vs S starch (50 g)
Seal 2003 (UK) **Study 2**	Double blinded cross-over	Evaluate the effect of different starches on carbohydrate metabolism in T2D subjects	13 adults (9 male and 4 female) with T2D, not taking medication	Starch suspensions containing differing levels of RS as well as SDS and RDS	**Glucose:** 10min intervals for 3hr pp; Daly et al 1998 **RS**: Englyst 1992	**Peak glucose:** 1.43 mmol/L lower than control (P < 0.05) **Insulin:** lower than control at all time points between 15 - 255 min (P value not provided)	R starch (50 g) vs S starch (50 g)
Seewi 1999 (Germany)	Double blinded cross-over	Evaluate the effect of leguminous versus maize starch on glucose homeostasis and other parameters	10 healthy adults (3 female and 7 male)	Soups prepared with different starches with varying % amylose content	**Glucose:** 15 min intervals for 3 hr pp; Beckman glucose analyser II **RS**: quantification not provided. % amylose quantification provided from manufacturer	**Peak glucose:** 0.53 mmol/L lower than control (P value not provided) **Insulin:** lower than control at 15, 30, 45, 60, 75, 90, 120, 150 min (P value not provided)	Fibre-depleted pure pea starch vs fibre-depleted unmodified maize starch
Shimotoyodome 2011 (Japan)	Single blinded cross-over	Evaluate the effect of RS4 supplementation on postprandial energy metabolism and blood glucose-dependent insulinotropic polypeptide	10 healthy male adults	Pancake meal prepared with waxy maize or RS4 starches	**Glucose:** 15, 30, 60, 90, 120, 180 min pp; blood glucose self-monitoring device (capillary) **RS**: not measured	**Peak glucose:** 0.61 mmol/L lower than control (P < 0.001) **Insulin:** Significantly lower than control at 60, 90,120,180 min (P < 0.05 or < 0.01). Non-significantly lower than control at 30 min.	Hydroxypropyl-distarch phosphate (HDP) meal vs waxy maize meal

Tachibe 2010 (Japan)	Cross-over	Determine the effect of RS4 on glycaemic responses in men	10 healthy male adults	4 cookies with differing types tapioca starch including type 4 RS	**Glucose:** 30, 60, 90, 120, 150, 180min pp; enzymatic test kit **Glucose** CII Test (capillary) **RS**: AOAC 985.29	**Peak glucose:** 2.03 mmol/L lower than control ($P < 0.05$) **Insulin:** not tested	Cross-linked starch cookie vs tapioca starch cookie
Tachibe 2011 (Japan)	Cross-over	Determine the effect of RS4 on glycaemic response and fermentability in men	10 healthy male adults	Starch suspensions of unmodified or crosslinked tapioca starch	**Glucose:** 30, 60, 90, 120, 150, 180min pp; enzymatic test kit CII Test (capillary) **RS**: AOAC 985.29	**Peak glucose:** 2.5 mmol/L lower than control ($P < 0.05$) **Insulin:** not tested	Highly cross-linked starch phosphate vs unmodified tapioca starch
Van Amelsvoort 1992 (Netherlands)	Cross-over	Evaluate the effect of amylose-amylopectin ratio on postprandial variables in males	22 healthy male adults 2 subjects withdrew with reasons provided that were unrelated to study	Lunch meal with amylopectin rich or amylose maize starch and rice.	**Glucose:** 0, 30, 60, 120, 240 min pp; gluco quant kit Boehringer Mannheim 1989 **RS**: quantification not provided. % amylose quantified by Takeda method	**Peak glucose:** 0.47 mmol/L lower than control. No P value provided. **Insulin:** lower at 30, 60, 120 min compared to control (P value not provided)	High amylose (fresh) vs low amylose (fresh)

*Confounders: Studies were controlled by cross-over design. Confounding is unlikely because acute measurements were taken, giving no time for change in subjects' diet or behaviour. ǂ Loss to followup described where relevant. ** Venous blood was tested for glucose estimation except when otherwise stated; pp: postprandial; SDS: T2DM: type 2 diabetes mellitus; slowly digested starch; RDS: rapidly digested starch (Englyst et al. 1992)

Table 3 Properties of the studies included in the **addition** of resistant starch review analysis

Reference and study location	Study design	Objectives	Participants & sample size	Interventions	Methods	Results	Arm used for review
Bodinham 2010 (UK)	Single blinded cross-over	Determine the effects of RS consumption on appetite compared to energy and available CHO matched placebo	20 healthy adult males	Test breakfast or lunch with either RS supplement or placebo	**Glucose:** 30 min intervals for 7 hr pp; tested enzymatically using a commercial kit	**Peak glucose:** 0.41 mmol/L lower than control (non-significant P value)	Meal supplemented with resistant starch vs placebo

					RS: AOAC 991.43	**Insulin:** lower than control at 30, 60, 90, 120 min (P = 0.029)	
Hallstrom 2011 (Sweden)	Cross-over	Evaluate the postprandial glucose response in vivo to bread products with an elevated amylose content	14 healthy adults	Bread with elevated amylose content and lactic acid	**Glucose:** 0,15,30,45,60,90,120 min pp; glucose oxidase method - HemoCue AB (capillary) **RS:** Akerberg method (Akerberg et al.1998)	**Peak glucose:** same concentration in test and control (3.0 mmol/L) **Insulin:** non-significantly lower than control at 60, 90, 120 min	Elevated amylose wheat with lactic acid (EAW-la) vs elevated amylose wheat bread (EAW). 3.3 g difference between test and control food
Haub 2012 (USA)	Single blinded cross-over	Determine the effect of two novel RS4 starches on postprandial glycaemia	10 healthy adults	Two novel potato derived RS based drinks	**Glucose:** 30,45,60, 90,120 min pp; YSI 2300 (capillary) **RS:** no method provided	**Peak glucose:** 0.21 mmol/L lower than control (non-significant P value) **Insulin:** not tested	Non-commercial resistant starch (PR+) vs dextrose control
Kinnear 2011 (Canada)	Cross-over	Investigate the effects of cooling and reheating on the GI of novel potato clones	10 healthy adults (5 male, 5 female)	New varieties of potato with differing levels of RS	**Glucose:** 15,30,45,60,90, 120 min pp; YSI 2300 (capillary) **RS:** Englyst 1992	**Peak glucose:** 0.27 mmol/L lower than control (P value not provided) **Insulin:** not tested	Experiment 1: fresh boiled selection 4 vs selection 3 potatoes
Klosterbuer 2012 (USA)	Double blinded cross-over	Evaluate the effect of starch and pullulan on glucose, insulin and gut hormone responses	20 healthy adults	Test breakfast with added starch	**Glucose:** 15, 30, 45, 60, 90,120, 180 min pp; hexokinase colorimetric method **RS:** "Accepted AOAC methods"	**Peak glucose:** 0.17mmol/L decrease compared to control (P value not provided) **Insulin:** slightly lower than control at 30, 45, 60 min (P value not provided)	RS meal vs control 24.4 g difference in RS

Marchini 1998 (Brazil)	Cross-over	Evaluate the lipid and glucose response after intake of raw resistant potato starch	10 healthy adults	Potato resistant starch supplemented meal	**Glucose:** -15,-1, 30 min intervals for 7 hr pp; Beckman analyser II **RS**: information provided from manufacturer	**Peak glucose:** 0.71 mmol/L higher than control; non-significant P value. **Insulin:** higher than control at 60, 150 min (P value not provided)	Resistant raw potato starch supplement vs No RS
Maziarz 2017 (USA)	Double blinded parallel	Determine the effect of high amylose maize type 2 on glucose homeostasis in overweight healthy adults	18 healthy overweight adults 7 subjects withdrew with reasons provided unrelated to study	Muffin with high maize RS2	**Glucose:** 0, 15, 30, 60, 120 min pp; hexokinase colorimetric method **RS:** information provided from manufacturer	**Peak glucose:** 0.33 mmol/L higher than control, non-significant P value. **Insulin:** Non-significant differences (increase at 15 min, decrease at 60 min) compared to control	High amylose maize RS2- muffin (baseline reading) vs control muffin (baseline reading)

*Confounders: Studies were controlled by cross-over design. Confounding is unlikely because acute measurements were taken, giving no time for change in subjects' diet or behaviour. Maziarz et al. (2017) was a parallel design in which participant characteristics were not significantly different between control and intervention groups.

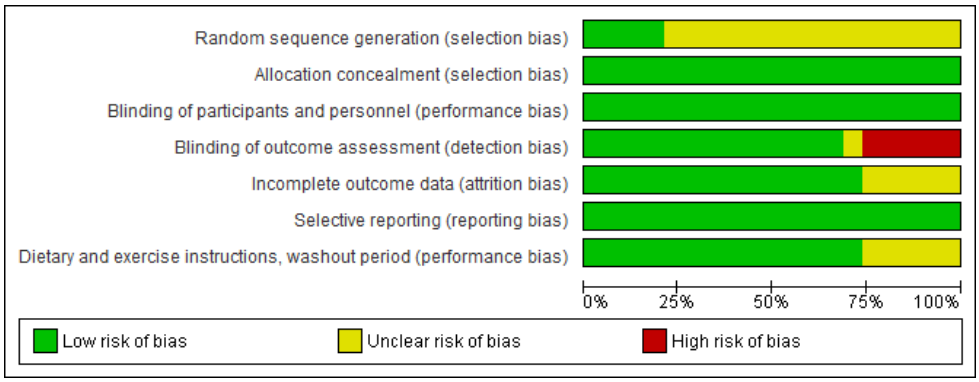

Figure 2A. Risk of bias graph of included replacement studies

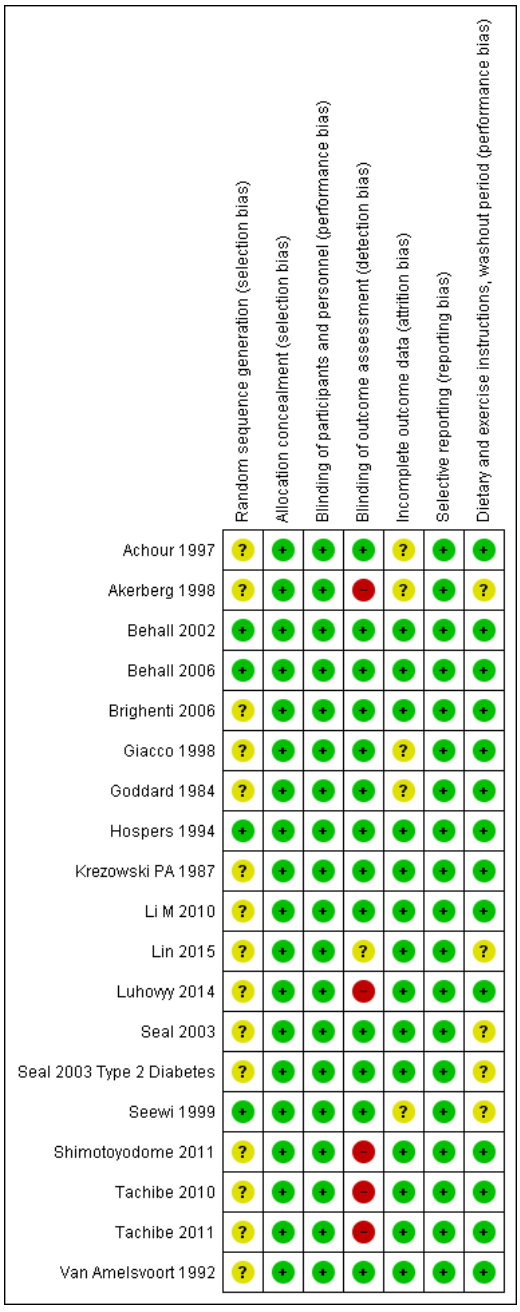

Figure 2B. Risk of bias analysis of included replacement studies

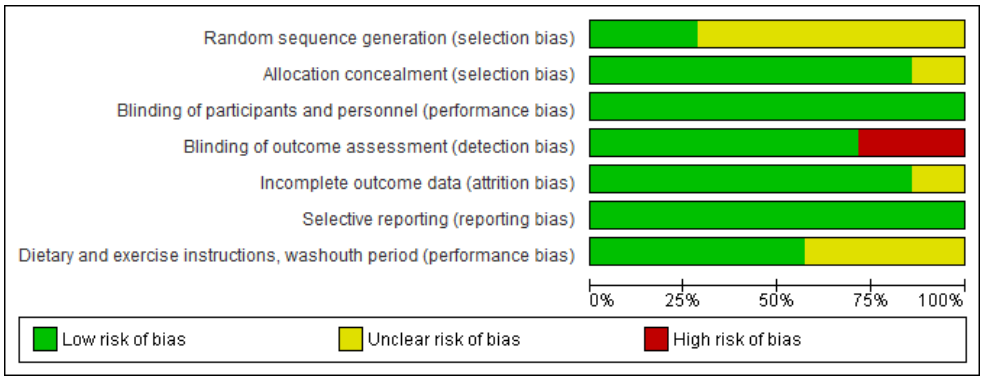

Figure 2C. Risk of bias graph of included addition studies

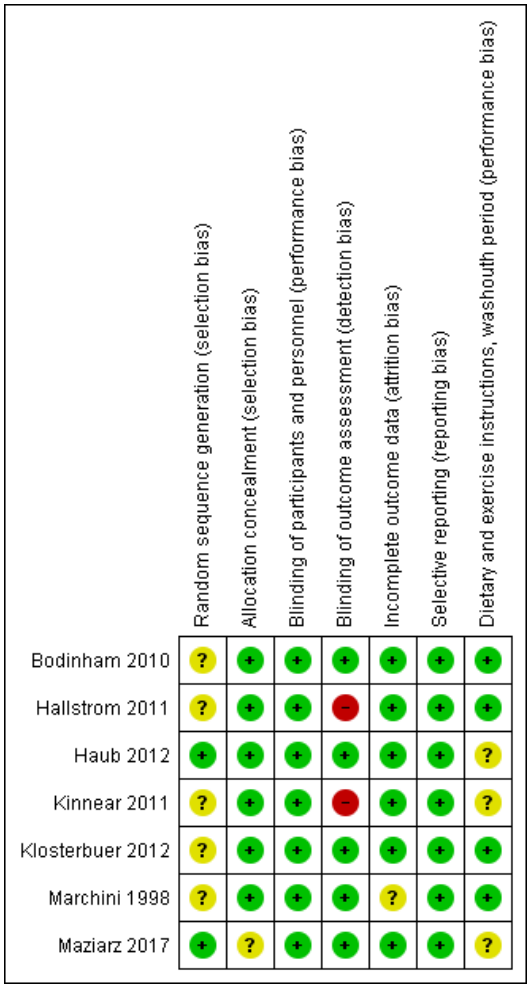

Figure 2D. Risk of bias analysis of included addition studies

2.3 Summary of evidence

2.3.1 Peak blood glucose concentration

Twenty five studies were included following full text review. Of these, seventeen studies and eighteen trials were included in the meta-analysis. The remaining eight studies did not provide either standard error measurements or appropriate P values to calculate variance and therefore were not used to extract data on peak glucose. Seven of these publications were replacement studies and reported a significant decrease in peak postprandial blood glucose in the resistant starch tests compared to control foods. One study (Klosterbuer et al. 2012) was an addition study that reported a slight decrease (0.17 mmol/L) in postprandial blood glucose in the high amylose food compared to low amylose food however the author did not provide statistics on the peak values.

Twenty four studies were cross-over design, with sample size ranging from 8 to 40, with an average size of 14. One trial with a parallel study design (Maziarz et al. 2017) had a sample size of 18. Three trials tested adults with type 2 diabetes (Giacco et al. 1998; Krezowski et al. 1987; Seal et al. 2003).

Figure 3A shows the dose of resistant starch tested and the difference in peak blood glucose concentration between the resistant starch and control phases for both replacement and addition studies. The amount of resistant starch varied between 2.5 g and 30.4 g. Several studies that provided information relating to amylose content (Seewi et al. 1999; Goddard et al. 1984) or commercial RS4 product (Shimotoyodome 2011) but did not provide exact quantities of resistant starch in both test and control foods were excluded from the scatterplot. Studies that quantified resistant starch using appropriate Association of Official Agricultural Chemists (AOAC) or other accepted methods were included in Figure 3A. However studies that used AOAC method 985.29 to estimate RS4 (Tachibe et al. 2010; Tachibe et al. 2011) were excluded as this method for total dietary fibre analysis has been found to overestimate RS4 content (McCleary et al. 2013).

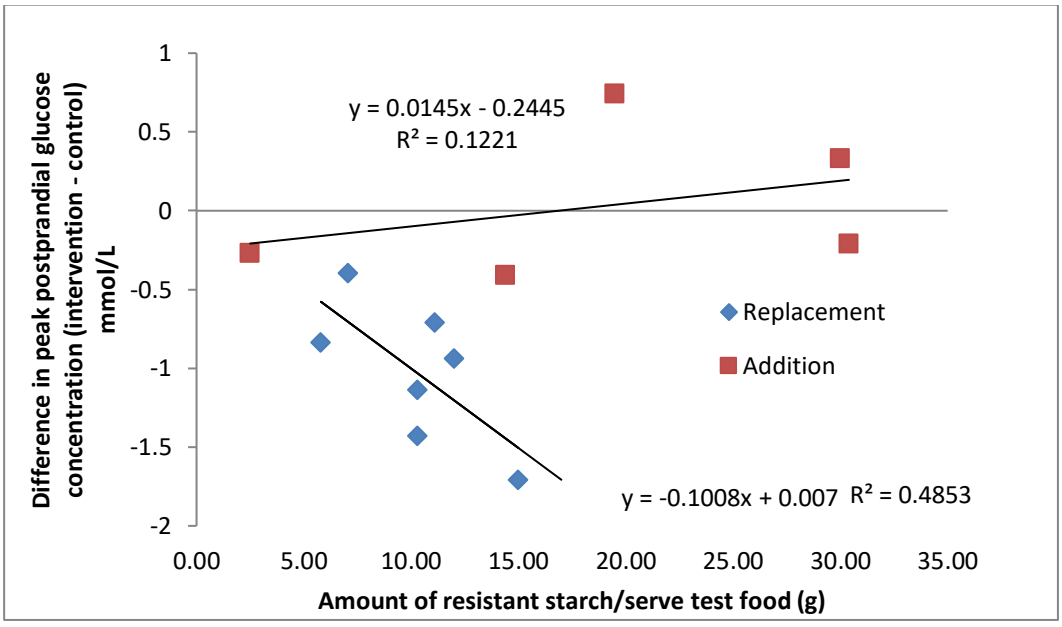

Figure 3A. Scatterplot of the dose[1] of resistant starch consumed and the difference in peak postprandial blood glucose concentrations compared to control for replacement and addition studies. [1]Dose in test foods was calculated as the difference between resistant starch levels in test and control foods

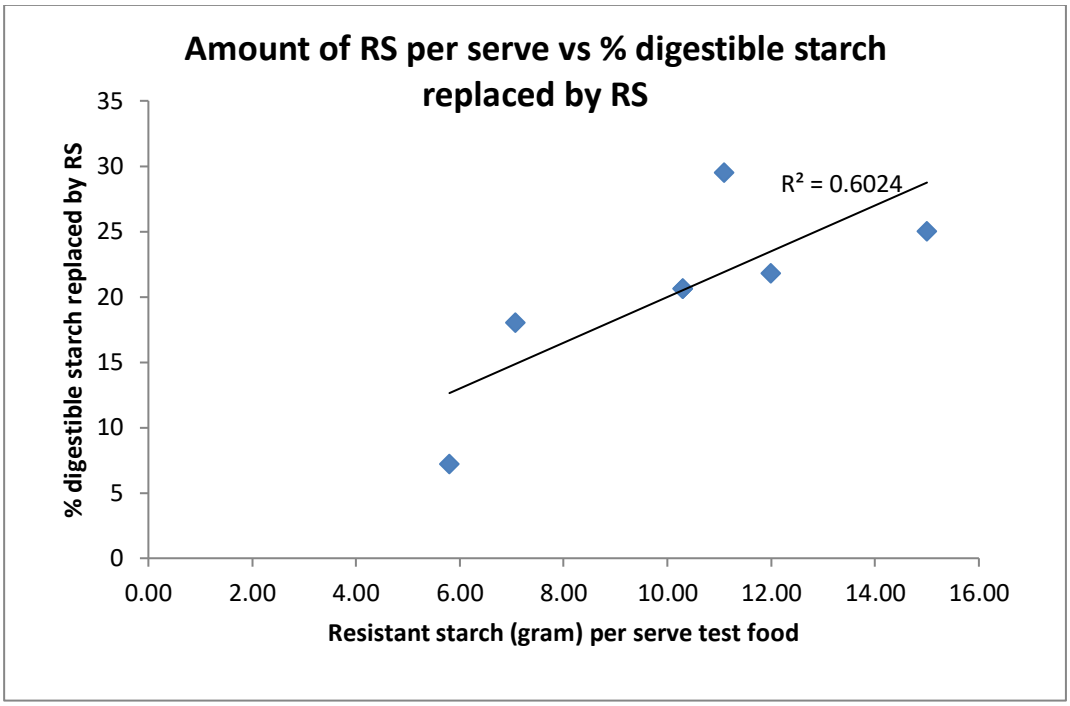

Figure 3B. Scatterplot of resistant starch per serve test food (gram) and percentage digestible starch replaced by RS. One study from figure 3A did not provide percentage starch information and could not be included in the graph.

The amount of resistant starch given in each test ranged from 2.5 g to 30.2 g for addition studies and from 5.8 g to 15 g for replacement studies. Most of the studies tested the effect of resistant starch as part of a meal however one replacement study tested the effect of a suspension (Seal et al. 2003). Studies of diabetic subjects were also included in the graph (Giacco et al. 1998; Seal et al. 2003).

A linear regression model that assumes equal weight to each study was added for both replacement and addition studies. For the replacement studies the slope of the line was -0.1 indicating that for every one gram of digestible starch that was replaced with resistant starch peak postprandial glucose concentration decreased by 0.1 mmol/L. Forty nine percent of this change can be attributed to resistant starch. Despite a large amount of variation in study design including type of resistant starch, method of quantitating resistant starch, use of normoglycaemic versus diabetic subjects, macronutrient content between test foods as well as food type, a moderate linear relationship exists between increased replacement of digestible starch with resistant starch and a decrease in peak postprandial blood glucose concentration.

In the case of addition studies the addition of one gram of resistant starch contributed to an increase of 0.02 mmol/L of postprandial blood glucose, $R^2 = 0.12$ indicating that adding resistant starch to a food does not contribute to a change in postprandial blood glucose concentration and therefore there is a low level of correlation between addition of resistant starch and decrease in postprandial blood glucose. For replacement studies $R^2=0.49$ indicates a moderate correlation between increase in level of resistant starch replacement and decrease in postprandial blood glucose.

Figure 3B shows a scatterplot of resistant starch per serve test food (gram) vs % digestible starch replaced by RS in which a moderate correlation exists between the amount of

resistant starch in the test food and percentage replacement of digestible starch with resistant starch (R^2=0.6).

Figure 4 shows the same scatter plot as Figure 3A, with standard errors for the difference in peak postprandial glucose concentrations and the amount of resistant starch per serve of test food.

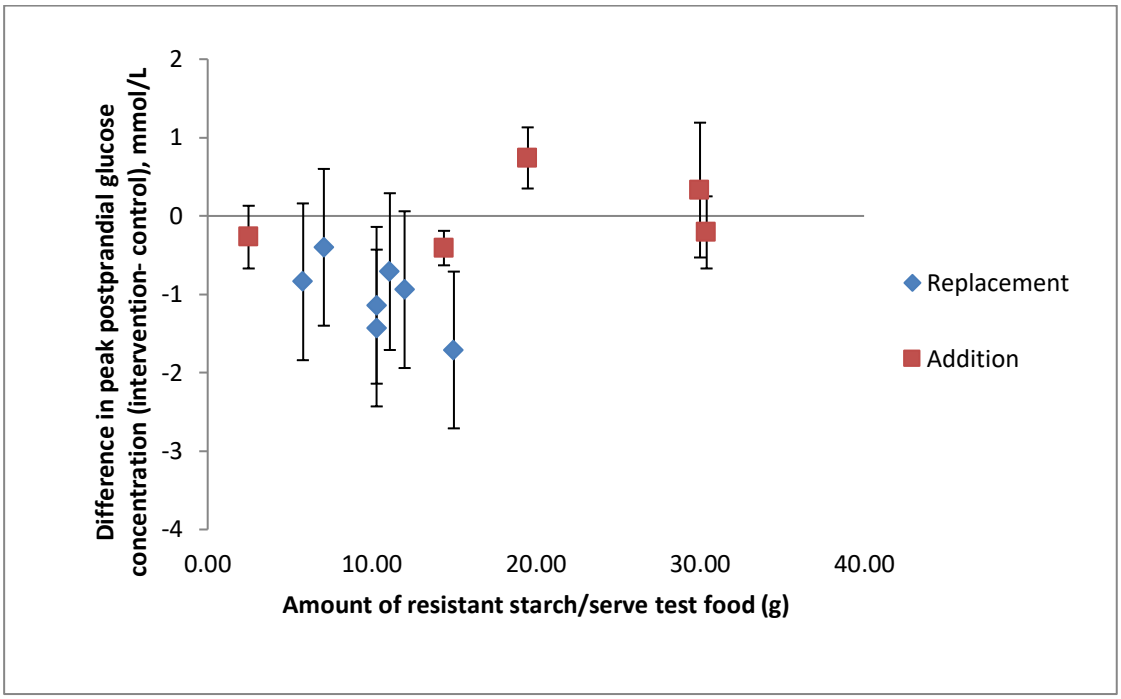

Figure 4. Scatterplot of the dose of resistant starch consumed and the difference in peak postprandial blood glucose concentrations compared to control with standard errors for replacement and addition studies.

Meta-analysis was undertaken for replacement and addition studies in which peak postprandial glucose was reported or could be calculated and a difference in resistant starch, % amylose or commercial resistant starch product was provided.

Replacing resistant starch with digestible starch caused an overall decrease in peak post-prandial blood glucose of 1.06 mmol/L (95% CI [-1.50, -0.61]) compared to control foods, with the confidence interval of one study crossing the line of no effect (Li et al. 2010). However there was a high level of heterogeneity between studies (I^2=95%). FSANZ noted that one study (Tachibe et al. 2010) had very narrow confidence intervals that contributed to heterogeneity. When excluded from the analysis heterogeneity decreased to 84% (data not shown). A smaller confidence interval would result if standard errors were mistakenly reported as standard deviations. Authors could not be contacted to clarify.

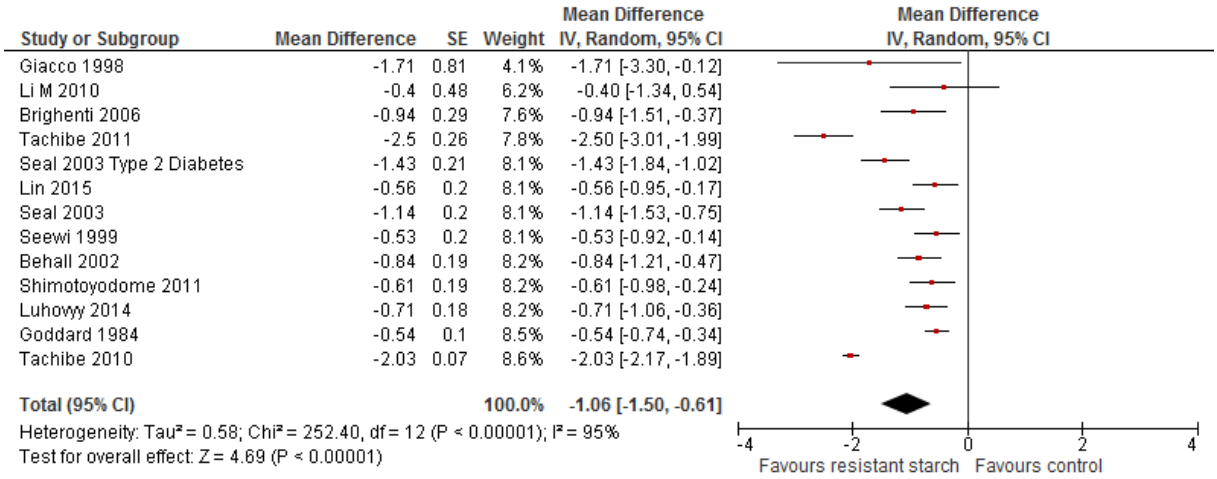

Figure 5. Forest plot of studies measuring peak postprandial blood glucose concentration following replacement of digestible starch with resistant starch.

By contrast, adding resistant starch to a food caused a slight decrease in peak postprandial blood glucose of 0.05 mmol/L (95% CI [-0.52, 0.41]) compared to control foods, with two of five studies showing an increase in peak blood glucose following consumption of resistant starch (Marchini et al. 1998; Maziarz et al. 2017). There was a moderate level of heterogeneity between studies (I^2=43%).

In order to determine the cause of heterogeneity between studies a range of subgroup analyses were performed.

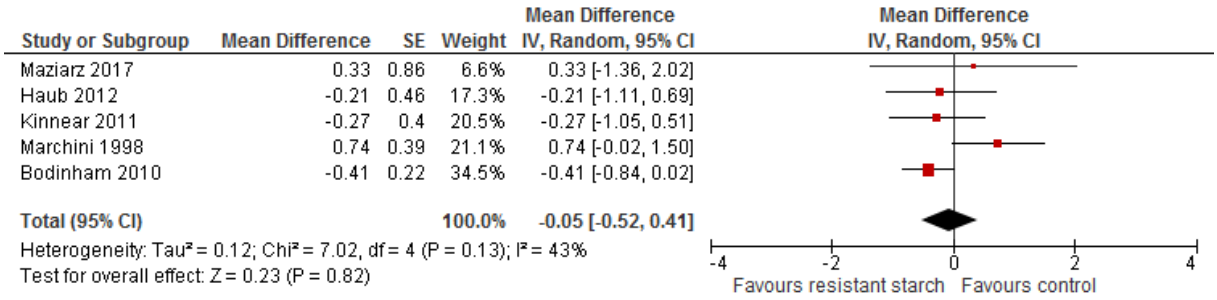

Figure 6. Forest plot of studies measuring peak postprandial blood glucose concentration following addition of resistant starch.

2.3.1.1 Subgroup analyses – Replacement with resistant starch

2.3.1.1.1 Dose of resistant starch

The high level of heterogeneity among replacement studies may be caused by differences in dose as shown in Figure 3A. Therefore a subgroup analysis based on dose of resistant starch was carried out for studies which quantified resistant starch levels (Figure 7). Groups were determined arbitrarily based on the range of doses tested. A significant decrease in postprandial blood glucose was noted in each subgroup, decreasing by 0.78, 1.05 and 1.71 mmol/L for the three subgroups: less than 7.1 g, 7.1–14 g and >14 g resistant starch. A non-significant difference was noted between subgroups when both normoglycaemic and diabetic subjects were assessed (P =0.49) however when diabetic subjects were removed from the analysis (Giacco et al. 1998; Seal et al. 2003 T2D trial) the level of heterogeneity decreased from 58% to 22% for the 7.1–14 g group (Figure 8). Therefore some of the heterogeneity from Figure 5 can be explained by dose of resistant starch and type of subjects that are assessed.

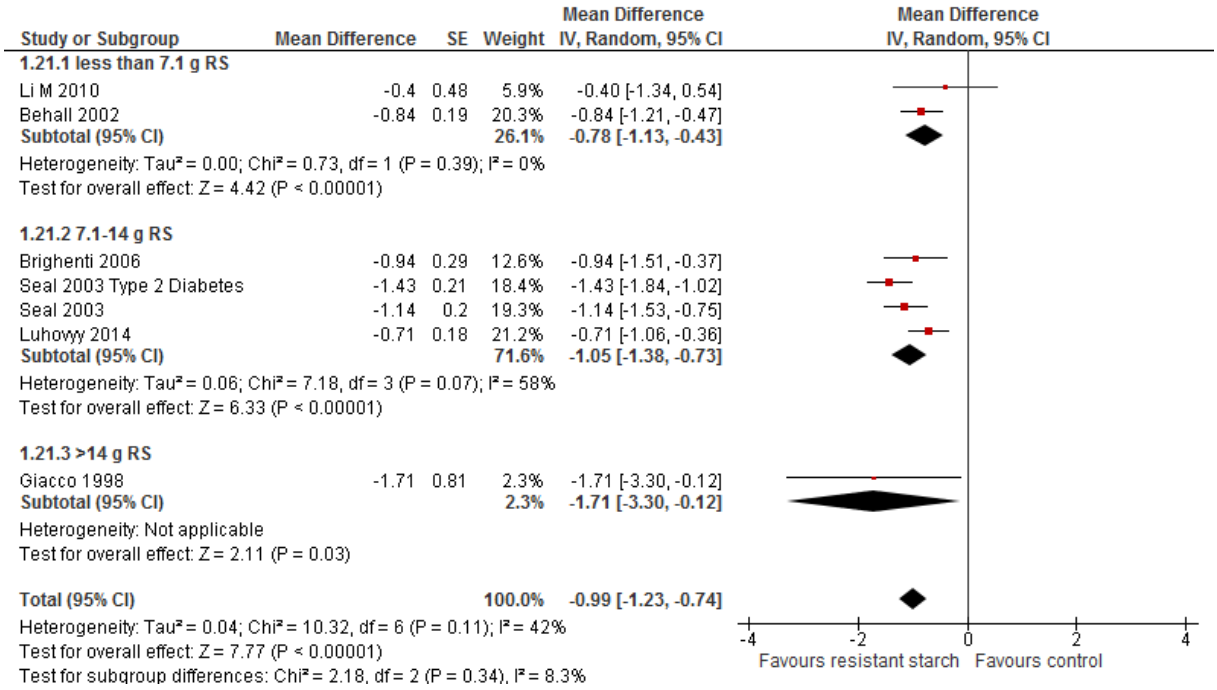

Figure 7. Forest plot of studies measuring peak postprandial blood glucose concentration following replacement of digestible starch with resistant starch by dose of resistant starch

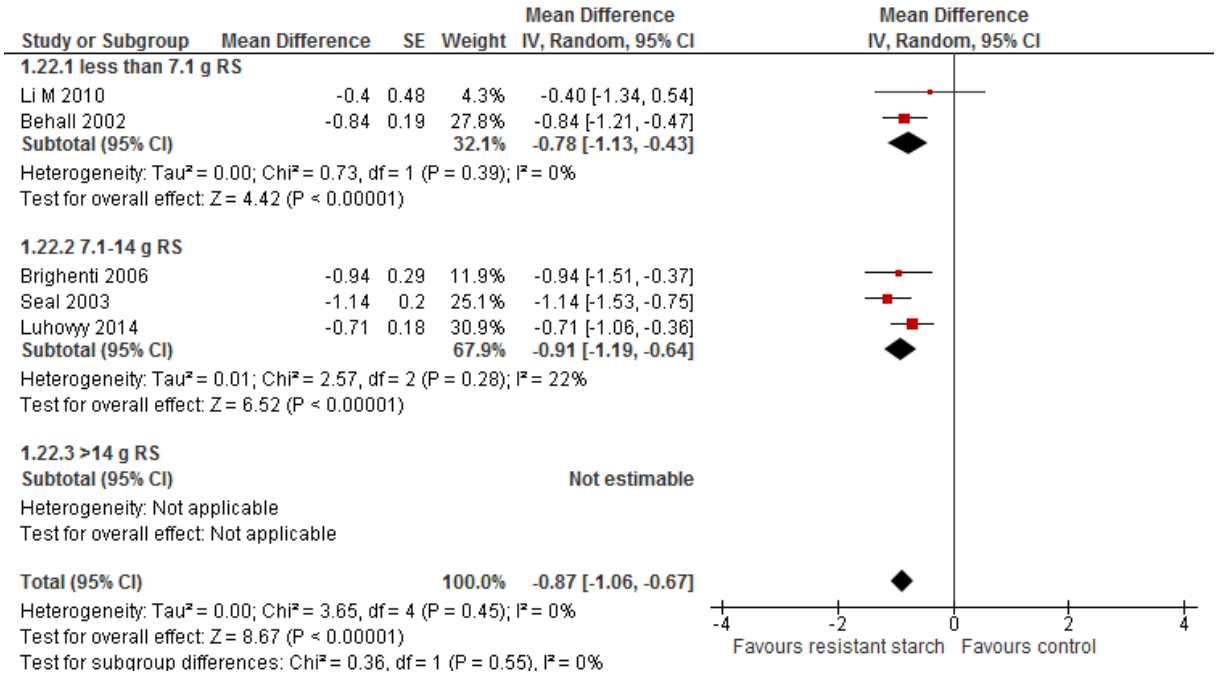

Figure 8. Forest plot of studies measuring peak postprandial blood glucose concentration following replacement of digestible starch with resistant starch in normoglycaemic subjects by dose of resistant starch.

2.3.1.1.2 Type of resistant starch

Resistant starch can be classified as RS1–5, with RS1–4 being considered in this review. In order to determine if the type of resistant starch had an effect on peak postprandial blood glucose levels a subgroup analysis was undertaken. RS2–4 were identified in included studies. It was noted that some studies included more than one type of resistant starch. Retrograded starch may have been present in some studies that assessed RS2 and one study that assessed retrograded starch also contained RS2 (Lin et al. 2015). Therefore this study was excluded from subgroup analysis.

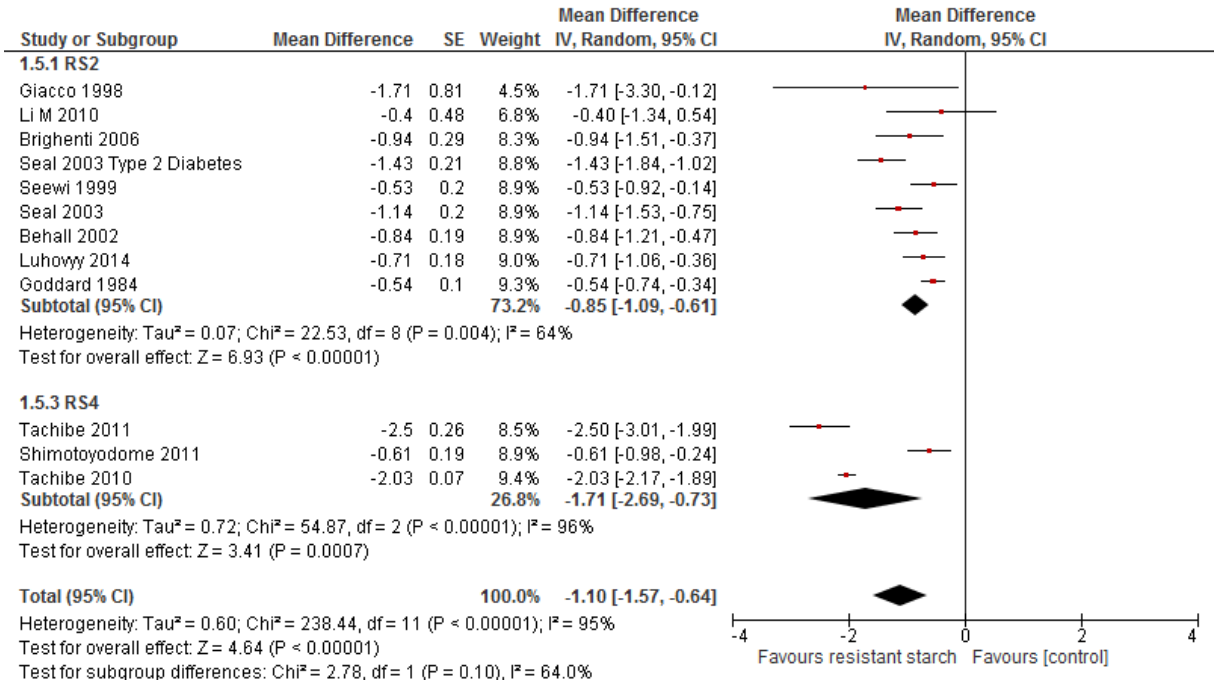

Figure 9. Forest plot of studies measuring peak postprandial blood glucose concentration following replacement of digestible starch with resistant starch by type of resistant starch.

The majority of studies used RS2 in the form of high amylose varieties of grains such as rice or wheat as part of a meal or a drink. Despite a substantial degree of heterogeneity (I^2=64%), a large and significant effect on peak blood glucose was seen in the RS2 studies, resulting in a decrease in peak postprandial blood glucose of 0.85 mmol/L 95% CI [-1.09, -0.61]). The three studies using RS4 cross-linked resistant starches (Tachibe 2010 and 2011; Shimotoyodome 2011) also showed a significant effect on peak postprandial blood glucose (-1.71 mmol/L [95% CI [-2.69, -0.73]). A high level of heterogeneity was also observed among these studies (I^2=96%). No significant difference was noted between subgroups (Figure 9).

2.3.1.1.3 Presentation of food

Study interventions were considered to be drink-based if they consisted of a starch solution or suspension without the presence of other macronutrients (e.g. Seal et al. 2003; Tachibe et al. 2011). Interventions that were classified as foods contained several macronutrients as well as carbohydrate.

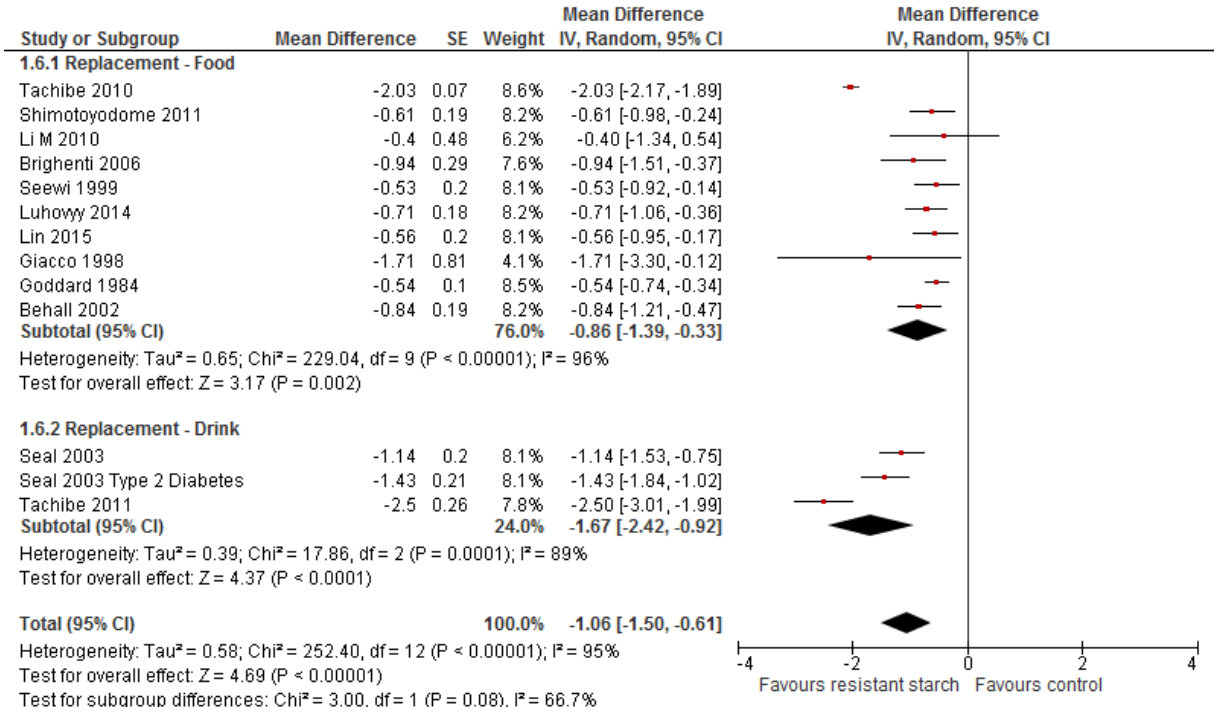

Figure 10. Forest plot of studies measuring peak postprandial blood glucose concentration following replacement of digestible starch with resistant starch by type of food.

The effect size was greater in drink studies than in food studies, with foods causing a decrease of 0.86 mmol/L (95% CI [-1.39, -0.33]) compared to 1.67 mmol/L in drinks (95% CI [-2.42, -0.92]). This result is to be expected as the rate of digestion and absorption decreases in the presence of other macronutrients (Birt et al. 2013).

2.3.1.1.4 Diabetes status

The effect of diabetic status on the relationship was also studied. Only two of the meta-analysed trials studied the effects of resistant starch on diabetic subjects (Giacco et al. 1998; Seal et al. 2003). A significant difference in effect on blood glucose was noted; -0.99 and -1.45 mmol/L for normoglycaemic and diabetic subjects respectively. A high level of heterogeneity was noted for normoglycaemic group (96%), but no heterogeneity was observed in the diabetic group. However the normoglycaemic group contained a larger number of studies with more possibility for variability in other factors among studies.

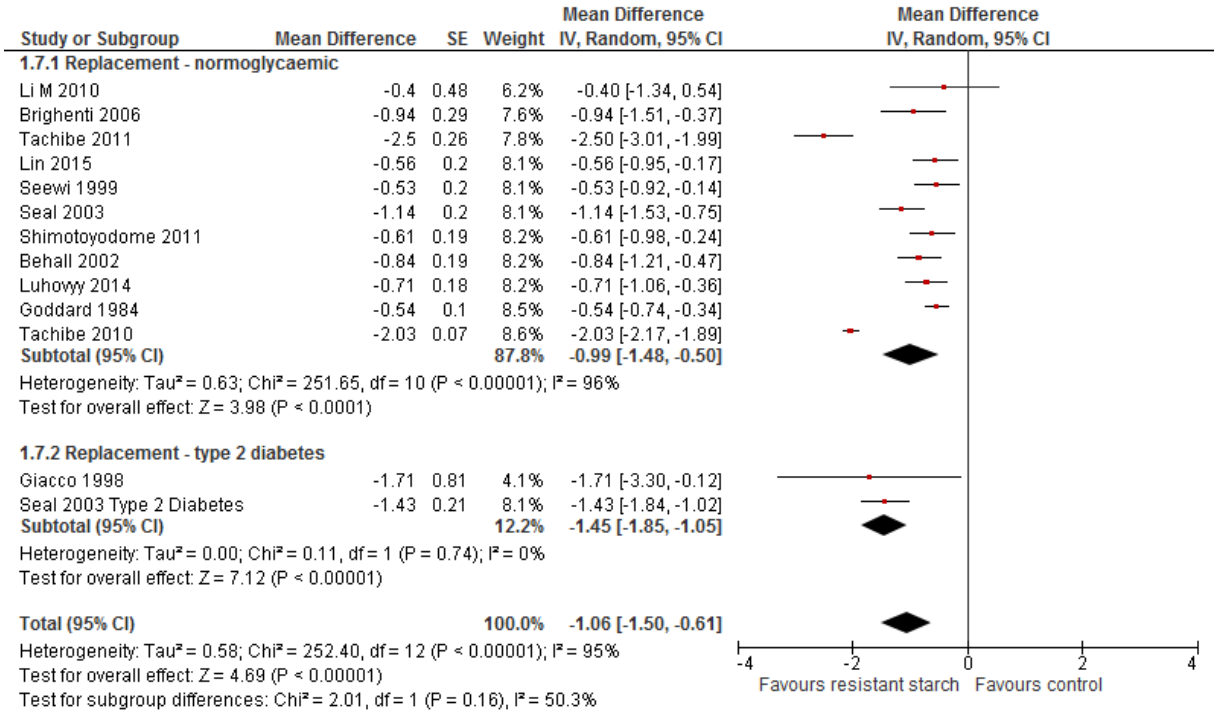

Figure 11. Forest plot of studies measuring peak postprandial blood glucose concentration following replacement of digestible starch with resistant starch by diabetes status.

2.3.1.1.5 Blood extraction method

Due to the risk of performance bias when capillary blood samples are used due to possible "milking" that causes an increase in tissue fluids in the sample thereby altering blood glucose readings (Colagiuri et al. 2003), a subgroup analysis was performed to compare results from venous and capillary blood collection methods. There was a non-significant difference between the groups (P = 0.21) indicating that blood collection methods were not responsible for variation in results. Heterogeneity was high for both the venous blood collection group (69%) and the capillary blood collection group (95%) (Figure 12).

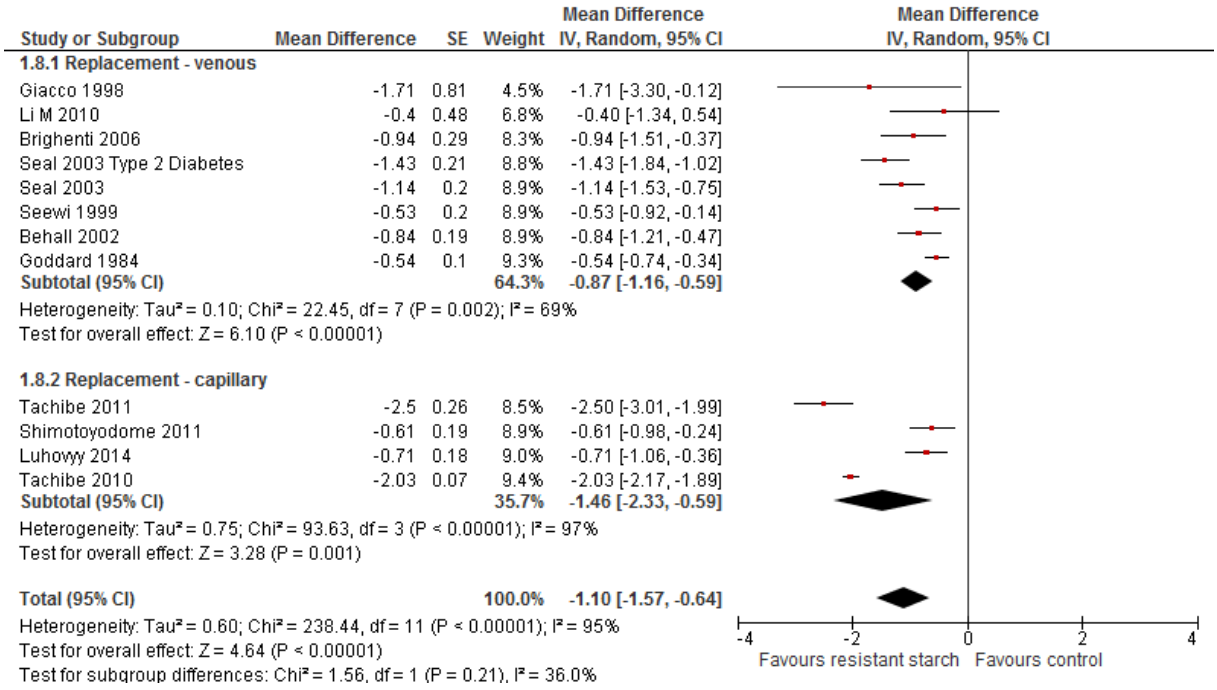

Figure 12. Forest plot of studies measuring peak postprandial blood glucose concentration following replacement of digestible starch with resistant starch by blood collection method.

2.3.1.1.6 Gender

Studies were grouped by gender. No studies were female-only but several stated that only male volunteers participated. One study that did not refer to gender was assumed to have recruited both male and female volunteers (Lin et al. 2015). No significant difference was observed between the groups (P= 0.17) with the men-only studies decreasing peak blood glucose by 1.46 mmol/L versus decreasing by 0.83 mmol/L in mixed gender studies. The level of heterogeneity was lower in the mixed gender studies compared to the men-only studies, 66% versus 97%, which indicates that heterogeneity is not due to gender but is due to some other factor (Figure 13).

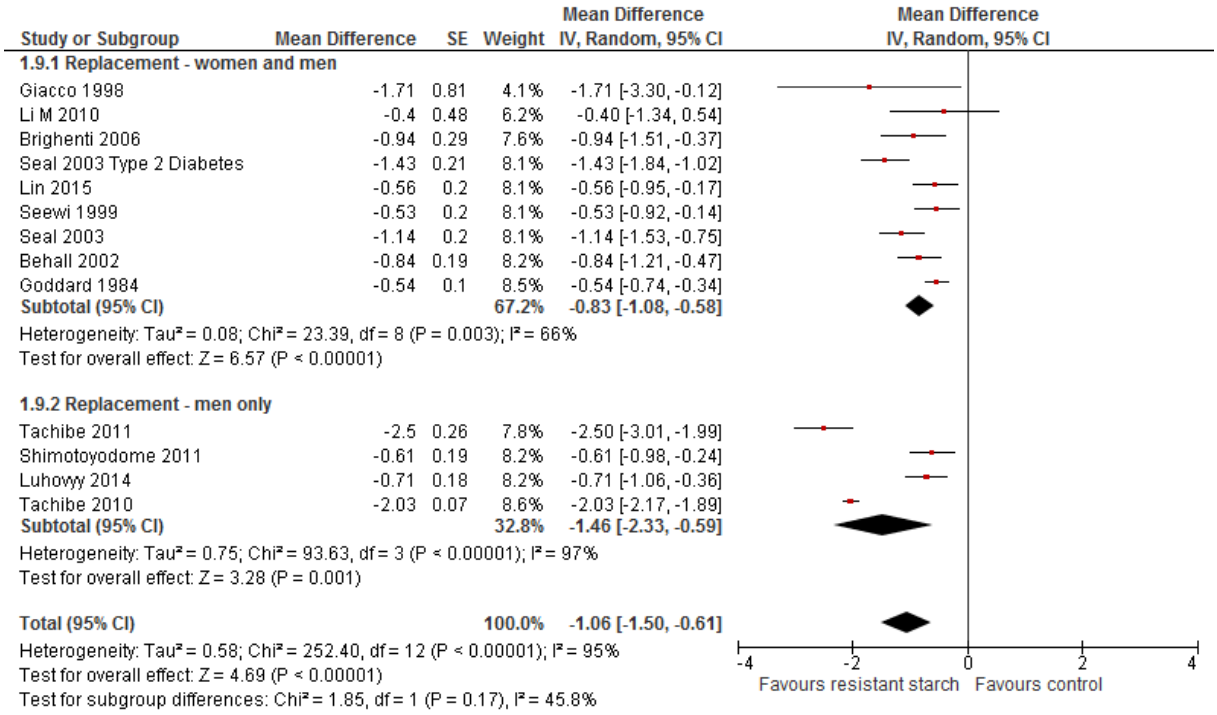

Figure 13. Forest plot of studies measuring peak postprandial blood glucose concentration following replacement of digestible starch with resistant starch by gender.

2.3.1.1.7 Funding Source

A subgroup analysis was undertaken in order to determine the effect of funding source (Figure 14). Funding sources were categorised as government or industry funded. Some industry funded studies were undertaken in university laboratories.

The level of heterogeneity was lower in government funded studies (I^2 = 23%) compared to industry sponsored studies (I^2 = 96%). However the difference between funding subgroups was non-significant (P = 0.11) and therefore conclusions cannot be drawn on the effect of funding source on the outcome.

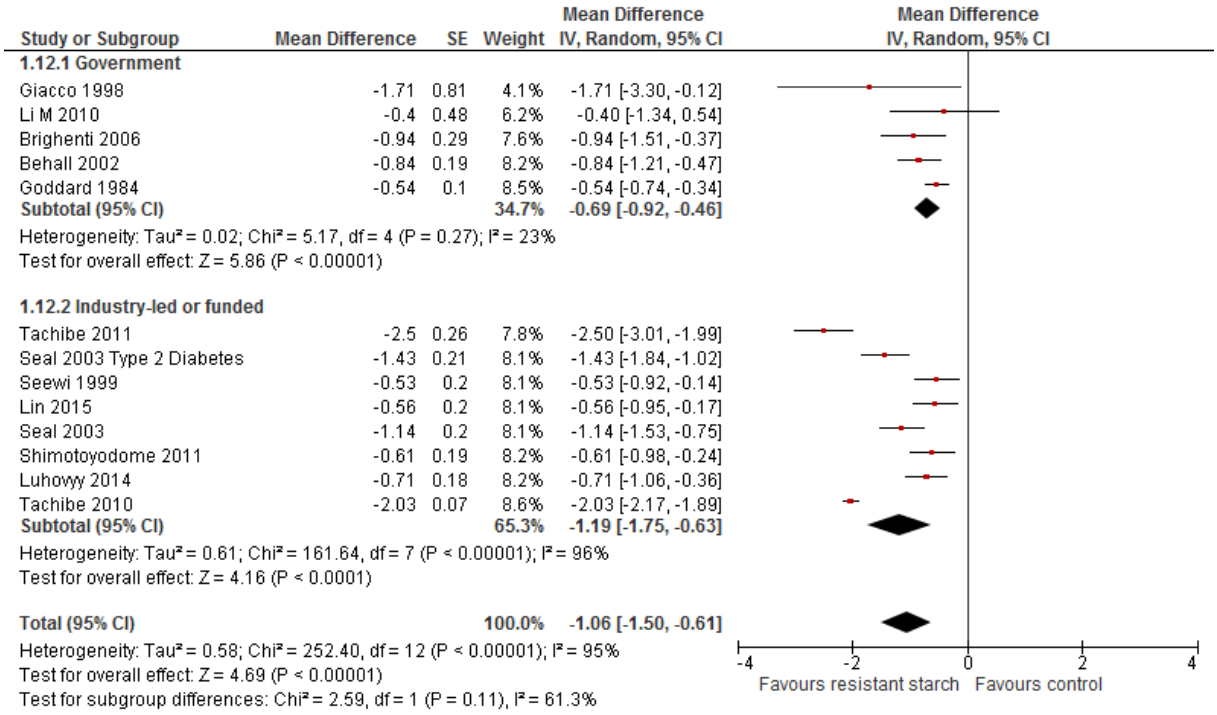

Figure 14. Forest plot of studies measuring peak postprandial blood glucose concentration following replacement of digestible starch with resistant starch by funding source.

2.3.1.1.8 High versus low quality studies

The quality of included studies was considered in Section 2.2.3. Overall the quality of included studies was considered to be high however some studies that did not provide a standardised meal or dietary instructions prior to testing were considered to be of lower quality. A subgroup analysis was carried out to determine the effect of high versus lower quality studies (Figure 15). Although the effect size was greater in high quality studies than lower quality studies, leading to a decrease of 1.13 mmol/L versus 0.91 mmol/L of postprandial blood glucose for lower quality studies compared to control foods, there was no statistical difference between the subgroups (P = 0.57).

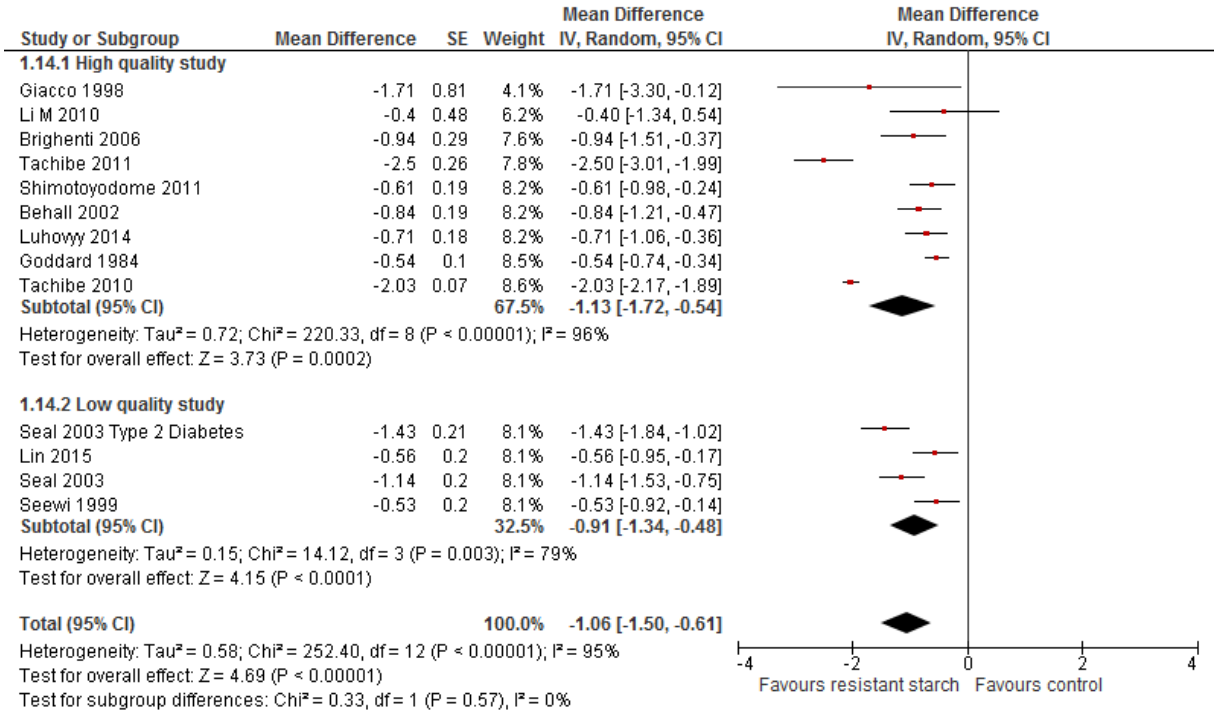

Figure 15. Forest plot of studies measuring peak postprandial blood glucose concentration following replacement of digestible starch with resistant starch by study quality.

2.3.1.1.9 Dose in High Quality Studies of Normoglycaemic subjects

When the subgroup analysis by dose was repeated for high quality studies there was no heterogeneity in the low or intermediate dose range of less than 7.1 g or 7.1-14 g (Figure 16). No studies were in the high dose range.

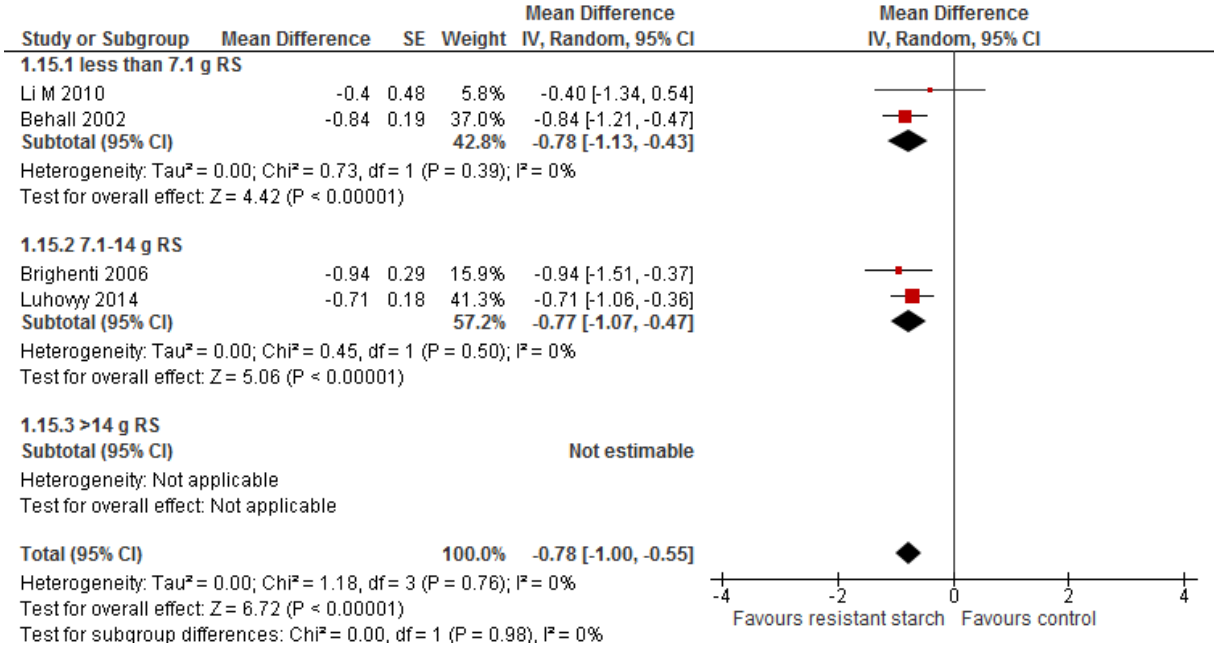

Figure 16. Forest plot of high quality studies measuring peak postprandial blood glucose concentration in normoglycaemic subjects following replacement of digestible starch with resistant starch by dose.

2.3.1.2 Subgroup analyses – Addition of resistant starch

2.3.1.2.1 Dose of resistant starch

Subgroup analysis was undertaken to determine if a difference in effect is observed based on quantity of resistant starch added to food with studies grouped as those with less than 7 g, 7 – 14.4 g or greater than 14.4 g resistant starch. Groups were determined arbitrarily based on the range of doses tested. There was no significant difference in the effect size between subgroups (P=0.17) (Figure 17).

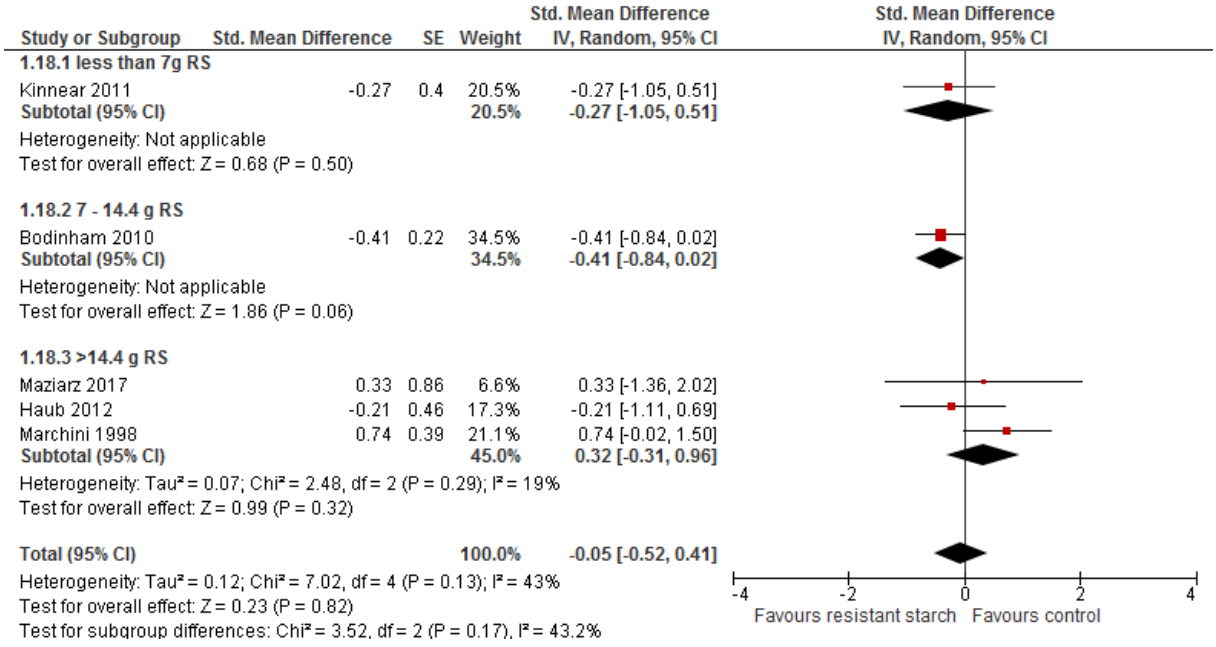

Figure 17. Forest plot of studies measuring peak postprandial blood glucose concentration following addition of resistant starch to food by dose of resistant starch.

2.3.1.2.2 Presentation of food

Only one addition study (Haub et al. 2012) used a starch suspension as the intervention which was classified as a drink. There was no significant difference between food type subgroups for addition studies (P = 0.70) (Figure 18).

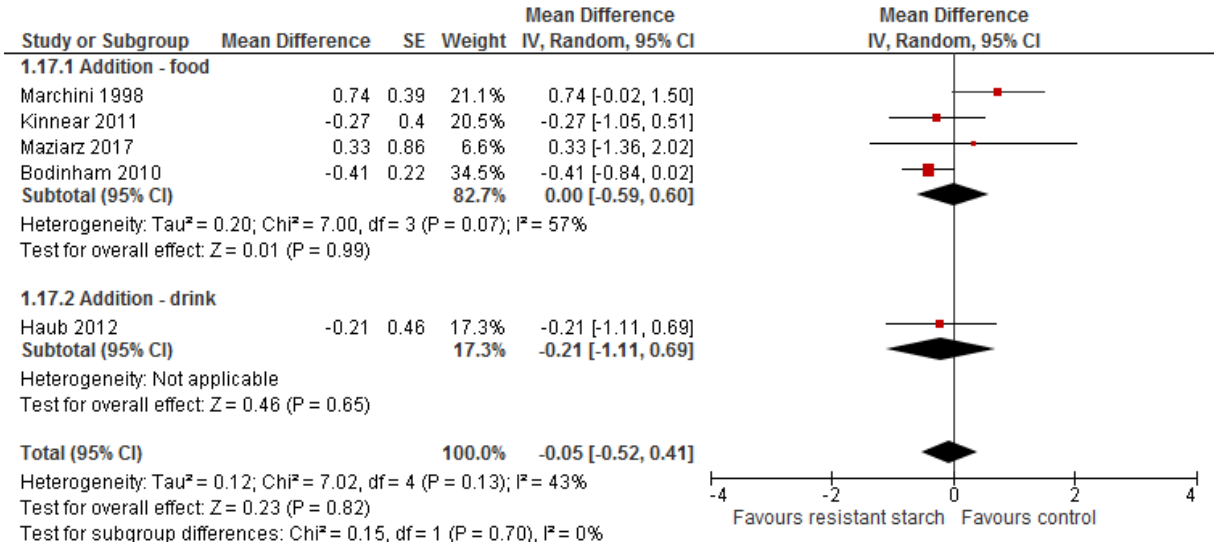

Figure 18. Forest plot of studies measuring peak postprandial blood glucose concentration following addition of resistant starch to food by presentation of food

2.3.1.2.3 Blood extraction method

There was no significant difference between blood extraction method subgroups for addition studies (P = 0.47) (Figure 19).

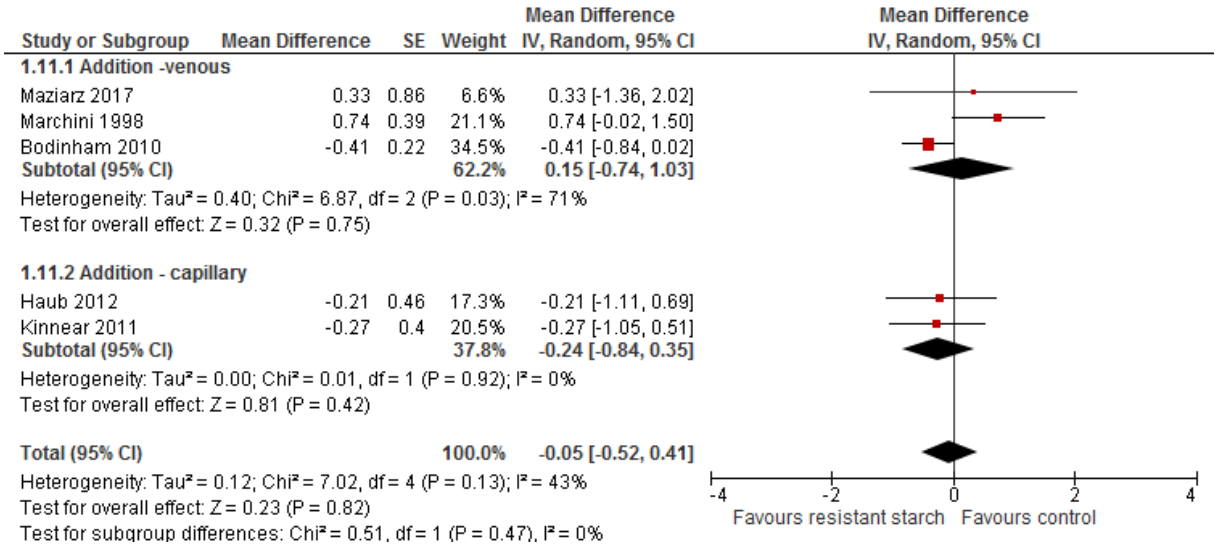

Figure 19. Forest plot of studies measuring peak postprandial blood glucose concentration following addition of resistant starch to food by blood extraction method.

2.3.1.2.4 Gender

Only one of the five addition studies included only male subjects (Bodinham et al. 2010). There was no significant difference between the subgroups (P=0.12) (Figure 20).

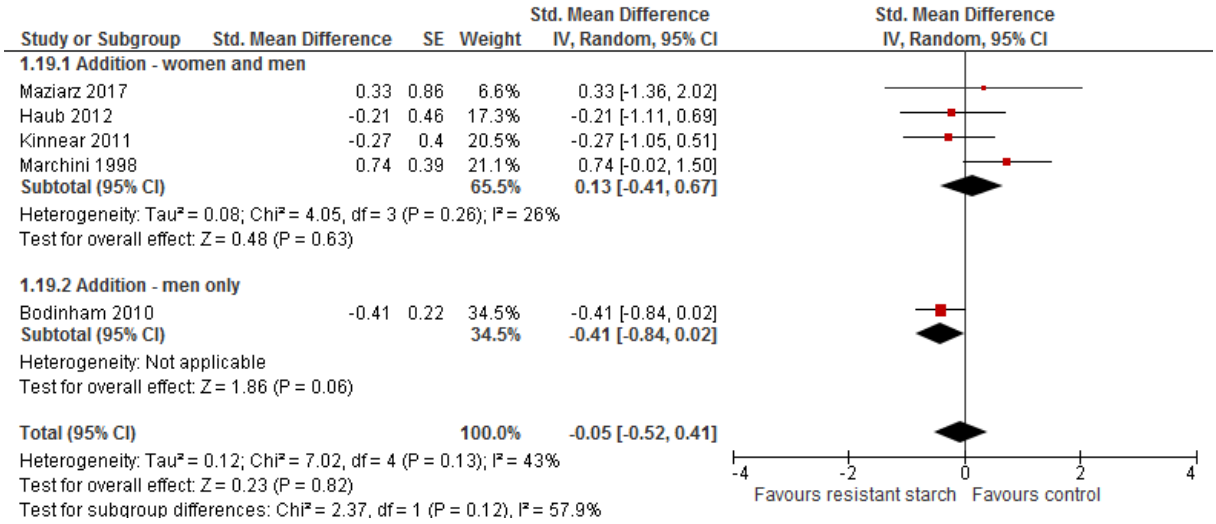

Figure 20. Forest plot of studies measuring peak postprandial blood glucose concentration following addition of resistant starch to food, by gender.

2.3.1.2.5 Study Design

There was no significant difference between study design subgroups for addition studies (P = 0.74) (Figure 21) although there is a higher level of heterogeneity in crossover studies (70%) compared to parallel studies (0%). As crossover studies provide stronger evidence in dietary intervention studies compared to parallel studies this indicates that the heterogeneity identified in this analysis is due to other factors.

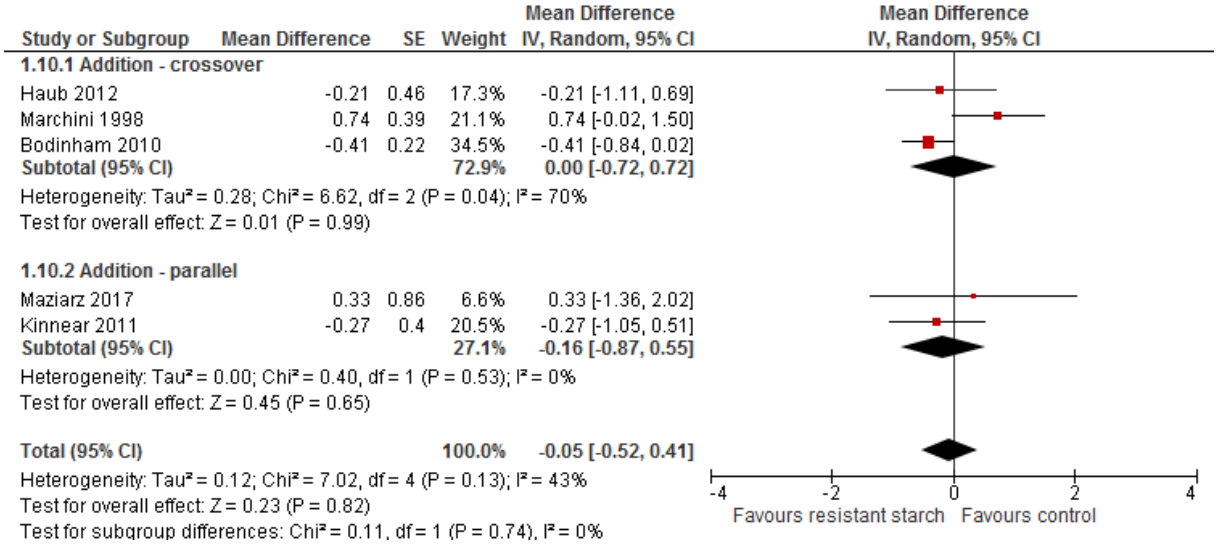

Figure 21. Forest plot of studies measuring peak postprandial blood glucose concentration following addition of resistant starch to food by study design.

2.3.1.2.6 Funding Source

Addition studies were either government or industry-led or industry funded. Again, there was no significant difference between funding source subgroups for addition studies (P = 0.13) (Figure 22).

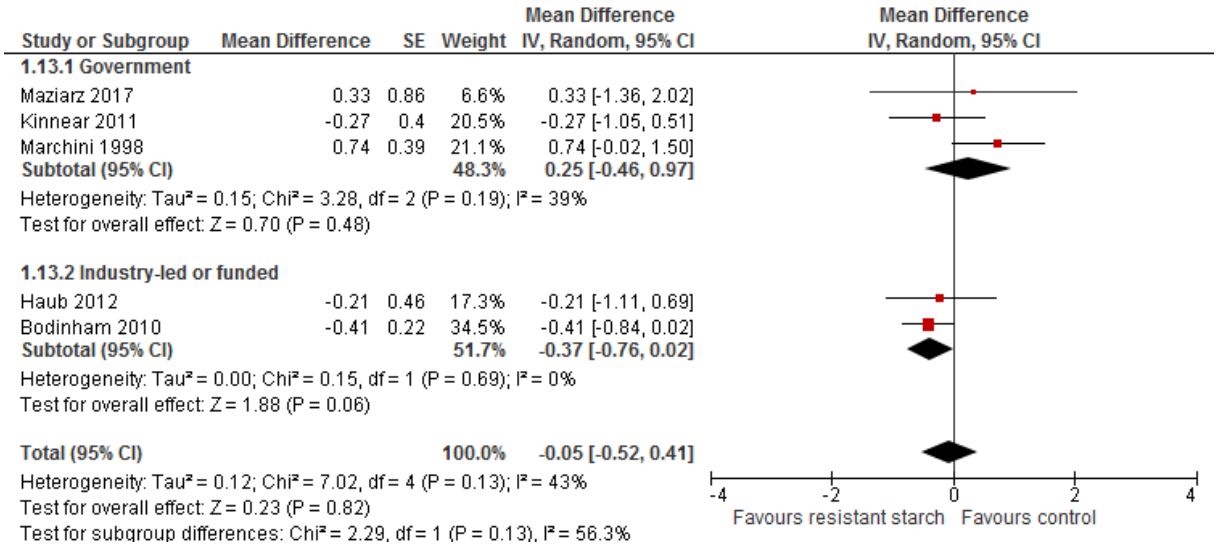

Figure 22. Forest plot of studies measuring peak postprandial blood glucose concentration following addition of resistant starch to food by funding source.

2.3.1.2.7 High versus low quality studies

Studies were determined to be of lower quality when a standardised meal or pre-testing dietary instructions were not provided to study participants. However subgroup analysis did not identify a significant difference in effect size between high and low quality studies (P=0.64) (Figure 23).

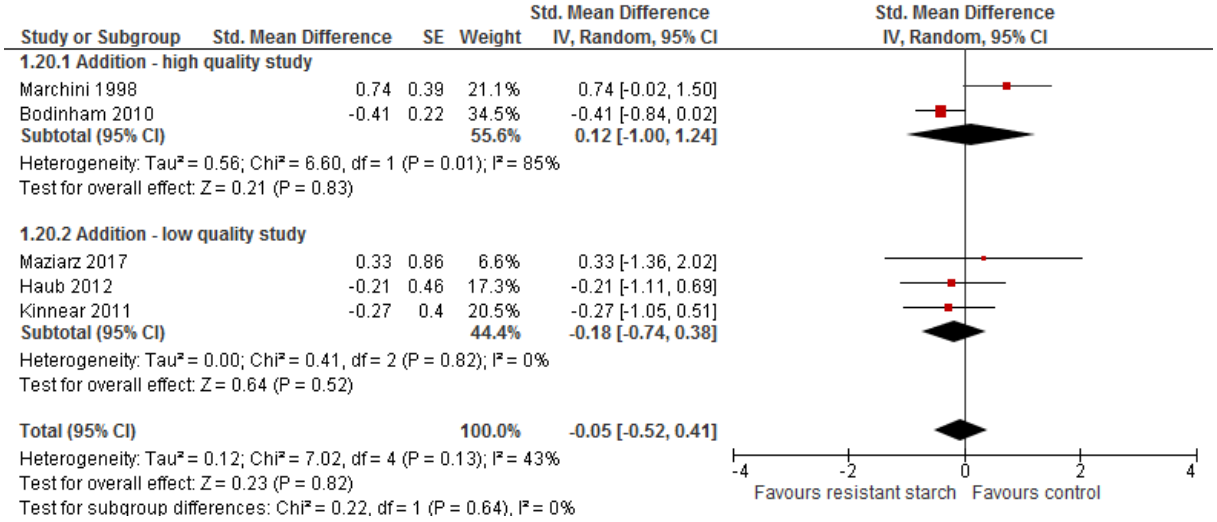

Figure 23. Forest plot of studies measuring peak postprandial blood glucose concentration following addition of resistant starch to food by study quality.

2.3.2 Publication bias

A wide range of resistant starch doses were tested in the included replacement studies and there were large differences in study design including total carbohydrate content, diabetic status of participants, form of food etc., therefore it is difficult to assess whether the asymmetry shown in Figure 24 reflects publication bias or variability in the methods among the studies (Sterne et al. 2011).

A funnel plot for addition studies was not undertaken as there are too few data points to assess asymmetry reliability.

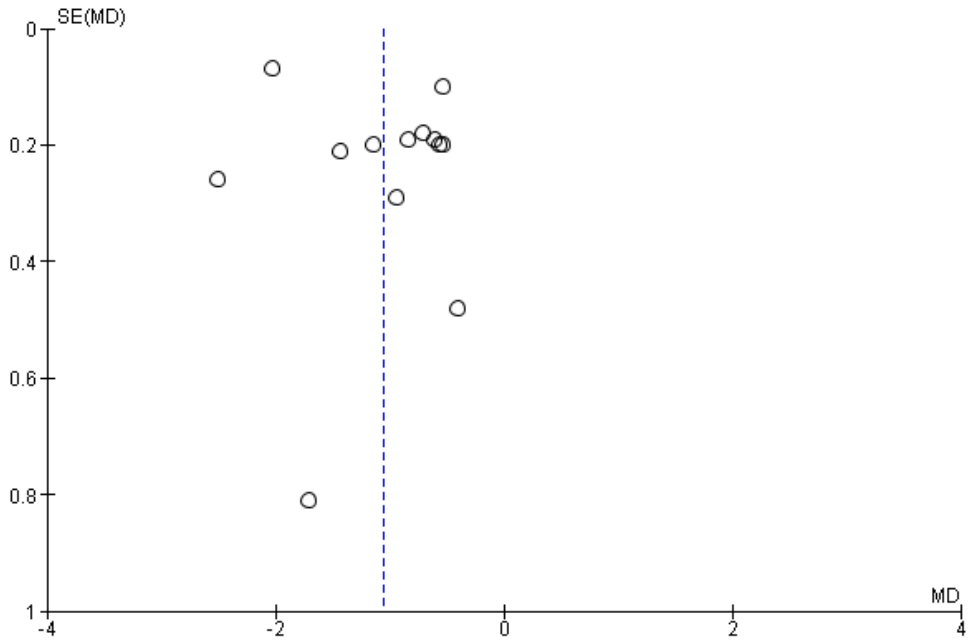

Figure 24. Funnel plot of effect sizes (MD: mean difference in mmol/L) versus standard errors (SE) around the mean on peak postprandial glucose concentration when digestible starch is replaced with resistant starch (positive numbers favour the control group).

3 Weight of evidence

For a food-health relationship to be substantiated there has to be a consistency of effect across high quality studies. The evidence base is strong for a causal relationship for a decrease in peak postprandial blood glucose when digestible starch is replaced with resistant starch. When analysed in high quality studies the effect size for the relationship is strong with resistant starch causing a decrease in peak postprandial blood glucose of 1.13 mmol/L (P = 0.0002) compared to control foods (Figure 15). Furthermore a moderate dose-response relationship was observed in studies in which resistant starch levels could be quantified with R^2 =0.49 (Figure 3A).

In contrast, fewer studies evaluated the relationship between addition of resistant starch and a decrease in peak postprandial blood glucose concentration compared to control foods. Two of these that were included in the meta-analysis were considered to be high quality (Bodinham et al. 2010; Marchini et al. 1998). The effect size was low in high quality studies with Z=0.21 (P = 0.83, Figure 23) indicating that a causal relationship does not exist between addition of resistant starch and a decrease in postprandial blood glucose. Two further studies (Hallstrom et al. 2011 and Klosterbuer et al. 2012) could not be included in meta-analysis as standard deviations were not provided. Klosterbuer and colleagues studied the effect of the addition of 25 g resistant starch to breakfast products in a double-blinded randomised controlled crossover study. The large dose of resistant starch resulted in a decrease of 0.17 mmol/L; a P value was not provided. The study by Hallstrom and colleagues did not affect peak postprandial blood glucose concentration following the addition of 3.3 g resistant starch. Furthermore the dose response relationship indicated that increasing the amount of resistant starch added to food did not affect peak postprandial blood glucose concentration (R^2=0.12, Figure 3A). Therefore based on the available evidence from high quality studies there is no

indication that addition of resistant starch to a food causes a decrease in postprandial blood glucose concentration.

Thus, based on the current evidence, the relationship between the replacement of digestible starch with resistant starch and a decrease in peak postprandial blood glucose concentration has been established to a high degree of certainty. The available evidence indicates to a moderate degree of certainty that a relationship does not exist between addition of resistant starch to a food and a decrease in peak postprandial blood glucose concentration.

3.1 Assessment of body of evidence

3.1.1 Consistency of relationship

Replacement studies

While the overall effect indicated a decrease in peak postprandial blood glucose when resistant starch replaced digestible starch in a food there was a high level of heterogeneity (I^2=96%) in high quality studies (Figure 15). Several subgroup analyses were undertaken to identify potential contributors to the heterogeneity including dose of RS, type of RS, presentation of food, diabetes status, blood extraction method, gender, funding source and quality of study. The level of heterogeneity decreased when studies were grouped by dose of resistant starch (Figure 7), presentation of food (Figure 10), diabetes status (Figure 11) and blood extraction method (Figure 12). Furthermore, included studies used a range of methods to quantify resistant starch (Table 2), which is recognised to cause varying results (Behall et al. 2002; Perera et al. 2010). Therefore FSANZ concludes that some of the heterogeneity observed for replacement studies can be attributed to several factors and therefore the observed heterogeneity does not alter our conclusion that a relationship exists between replacement of digestible starch with resistant starch in a food and a decrease in peak postprandial blood glucose concentration.

Addition studies

High quality addition studies showed a non-significant increase in peak postprandial blood glucose concentration (P=0.83) which FSANZ regards as showing no effect. Although the heterogeneity was high (I^2=85%) the confidence intervals of all studies cross the line of no effect. Therefore, based on the current evidence a relationship does not exist between addition of resistant starch to a food and a decrease in peak postprandial blood glucose concentration..

3.1.2 Causality

Randomised controlled trials are a strong design for inferring causality. All studies that were included in this review were randomised controlled trials. The RCTs in the replacement review included 225 adults, with high quality studies testing 154 adults. The review of addition studies included 68 subjects, 30 of whom were in high quality studies.

Studies were not downgraded for risk of bias as FSANZ concluded that the overall risk of bias in the body of evidence was low (Section 2.2.3).

Studies that provided standardised meals prior to consumption of test foods or dietary instructions were considered to be high quality.

Neither relationship was downrated for indirectness. Evidence was not found to be indirect in any of 4 potential categories as defined in the GRADE guidelines for imprecision (Guyatt et al. 2011)

- subjects did not differ from those of interest. The evidence base comprises mostly of data from normoglycaemic subjects and therefore represents the population of interest.
- The interventions that were tested did not differ from the intervention of interest. All included studies measured the addition of resistant starch to a food or the replacement of digestible starch with resistant starch in a food.
- The outcome did not differ from that of primary interest. All included studies measured postprandial blood glucose concentration at several intervals following consumption of food.
- The intervention of interest was tested directly with standardised methods.

The relationship between replacement of digestible starch with resistant starch in a food and a decrease in peak postprandial blood glucose concentration was not downrated for imprecision. 225 participants contributed to the evidence for mean effect estimate and the confidence interval of mean effect estimate of -1.50 to -0.61 indicated that imprecision was not of concern (Guyatt et al. 2011a) .

The relationship between addition of resistant starch in a food and decrease in peak postprandial blood glucose concentration had a small total sample size of 50 subjects in crossover design and 18 subjects in parallel design. Furthermore the confidence interval of effect estimate crossed the line of no effect for all trials as well as for high quality trials. Therefore this relationship was downgraded by one level for imprecision.

FSANZ concludes that there is a causal relationship between replacement of digestible starch with resistant starch and a decrease in peak postprandial blood glucose concentration. The degree of certainty in this relationship is ‘High’. However a causal relationship was not demonstrated between addition of resistant starch to a food and a decrease in peak postprandial blood glucose concentration, with a ‘Moderate’ degree of certainty.

3.1.3 Plausibility

The replacement of digestible starch with resistant starch is a plausible way of lowering peak postprandial blood glucose. Digestible starch is rapidly broken down into its constituent parts including maltose, maltotriose, α-dextrins, and glucose (Lovegrove et al. 2017). However resistant starch cannot be hydrolysed by α-amylase and remains intact until it reaches the large intestine. Partial or total fermentation of resistant starch can then occur by bacterial microflora in the large intestine. Therefore resistant starch does not contribute to an increase in peak postprandial blood glucose concentration and replacing digestible starch with resistant starch could plausibly result in a decrease in postprandial blood glucose. Furthermore, resistant starch delays gastric emptying and decreases absorption of macronutrients and therefore the addition of resistant starch to a food could also decrease postprandial blood glucose.

3.2 Applicability to Australia and New Zealand

3.2.1 Intake required for effect

Recent data on resistant starch intakes in Australia and New Zealand are not available. Australian intake of resistant starch based on the 1995 National Nutrition Survey database of 13,858 Australians is 10.7 g/day for adult males over 19 years and 8.2 g/day for females (Roberts et al. 2004). An approximation of resistant starch consumption in New Zealand was calculated as 6.5 g and 4.8 g for males and females age 10 and over (Baghurst and Baghurst, 1996). However these daily intake calculations for both countries are considered to be an underestimate since methods of analysis for resistant starch have been refined in the last 20 years.

Resistant starch is found naturally in a range of foods including white bread (1%), wholemeal bread (1- 6%), peas (4.9 - 6.3%) whole grain rice (11.8%), and unripe bananas (41- 59% dry weight) (Perera et al. 2010), however it is widely recognised that the method of quantification as well as food variety, cooking method can alter resistant starch estimates (Chiu and Stewart, 2013; Perera et al. 2010; Roberts et al. 2004).

The range of dose of resistant starch varied among included studies. For studies in which resistant starch could be quantified, the dose varied from 2.5 to 30.4 g for addition studies and from 5.8 g to 15 g for replacement studies. No effect was noted at any dose in addition studies however a decrease in postprandial blood glucose was observed at the lowest tested replacement dose of 5.8 g, equivalent to a replacement of 7% of total starch with resistant starch and approximately half of the average daily consumption rate for adult males in Australia, that was determined using 1995 national nutrition survey data.

Some bread products are currently available in Australia, delivering 1.5 g RS per 74 g serving size which is equivalent to approximately 5.5% total starch indicating that a 7% substitution rate may feasible within a single serving of bread or other foods.

Palatability was discussed in some studies in which large doses of resistant starch were tested. In one study it was noted that 40 g of hi-maize (equivalent to 24 g RS 2) was the highest quantity that could be added to a portion of a mousse before there were adverse effects on taste or texture (Bodinham et al. 2010). However the primary use for high amylose flour is more likely to be in cereal products and baked goods. A slight decrease in palatability was reported in high (22 g) or low (11 g) dose cookies compared to control foods (9% and 5% less palatable respectively) in the subjective palatability score (Luhovvy et al. 2014). No issue of palatability or adverse effects were discussed in other included studies using moderate or high quantities of RS 2 or RS4 (Brighenti et al. 2006; Seal et al. 2003; Tachibe et al. 2010; Tachibe et al. 2011). Therefore the minimum effective dose of 5.8 g should not cause negative palatability effects.

3.2.2 Target population

All studies but three (Giacco et al. 1998, Krezowski et al. 1987, Seal et al (T2D), 2003) were carried out on healthy, normoglycaemic adults. None of the included studies were conducted in New Zealand or Australia however FSANZ did not consider that dietary differences would influence the outcomes. No studies were identified in children.

3.2.3 Extrapolation from supplements

Not assessed due to the absence of evidence.

3.2.4 Adverse effects

An increase in insulin secretion compared to control foods would be considered an adverse effect. The effect of resistant starch on postprandial blood insulin levels were considered a priori. Insulin levels were tested in all but four studies (Kinnear et al. 2011; Luhovvy et al. 2014; Tachibe et al. 2010, Tachibe et al. 2011). In all replacement studies insulin levels were either lower or similar to those following consumption of control foods (Table 2). A small increase in insulin levels was reported at some time points in two addition studies (Table 3) (Marchini et al. 1998, 60 min and 150, no P values provided; Maziarz et al. 2017 non-significant difference at 15 min). However overall insulin secretion levels were similar in addition studies compared to control foods. A slight increase at some time points is unsurprising considering that an increased amount of carbohydrate is present in these studies.

Adverse effects of minor abdominal discomfort including bloating and flatulence were identified in some subjects in which large doses of resistant starch were tested. Behall and colleagues noted that some subjects that consumed high doses of resistant starch in the

form of high-amylose meals or diets experienced bloating and flatulence (Behall et al. 2002). A study that tested the effect of consuming 32 g resistant starch per day over a four week period in 24 healthy men reported that 91% of subjects that consumed RS3 and 82% of subjects that consumed RS2 reported flatulence compared to 55% of the control group. 41% of RS3 and 28% of RS2 subjects reported bloating compared to 9% of the glucose control group (Heijnen et al.1998). Another study by the same author also noted that one of ten subjects reported mild abdominal complaints in the evening of the measurement day following consumption of the 27 g of resistant starch (Heijnen et al. 1995). Muir and colleagues reported moderate levels of flatulence when subjects consumed 20 g resistant starch over one day (with a median value of 6 on a subjective symptom scale from 0 to 10 (Muir et al. 2004). No other adverse effects were identified in included studies.

4 Conclusion

Based on the evidence presented in this review it was possible to establish with a 'high' degree of certainty a relationship exists between replacement of digestible starch with resistant starch in a food and a decrease in peak postprandial blood glucose concentration. It was established with a moderate degree of certainty that a relationship does not exist between the addition of resistant starch to a food and a decrease in peak postprandial blood glucose concentration.

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Appendix 1: Search terms

The following search terms were used to identify studies for including in the review:

EMBASE – OVID platform
Database was searched on 29 February 2016 and 245 articles were identified.

#1	MeSH descriptor: [Blood Glucose] explode
#2	MeSH descriptor: [Hyperglycemia] explode
#3	glucose or "postprandial glucose" or "postprandial blood glucose" or "postprandial hyperglycemia" or "postprandial hyperglycaemia" or "postprandial hyperglycemias" or "postprandial hyperglycaemias" or "postprandial hypoglycemia" or "postprandial hypoglycaemia"
#4	#1 or #2 or #3
#5	MeSH descriptor: [Starch] explode
#6	MeSH descriptor: [Amylose] explode
#7	starch or resistant starch or "resistant starch" or RS1 or RS2 or RS3 or RS4 or amylose or high amylose or "high amylose" or amylomaize
#8	#5 or #6 or #7
#9	#4 and #8
#10	randomized controlled trial or "controlled clinical trial" or randomi*ed or placebo or randomly or trial or groups
#11	#9 and #10 in Trials

Cochrane CENTRAL
Database was searched on 25 February 2016 and 388 articles were identified.

#1	MeSH descriptor: [Blood Glucose] explode all trees
#2	MeSH descriptor: [Hyperglycemia] explode all trees
#3	glucose or "postprandial glucose" or "postprandial blood glucose" or "postprandial hyperglycemia" or "postprandial hyperglycaemia" or "postprandial hyperglycemias" or "postprandial hyperglycaemias" or "postprandial hypoglycemia" or "postprandial hypoglycaemia"
#4	#1 or #2 or #3
#5	MeSH descriptor: [Starch] explode all trees
#6	MeSH descriptor: [Amylose] explode all trees
#7	starch or resistant starch or "resistant starch" or RS1 or RS2 or RS3 or RS4 or amylose or high amylose or "high amylose" or amylomaize
#8	#5 or #6 or #7
#9	#4 and #8
#10	randomized controlled trial or "controlled clinical trial" or randomi*ed or placebo or randomly or trial or groups
#11	#9 and #10 in Trials

Medline – PubMed portal
Database was searched on 25 February 2016 and 662 articles were identified.

#1	Search (starch[MeSH Terms]) OR amylose[MeSH Terms]
#2	Search (((((((starch[Text Word]) OR amylose[Text Word]) OR resistant starch[Text Word]) OR RS1[Text Word]) OR RS2[Text Word]) OR RS3[Text Word]) OR RS4[Text Word]) OR high amylose[Text Word]) OR amylomaize[Text Word]
#3	Search (#1) OR #2
#4	Search ((postprandial hyperglycemia[MeSH Terms]) OR postprandial hyperglycemias[MeSH Terms]) OR blood glucose[MeSH Terms]
#5	Search (((glucose[Text Word]) OR postprandial glucose[Text Word]) OR postprandial blood glucose[Text Word]) OR postprandial hyperglycemia*[Text Word]
#6	Search (#4) OR #5
#7	Search (#3) AND #6
#8	Search ((((((("randomized controlled trial"[Publication Type]) OR "controlled clinical trial"[Publication Type]) OR randomi*ed[Title/Abstract]) OR placebo[Title/Abstract]) OR randomly[Title/Abstract]) OR trial[Title/Abstract]) OR groups[Title/Abstract]
#9	Search (#7) AND #8
#10	Search (animals[MeSH Terms]) NOT "humans"[MeSH Terms]
#11	Search (#9) NOT #10

Appendix 2: Studies excluded at full text review

Reference	Exclusion Reason
Abraha (1998)	Resistant starch not studied
Ahmad (2009)	Resistant starch not studied
Aldughpassi (2012)	Inadequate control group
Al-Tamimi (2010)	Digestible starch in control food was >110 % of replaced starch
Amelsvoort (1990)	Resistant starch not studied
Ames (2015)	Inadequate control group
Anderson (1990)	Resistant starch not studied
Anderson (2010)	Inadequate control group
Argyri (2013)	Resistant starch not studied
Asp (1996)	Unsuitable publication type
Asp (2006)	Resistant starch not studied
Asskali (2000)	Resistant starch not studied
Asskali (2001)	Resistant starch not studied
Axelsen (1997)	Resistant starch not studied
Axelsen (1999)	Resistant starch not studied
Axelsen (1999)	Resistant starch not studied
Axelsen (2000)	Resistant starch not studied
Baker (1984)	Resistant starch not studied
Bantle (1983)	Resistant starch not studied
Bantle (1986)	Resistant starch not studied
Bantle (1992)	Resistant starch not studied
Bantle (1993)	Resistant starch not studied
Behall (1988)	Subjects not randomised
Behall (1989)	Long term study
Behall (1995)	Long term study
Behall (2002)	Postprandial blood glucose not measured
Behall (2005)	Insufficient dietary information
Bhattacharya (2007)	Participants suffered disease affecting glucose metabolism
Bhattacharya (2015)	Participants suffered disease affecting glucose metabolism
Ble-Castillo (2014)	Long term study
Ble-Castillo (2015)	Unsuitable publication type
Bodinham (2012)	Long term study
Bodinham (2013)	No peak blood glucose
Bodinham (2014)	Long term study
Bornet (1987)	Resistant starch not studied
Bornet (1989)	Insufficient dietary information
Bornet (1990)	Resistant starch not studied
Bornet (1990)	Unsuitable study design
Bracken (2014)	Insufficient dietary information
Brand (1990)	Resistant starch not studied
Chiu (2013)	Insufficient dietary information
Correia (2008)	Participants suffered disease affecting glucose metabolism
Crapo (1980)	Resistant starch not studied

Reference	Exclusion Reason
Crapo (1988)	Resistant starch not studied
Culling (2009)	Resistant starch not studied
Daly (1998)	Resistant starch not studied
de (1995)	Long term study
Dodevska (2016)	Long term study
Edwards (2015)	Participants suffered disease affecting glucose metabolism
Ekstrom (2013)	Inadequate control group
Ells (2005)	Resistant starch not studied
Englyst (1999)	Resistant starch not studied
Erkelens (1985)	Resistant starch not studied
Gannon (1998)	Resistant starch not studied
Garcia-Rodriguez (2013)	Inadequate control group
Gargari (2015)	Long term study
Gentile (2015)	Postprandial blood glucose not measured sufficiently
Goodpaster (1996)	Inappropriate study design
Gower (2016)	Long term study
Granfeldt (1994)	Subjects not randomised
Granfeldt (1995)	Subjects not randomised
Granfeldt (1995)	Resistant starch not studied
Haub (2010)	Inadequate control group
Heaton (1988)	Resistant starch not studied
Heijnen (1995a)	Postprandial blood glucose not measured sufficiently
Heijnen (1995b)	Digestible starch in control food was >110 % of replaced starch
Heijnen (1996)	Long term study
Heijnen (1998)	Long term study
Hettiaratchi (2011)	Subjects not randomised
Hoebler (1999)	Subjects not randomised
Hoste (2009)	Unsuitable publication type
Howe (1996)	Long term study
ISRCTN26222607 (2005)	Resistant starch not studied
Jarvi (1999)	Resistant starch not studied
Jenkins (1998)	Long term study
Jimenez-Dominguez (2015)	Long term study
Johannsen (2007)	Inadequate control group
Johansson (2013)	Postprandial blood glucose not measured
Johnston (2010)	Long term study
Karimi (2016)	Long term study
Karupaiah (2011)	Subjects not randomised
Keogh (2007)	Long term study
Klinken (2015)	Unsuitable publication type. Related paper identified and included in review.
Konings (2014)	Resistant starch not studied

Reference	Exclusion Reason
Kwak (2012)	Long term study
Larsen (1996)	Inadequate control group
Li (2011)	Postprandial blood glucose not measured
Lintas (1995)	Inadequate control group
Lobley (2013)	Long term study
Lyon (2011)	Resistant starch not studied
Maki (2012)	Long term study
Martino (2013)	Resistant starch not studied
Meynier (2015)	Resistant starch not studied
Meynier (2015)	Unsuitable publication type
Miller (1994)	Resistant starch not studied
Mohan (2016)	Inadequate control group
Nichenametla (2014)	Long term study
Nilsson (2008)	Long term study
Nilsson (2010)	Long term study
Noakes (1996)	Long term study
Nordgaard (1995)	Postprandial blood glucose not measured
O'Connor (2015)	Unsuitable publication type
O'Connor (2016)	Inadequate control group
Olesen (1994)	Subjects not randomised
Otto (1982)	Resistant starch not studied
Park (2004)	Long term study
Penn (2010)	Long term study
Peronnet (2015)	Resistant starch not studied
Poquette (2014)	Inadequate control group
Quilez (2007)	Inadequate control group
Raben (1994)	Subjects not randomised
Ranganathan (1994)	Design could not be considered as either addition or replacement study
Reiser (1979)	Resistant starch not studied
Reiser (1989)	Resistant starch not studied
Robertson (2003)	Long term study
Robertson (2005)	Long term study
Robertson (2012)	Unsuitable publication type
Robertson (2012)	Long term study
Rodin (1991)	Resistant starch not studied
Sands (2009)	Resistant starch not studied
Schioldan (2015)	Unsuitable publication type
Schioldan (2017)	Long term study
Smith (2012)	Resistant starch not studied
Swan (1966)	Resistant starch not studied
Swanson (1992)	Long term study
Tagliabue (1995)	Postprandial blood glucose not measured
Trinidad (2013)	Subjects not randomised
Vonk (2000)	Subjects not randomised
Westrate (1993)	Inadequate control group

Reference	Exclusion Reason
Wolever (1996)	Resistant starch not studied
Wolever (2016)	Inadequate control group
Wolf (2001)	Inadequate control group
Wong (1981)	Resistant starch not studied
Yamada (2005)	Subjects not randomised
Zenel (2015)	Variation in resistant starch too low to assess effect
Zhang (2007)	Postprandial blood glucose not measured

Appendix 3: Risk of bias table for studies in the systematic review

Reference	Random sequence generation (selection bias)		Allocation concealment (selection bias)*		Blinding of participants and personnel (performance bias)*		Blinding of outcome assessors (detection bias); type of blood sample drawn and analysed*		Incomplete outcome data (attrition bias)		Selective reporting (reporting bias)		Other (dietary and exercise instructions; testing interval in cross-over studies)	
Achour 1997	**?**	Not described	**Low**	Not described	**Low**	Not described	**Low**	Venous, standard method	**?**	Not described	**Low**	Expected outcome reported	Low	No alcohol or exercise for 3 days before, standardised low residue dinner night before. 1 week washout
Akerberg 1998	**?**	Not described	**Low**	Not described	**Low**	Not described	**High**	Finger prick blood sample	**?**	Not described	**Low**	Expected outcome reported	?	Overnight fast. 1 week washout
Behall 2002	**Low**	Williams Latin Square design	**Low**	Not described	**Low**	Not described	**Low**	Venous, standard method	**Low**	1/26, dropout unrelated to study	**Low**	Expected outcome reported	Low	Standard equilibration diet for 2 days before.
Behall 2006	**Low**	Williams Latin Square design	**Low**	Not described	**Low**	Not described	**Low**	Venous, standard method	**Low**	1/10, dropout unrelated to study	**Low**	Expected outcome reported	Low	Standard equilibration diet for 2 days before.
Brighenti 2006	**?**	Not described	**Low**	Not described	**Low**		**Low**	Venous blood and semi-automatic glucose analyser	**Low**	Zero attrition rate	**Low**	Expected outcome reported	Low	Avoid smoking during test day, maintain usual physical activity during study period, standardised dinner night before. 1 week washout
Giacco 1998	**?**	Not described	**Low**	Not described	**Low**	Not described	**Low**	Venous, standard method	**?**	Not described	**Low**	Expected outcome reported	Low	12 hour fast. 2 day low fibre isoenergetic diet before each arm.

Reference	Random sequence generation (selection bias)		Allocation concealment (selection bias)*		Blinding of participants and personnel (performance bias)*		Blinding of outcome assessors (detection bias); type of blood sample drawn and analysed*		Incomplete outcome data (attrition bias)		Selective reporting (reporting bias)		Other (dietary and exercise instructions; testing interval in cross-over studies)	
Goddard 1984	**?**	Not described	**Low**	Not described	**Low**	Not described	**Low**	Venous, standard method	**?**	Not described	**Low**	Expected outcome reported	?	Overnight fast.1-2 week washout
Hospers 1994	**Low**	Block design	**Low**	Not described	**Low**		**Low**	Venous, standard method	**Low**	Zero attrition rate	**Low**	Expected outcome reported	Low	Instructed to refrain from eating legumes, onions, leek, pea-soup, garlic or strong spices, to avoid excessive intake of alcohol and snacks for the 2 day before experimental day. Ate normal breakfast, two and half hour fast before pasta lunch. At least one day washout.
Krezowski 1987	**?**	Not described	**Low**	Not described	**Low**	Not described	**Low**	Venous, standard method	**Low**	Zero attrition rate	**Low**	Expected outcome reported	Low	Diet with at least 200 g CHO/day with adequate food energy for 3 days before testing. 3+ week washout
Li 2010	**?**	Stratified randomis-ation with no method provided	**Low**	Not described	**Low**	Not described	**Low**	Venous, standard method	**Low**	Zero attrition rate	**Low**	Expected outcome reported	Low	Avoid hydrogen producing foods, high fibre food, alcohol, beverages and others and recorded consumption for

Reference	Random sequence generation (selection bias)		Allocation concealment (selection bias)*		Blinding of participants and personnel (performance bias)*		Blinding of outcome assessors (detection bias); type of blood sample drawn and analysed*		Incomplete outcome data (attrition bias)		Selective reporting (reporting bias)		Other (dietary and exercise instructions; testing interval in cross-over studies)	
														24hr before. 1 week washout
Lin 2015	**?**	Not described	**Low**	Not described	**Low**	Not described	**?**	Venous, standard method	**Low**	Zero attrition rate	**Low**	Expected outcome reported	?	No pretesting instructions described. 1 day washout
Luhovyy 2014	**?**	Not described	**Low**	Not described	**Low**	Double blind	**High**	Finger prick blood testing	**Low**	Zero attrition rate	**Low**	Expected outcome reported	Low	10-12 hr fast, following std breakfast 4 hr before arrival. 1 week washout
Seal 2003	**?**	Not described	**Low**	Not described	**Low**	Double blind	**Low**	Venous, standard method	**Low**	Zero attrition rate	**Low**	Expected outcome reported	?	No alcohol or strenuous exercise 24hr before, fasting from 9pm night before. 1 week or 1 month (females) washout. Standardised meal for T2D subjects
Seewi 1999	**Low**	Random-generator program	**Low**	Not described	**Low**	Double blinded	**Low**	Venous, standard method	**?**	Not described	**Low**	Expected outcome reported	?	Overnight fast
Shimotoyodome 2011	**?**	Not described	**Low**	Not described	**Low**	Single blinded	**High**	Finger prick blood testing	**Low**	Zero attrition rate	**Low**	Expected outcome reported	Low	2 day before study abstain from alcohol and exercise. Standardised dinner 8 - 8.30pm night before. Refrain from food and water 12hr and

Reference	Random sequence generation (selection bias)		Allocation concealment (selection bias)*		Blinding of participants and personnel (performance bias)*		Blinding of outcome assessors (detection bias); type of blood sample drawn and analysed*		Incomplete outcome data (attrition bias)		Selective reporting (reporting bias)		Other (dietary and exercise instructions; testing interval in cross-over studies)	
														3hr before test meal respectively. 1 week washout
Tachibe 2010	**?**	Not described	**Low**	Not described	**Low**	Not described	**High**	Finger prick blood testing	**Low**	Zero attrition rate	**Low**	Expected outcome reported	Low	Consume a pre-prepared dinner at 9pm then 12hr fast. Avoid alcohol, excessive eating and excessive physical exercise over the experimental period. 7 day washout
Tachibe 2011	**?**	Not described	**Low**	Not described	**Low**	Not described	**High**	Finger prick blood testing	**Low**	Zero attrition rate	**Low**	Expected outcome reported	Low	Consume a pre-prepared dinner at 9pm then 12 hr fast. Avoid alcohol, excessive eating and excessive physical exercise over the experimental period. 3 day washout
Van Amelsvoort 1992	**?**	Not described	**Low**	Not described	**Low**	Not described	**Low**	Venous, standard method	**Low**	2/24 reasons unrelated to study	**Low**	Expected outcome reported	?	Instructions provided - normal activity pattern. 1 week washout
Addition Studies														

Reference	Random sequence generation (selection bias)		Allocation concealment (selection bias)*		Blinding of participants and personnel (performance bias)*		Blinding of outcome assessors (detection bias); type of blood sample drawn and analysed*		Incomplete outcome data (attrition bias)		Selective reporting (reporting bias)		Other (dietary and exercise instructions; testing interval in cross-over studies)	
Bodinham	**?**	Not described	**Low**	Not described	**Low**	Single blinded	**Low**	Venous, standard method	**Low**	Zero attrition rate	**Low**	Expected outcome reported	Low	Overnight fast, identical evening meal before fast, avoid alcohol, caffeine and strenuous exercise for at least 24hr before. At least one week washout
Hallstrom 2011	**?**	Not described	**Low**	Not described	**Low**	Not described	**High**	Finger prick blood testing	**Low**	Zero attrition rate	**Low**	Expected outcome reported	Low	No tobacco, antibiotics, probiotics during and 2 weeks before the test period. Avoid strenuous exercise, alcohol or eat meals rich in fibre the day before testing. Eat a low fibre dinner at 6pm night before testing and eat the same meal each night before testing
Haub 2012	**Low**	Williams Latin Square	**Low**	Not described	**Low**	Single blinded	**Low**	Venous, standard method	**Low**	Zero attrition rate	**Low**	Expected outcome reported	?	10 hour fasting

Reference	Random sequence generation (selection bias)		Allocation concealment (selection bias)*		Blinding of participants and personnel (performance bias)*		Blinding of outcome assessors (detection bias); type of blood sample drawn and analysed*		Incomplete outcome data (attrition bias)		Selective reporting (reporting bias)		Other (dietary and exercise instructions; testing interval in cross-over studies)	
Kinnear 2011	**?**	Not described	**Low**	Not described	**Low**	Not described	**High**	Finger prick blood testing	**Low**	Zero attrition rate	**Low**	Expected outcome reported	?	10-12hr overnight fasting. At least 1 day washout
Klosterb-uer 2012	**?**	Not described	**Low**	Not described	**Low**	Not described	**Low**	Venous blood and automatic glucose analyser	**Low**	Zero attrition rate	**Low**	Expected outcome reported	Low	Instructed to follow a low-fibre diet and avoid fibre supplements, alcohol and excessive exercise for 24hr before each study visit. 12 hour fast before testing. At least 3 week washout
Marchini 1998	**?**	Not described	**Low**	Not described	**Low**	Not described	**Low**	Venous, standard method	**?**	Not described	**Low**	Expected outcome reported	Low	No alcohol and exercise for 3 days before expt, 12hr min fast, eat normal diet with fibre and resistant starch less than 5 gram per day. Overnight washout
Maziarz 2017	**Low**	Random number generator	**?**	Parallel design and not described	**Low**	Double blind	**Low**	Venous, standard method	**Low**	7/25, reasons unrelated to study	**Low**	Expected outcome reported	?	Overnight fast. At least one day washout

*Because the outcome is measured within hours of the test, and test foods are supplied, there is no opportunity for lack of blinding to affect adherence during the testing phase, studies which did not describe their methods clearly were considered to have low risk of bias for allocation concealment if they used a cross-over design, or low risk of

performance bias if they used a cross-over design and there was no choice by subjects in the quantity consumed and low risk of detection bias if they collected a venous blood sample and was analysed using a standard method that could not involve technician variation

Appendix 4: GRADE summary of findings table.

Question A: Does replacement of digestible starch with resistant starch affect peak postprandial blood glucose concentration?
Source: FSANZ systematic review of evidence

Quality assessment of body of evidence							Participants			Mean effect estimate mmol/L [95% CI]	Quality (degree of certainty in relationship)
Number of trials	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Considerations	Cross-over	P-INT.	P-CTL		
Effect of all trials on postprandial blood glucose											
13	RCTs	none	none	none	none	dose-response curve	225	N/A	N/A	-1.06 [-1.50, -0.61]	⊕⊕⊕⊕ High
Effect of high quality trials on postprandial blood glucose											
11	RCTs	none	none	none	none	dose-response curve	154	N/A	N/A	-1.13 [-1.72, -0.54]	⊕⊕⊕⊕ High

P-INT: participants in intervention arm of parallel trials; P-CTL: participants in control arm of parallel trials

Question B: Does addition of digestible starch to a food affect peak postprandial blood glucose concentration?
Source: FSANZ systematic review of evidence

Quality assessment of body of evidence							Participants			Mean effect estimate mmol/L [95% CI]	Quality (degree of certainty in relationship)
Number of trials	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Considerations	Cross-over	P-INT.	P-CTL		
Effect of all trials on postprandial blood glucose											
5	RCTs	none	none	none	serious[1]	dose-response curve	50	9	9	-0.05 [-0.52, 0.41]	⊕⊕⊕ Moderate
Effect of high quality trials on postprandial blood glucose											
2	RCTs	none	none	none	serious[1]	dose-response curve	30	N/A	N/A	0.12 [-1.00,1.24]	⊕⊕⊕ Moderate

P-INT: participants in intervention arm of parallel trials; P-CTL: participants in control arm of parallel trials
[1]*Small total sample sizes were down-graded for imprecision*