



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

**Systematic review of the evidence for a
relationship between
 β -glucan from oats or barley and
peak postprandial blood glucose concentration**

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Date: April 2016

Table of Contents

Executive Summary	i
1. Introduction.....	1
1.1 Food or property of food.....	1
1.2 Health effect.....	2
1.3 Proposed relationship.....	2
2. Evaluation of evidence	3
2.1 Methods	3
2.1.1 Search strategy.....	3
2.1.2 Inclusion and exclusion criteria.....	3
2.1.3 Study selection, data extraction and quality assessment.....	4
2.1.4 Statistical analyses.....	4
2.1.5 Subgroup analyses	5
2.2 Results.....	5
2.2.1 Search results and included studies	5
2.2.2 Quality assessment of studies and strata	7
2.3 Summary of evidence.....	8
2.3.1 β -glucan from oats or barley and peak postprandial blood glucose	8
2.3.2 Publication bias.....	9
3. Weight of evidence	10
3.1 Assessment of body of evidence.....	10
3.1.1 Consistency	10
3.1.2 Causality	10
3.1.3 Plausibility	10
3.2 Applicability to Australia and New Zealand.....	11
3.2.1 Intake required for the effect.....	11
3.2.2 Target population	11
3.2.3 Extrapolation from supplements	11
3.2.4 Adverse effects	11
4. Conclusion	12
5. Acknowledgment	12
6. References.....	12
Appendix 1: Database search strategy	18
Appendix 2: Studies excluded at full text review	20
Appendix 3: Characteristics of included strata	23
Appendix 4: Summary of risk of bias for the included strata	24
Appendix 5: Risk of bias of strata included in the systematic review.....	25
Appendix 6: GRADE summary of findings tables.....	26

Executive Summary

<i>Does the dietary intake of β-glucan from oats reduce peak postprandial blood glucose concentration?</i>	
Food-health relationship	Intake of β -glucan from oats reduces peak postprandial blood glucose concentration
Degree of certainty (GRADE rating)	⊕ Very Low
Component	Notes
<i>Body of evidence</i>	The three strata from two randomised controlled trials (RCTs) that were included in the systematic review tested 4 g of an enzymatically-modified β -glucan derived from oats on 15 healthy subjects. Each of the subjects received the modified β -glucan as a drink containing 50 g of glucose. All data come from a single research group.
<i>Consistency</i>	All three strata from the RCTs showed a reduction in peak postprandial blood glucose concentration after consuming the glucose-based beverage containing 4 g of an enzymatically-modified β -glucan derived from oats.
<i>Causality</i>	When sufficiently powered, an RCT is a strong study design for demonstrating a causal relationship between intake of food or a property of food and a health outcome. However, consideration of several factors has resulted in the conclusion that the data do not provide strong causal evidence for the relationship in question. These considerations include (i) uncertainty in the degree of similarity of the tested modified β -glucan and the naturally-occurring β -glucans in oats; (ii) the modified β -glucan was provided to a low number of subjects; and (iii) the modified β -glucan was provided at only one dose level of 4 g, an amount unlikely to be present in a single serving of food. Therefore, a causal relationship for an amount that is more likely to be achieved in a single serving of food cannot be established by extrapolation.
<i>Plausibility</i>	It is plausible that β -glucan from oats reduces peak postprandial blood glucose concentration by increasing fluid viscosity in the gastrointestinal tract, thereby reducing glucose uptake.
<i>Generalisability</i>	Not applicable because of the low quality of the evidence, the small size of the population sample and lack of generalisability to the naturally-occurring β -glucans in oats for consumption by healthy individuals.

Does the dietary intake of β -glucan from barley reduce peak postprandial blood glucose concentration?

Food-health relationship	Intake of β -glucan from barley reduces peak postprandial blood glucose concentration
Degree of certainty (GRADE rating)	Not assessable

Component	Notes
Body of evidence	No RCT measured the effect of pure β -glucan from barley. All studies, including those which investigated extracted/concentrated barley, included other fibres and food components in addition to β -glucan. Therefore, the relationship could not be assessed.
Consistency	Consistency could not be assessed because there were no trials which would allow the effect of β -glucan from barley to be separated from the effects of other components in the food products.
Causality	When sufficiently powered, an RCT is a strong study design for demonstrating a causal relationship between intake of food or a property of food and a health outcome. However, because no available RCT used pure β -glucan from barley, no conclusion can be drawn regarding the consumption of β -glucan from barley and a reduction in peak postprandial blood glucose concentration.
Plausibility	It is plausible that β -glucan from barley reduces peak postprandial blood glucose concentration by increasing fluid viscosity in the gastrointestinal tract, thereby reducing glucose uptake.
Generalisability	Not applicable due to the lack of the evidence.

FSANZ has conducted a systematic review on the intake of β -glucan derived from oats or barley on the reduction of peak postprandial blood glucose concentrations in humans. In doing this review, FSANZ has 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*.

Of the 1192 articles retrieved from the literature search for evidence to assess the food-health relationships in question, all but 48 articles were rejected based on their titles and abstracts. Forty-six of the 48 articles were rejected after full-text screening because they did not meet the *a priori* inclusion criteria – mainly due to the use of interventions that confound the interpretation of data such as the use of dietary fibres that contain β -glucan-like substances which are known to affect glucose absorption.

Two related articles were included in the review and both originated from a single Canadian research group. For the purpose of meta-analysis, data from three of the nine reported strata were extracted from the blood glucose concentration-time curves that were shown in the articles. These strata were comprised of the same 15 subjects. The analysis showed a significant effect (-0.96 mmol/L, 95% CI: -1.34, -0.58) that favoured intervention. However, the interventions described in both articles were semi-synthetic β -glucans that were obtained by enzymatic hydrolysis of oat-derived β -glucans. Furthermore, they were used in amounts that are unlikely to be present in a single serving of food.

With low risks of selection (random sequence generation), performance (blinding of subjects), attrition and reporting biases combined with unclear risk of selection (allocation concealment), and detection biases in all three included strata, an overall moderate risk of bias was determined for the three strata that were included in the meta-analysis.

The relationship was down rated because the rheological properties of the semi-synthetic β -glucans compared with those of the naturally occurring β -glucans in oats is unclear, there were few subjects and authors do not describe whether subjects were given instructions that reduce the variation in test results due to background diet and exercise. Furthermore, the amounts used in the interventions limit any conclusions that can be made about generalisability to Australian and New Zealand populations.

FSANZ concludes that there is a “very low” degree of certainty in the relationship between the intake of β -glucan from oats and the reduction in peak postprandial blood glucose concentration. The available evidence also relates to a quantity of β -glucan that is unlikely to be achieved in a single eating occasion.

As there were no studies that tested purified β -glucan derived from barley, FSANZ concludes that the relationship between the intake of β -glucan from barley and the reduction in peak postprandial blood glucose concentration is not assessable.

1. Introduction

In 2012, the European Union authorised the health claim that: “Consumption of β -glucans from oats or barley as part of a meal contributes to the reduction of the blood glucose rise after that meal”. The conditions for using this claim states that it “may be used only for food which contains at least 4 g of β -glucans from oats or barley for each 30 g of available carbohydrates in a quantified portion as part of the meal. In order to bear the claim information shall be given to the consumer that the beneficial effect is obtained by consuming the β -glucans from oats or barley as part of the meal” (The European Commission 2012).

In examining the evidence to support this claim, the European Food Safety Authority (EFSA) concluded that the claim was established based on human dietary intervention studies investigating the effects of concentrated dietary fibres derived from oats or barley on postprandial glycaemic responses (EFSA 2011). Changes in the postprandial glucose concentrations in the studies that were considered by EFSA were nominally ascribed to the β -glucans in the meals. The conclusion by EFSA was drawn from a narrative review of the scientific literature. EFSA did not perform a systematic review of the literature.

FSANZ is considering whether a relationship between the intake of β -glucan derived from oats or barley in a meal and reduced peak postprandial blood glucose concentration can be incorporated into Schedule 4 – Nutrition, health and related claims in the *Australia New Zealand Food Standards Code*. FSANZ considers that 4 g of β -glucan, which is the amount of β -glucan stated in the EU authorised health claim, is unlikely to be obtained from a single food on a single eating occasion but that smaller amounts could be obtained. No relevant systematic reviews on the topic were identified.

The purpose of this paper is to systematically review the totality of available evidence for the relationships between the intake of β -glucan derived from oats or barley in a meal and a reduction in peak postprandial blood glucose concentration.

1.1 Food or property of food

β -Glucans are non-starch polysaccharides made of glucose molecules linked by β -glycosidic bonds and located in the endosperm cell walls (Wood 2002; Vasanthan and Temelli 2008). The content and molecular weight of β -glucan varies between and within cereals, with higher molecular weight forms having greater viscosity and lower water-solubility (Kim and White, 2013). High levels of β -glucan are found in the bran of oats (*Avena sativa*) and barley (*Hordeum vulgare*) with an average content between 3.7 and 6.5% w/w, with much lower amounts in other grains such as wheat and rye (Wood 2002; Shewry et al. 2013). Technologies for concentrating and extracting β -glucan from oats and barley can increase β -glucan by up to 30% by dry separation processes and up to 65% by wet separation processes (Vasanthan and Temelli 2008; Limberger-Bayer et al. 2014). Specialised plant breeding programs can also produce cultivars with naturally higher amounts of β -glucan, e.g. BarleyMaxTM produced by the Commonwealth Scientific and Industrial Research Organisation (CSIRO) contains 10% w/w β -glucan (Topping et al. 2003). Other sources of β -glucan include baker's yeast and fungi. However, it is important to note that β -glucan from those alternative sources is not chemically identical to that from oats and barley (Manzi and Pizzoferrato 2000).

For the purpose of this food-health relationship, only purified β -glucans derived from oats or barley were considered (see section 2.1.2). Whole grain oats and barley, and fibre concentrates derived from these grains, are not considered in this review.

1.2 Health effect

An increase in blood glucose concentration after a meal is a normal physiological response as glucose is liberated from food and then absorbed (Venn and Green 2007). This rise in blood glucose promotes insulin release from the islet cells of the pancreas into the bloodstream, which in turn facilitates glucose 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, which stimulates the liver to convert stored glycogen into glucose. Thus the interplay between insulin and glucagon keeps blood glucose concentrations tightly controlled.

There are a number of ways of investigating changes in blood glucose concentration after a meal. Fasting serum or plasma glucose levels are measured and then, following an intervention, blood samples are typically taken every 10, 15 or 30 minutes for between 120 minutes to five hours. Blood samples are taken using an indwelling catheter. In the literature, commonly reported measures of postprandial blood glucose include: time to peak, rate of rise, peak, incremental peak, mean, incremental mean, 2-hour glucose, area under the blood glucose concentration curve (AUC) (which may be over differing time points), and incremental area under the blood glucose concentration 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 true peak. In addition, the true peak might occur at different times in people consuming different types of food or in people with normal as compared to those with abnormal glucose metabolism. There is no agreement among researchers as to which of these various outcome measures is the most relevant for assessing the physiological impact of changes in postprandial blood glucose concentrations.

After consultation with FSANZ's Health Claims Scientific Advisory Group, peak glucose was chosen as the most appropriate measure of postprandial blood glucose concentration 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 meal or glucose drink 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 glucose concentration was defined as ≤ 5.5 mmol/L, impaired glucose tolerance was defined as 5.6–6.9 mmol/L and diabetes was defined as ≥ 7.0 mmol/L (Diabetes Australia 2012).

1.3 Proposed relationship

FSANZ regards the reference to 'as part of a meal' in the EU claim under consideration to be a wording condition of General Function Claims under Article 13.1 in the EU. The relationship assessed by FSANZ therefore examined relevant evidence from studies in which the interventions were presented as 'meals' that did not necessarily contain macronutrients such as fat and protein.

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

- Dietary intake of β -glucan from oats reduces peak postprandial blood glucose concentration
- Dietary intake of β -glucan from barley reduces peak postprandial blood glucose concentration

2. Evaluation of evidence

A systematic review of the literature was performed to assess the proposed food-health relationships.

2.1 Methods

2.1.1 Search strategy

A search was conducted in PubMed and Cochrane CENTRAL on 8 January 2016 and in Embase® (OVID) on 15 January 2016. Detailed search strategies are presented in Appendix 1. Hand-searching was performed on the reference lists of articles screened on full-text.

2.1.2 Inclusion and exclusion criteria

The eligibility criteria are summarised in Table 1. To be included in the systematic review, an article must state that the trial was randomised or described an allocation method that suggests randomisation, such as Latin Square, and have included an appropriate control group. Parallel and cross-over designs were acceptable. Sequential designs were excluded because in such designs all subjects receive meals in the same order without randomisation.

With a sufficient washout period before the intervention, the absence of double-blinding for participants or observers was not treated as an exclusion criterion because the postprandial blood glucose concentration is measured within two hours of the intervention by standard laboratory methods. Therefore, there is limited opportunity for non-compliance factors by participants or observers to affect the assessment results.

For a study to be included, the β -glucan must be derived from either oats or barley and be of sufficient purity to unequivocally ascribe any postprandial blood glucose concentration effects to β -glucan. When the purity of the β -glucan was such that it contained other dietary fibres, polysaccharides or other compounds that can affect glucose absorption, the study was excluded because the changes in postprandial glucose cannot be unequivocally ascribed to β -glucan. Similarly, studies testing pure β -glucan from oats or barley mixed with other dietary fibres from similar or other sources were excluded unless the control group received the same vehicle or meal without the purified β -glucan.

Table 1. PICOTS criteria for study selection

Population	Non-acutely ill people.
Intervention	β -Glucan extracted and purified from either oats or barley and consumed with a meal. The purity of the β -glucan used in the intervention must be such that any reduction in peak postprandial blood glucose concentration can be unequivocally ascribed to β -glucan.
Comparator	Placebo or same foods without β -glucan.
Outcome	Peak postprandial blood glucose concentration.
Time	At least 90 minutes of reported postprandial blood glucose concentration measurements.
Study design	Randomised controlled trial (RCT).

The β -glucan intervention had to occur at a single meal, with blood glucose concentrations measured after that meal for at least 90 minutes.

Trials involving acutely ill subjects were excluded. Studies in subjects using medication that affect or control blood glucose were not excluded, unless medication regimes were different between the control and the test groups.

2.1.3 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 and exclusion criteria. Screening was conducted by one researcher.

Peak postprandial blood glucose concentration was, for the purpose of our meta-analysis, defined as the *maximum point on the blood glucose concentration-time curve or the maximum result that was recorded over the blood sampling period*. If blood glucose concentration-time curves were reported, then the web-based open access software package WebPlotDigitizer V3.9 was used to extract data, otherwise numeric data was used to calculate the mean effect size.

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 the study reported changes in postprandial blood glucose concentrations for multiple arms of β -glucan intervention, and there was no variation in the quantity of both β -glucan and glucose in the test meal, the arm chosen was the one in which the meal most closely approximated that which would be consumed in a normal diet. For instance in the case of a multi-arm study that tested modified oat- or barley-derived β -glucans, the arm (or arms) which tested the β -glucan that was most similar to that found in oats or barley would be used in the meta-analysis.

Blood glucose concentration results, information regarding the composition of the interventions, and the risk of bias assessment were extracted by two investigators. An assessment of the quality of each of the included strata was based on consideration of the following:

- a) a clearly stated hypothesis
- b) minimisation of bias
- c) adequate control for confounding
- d) the study participants' background diets and other relevant lifestyle factors
- e) study duration and follow-up adequate to demonstrate the health effect
- f) the statistical power to test the hypothesis.

The individual and the overall risk of bias of included studies was conducted according to the Cochrane Handbook (Higgins and Green 2011). The quality of the body of evidence was assessed using the GRADE Framework (Guyatt et al. 2008; Guyatt et al. 2011).

2.1.4 Statistical analyses

Following data extraction, changes in peak postprandial blood glucose concentrations were calculated. Given that the included studies are a crossover design, the difference in peak postprandial blood glucose concentrations was calculated as the following:

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

The standard error (SEM) for the difference in blood glucose concentrations was calculated as:

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

The correlation coefficient (r) in the above formula was imputed as 0.6 based on the intra-class correlation obtained from a linear mixed model fitted to data obtained from 150 people from whom up to 12 replicate measurements of capillary blood glucose were taken at baseline and 30 minutes after consuming 50 g of 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 the generic inverse variance method. The meta-analysis was performed using RevMan version 5.3 (The Nordic Cochrane Centre 2014).

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”. 0%, 25%, 50% and 75% can be interpreted as indicating no, low, medium and high heterogeneity, respectively (Higgins et al. 2003; Higgins and Green 2011).

2.1.5 Subgroup analyses

No sub-group analysis has been carried out because of the small number of included studies and populations to compare.

2.2 Results

2.2.1 Search results and included studies

The screening of articles retrieved from the literature search is detailed in Figure 1. Studies excluded after full text examination are listed in Appendix 2.

There were 48 articles screened on full text of which 46 were excluded because the studies reported in those articles did not meet one or more of the PICOTS criteria, mainly due to uncontrolled confounders (e.g. other ingredients such as soluble β -glucan-like dietary fibres) in the intervention that are known to influence postprandial blood glucose.

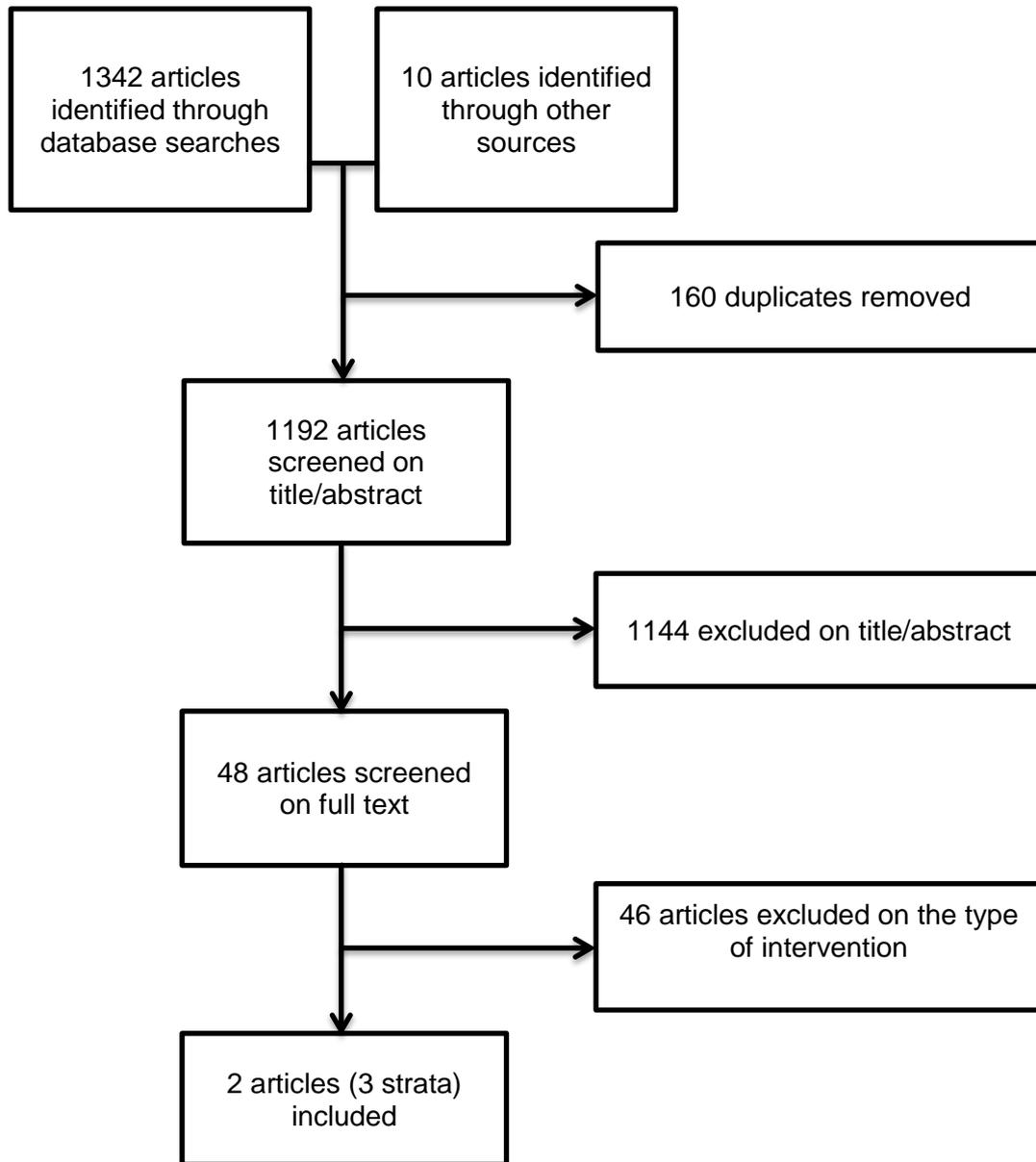


Figure 1. PRISMA diagram of the study screening process

Three strata from two studies (Kwong et al. 2013a; 2013b) were included (Appendix 3). These studies report the effects of β -glucan intake on postprandial blood glucose concentrations in adults. Two highly purified β -glucans with differing mean molecular weights (580 kDa and 145 kDa) were used as the interventions. Both were obtained by a controlled enzymatic hydrolysis of a commercially available oat-derived β -glucan extract.

The test meals presented to the subjects were beverages and viscoelastic gels containing 50 g of glucose. The beverages contained 4 g of either the 580 kDa or 145 kDa β -glucans, whereas the gels contained either 4 g of the 145 kDa β -glucan, 2 g each of the two β -glucans, or 3 g of the 580 kDa and 1 g of the 145 kDa β -glucans. Both the beverage and the gel test meals did not contain other macronutrients such as protein and fat. The control beverage meals were identical in composition, colour, and flavour except that β -glucan was not added.

The two Kwong et al. articles reported a total of nine separate strata, all of which were conducted on the same group of 15 healthy subjects (7 males/8 females, average age 37 ± 3 years and BMI $27 \pm 1 \text{ kg m}^{-2}$). In Kwong et al. (2013a), the interventions were presented as 130 mL beverages and gels, and there were five strata and one control group (which received a beverage). Kwong et al. (2013b) reported four strata with two independent control groups to test the postprandial glycaemic response of the two β -glucans presented as beverages with volumes of 250 and 600 mL.

To prevent double counting, one intervention arm from each sequence was used in the meta-analysis (Higgins and Green 2011). Furthermore, the arms testing the β -glucan with a molecular weight of 580 kDa was chosen in preference to the lower molecular weight β -glucan arms because the former is closer to the molecular weight range (1250-1990 kDa) of the naturally occurring β -glucan in oats (Ajithkumar et al. 2005; Andersson and Börjesdotter 2011).

As noted above, the definition of peak postprandial blood glucose concentration is defined as the maximum recorded blood glucose concentration over the blood sampling period. Hence, the difference between the peak postprandial glucose concentration in the intervention group and that in the control group was used as the effect size in the meta-analysis. However, it should be noted that in two of the three strata that were included in the meta-analysis, the effect sizes that were calculated using the summary numeric data reported in the two articles did not accord with the effect sizes that were calculated using the corresponding graphical data. The mean difference in the peak postprandial blood glucose concentration for the stratum in which the intervention was received as a 250 mL beverage containing 4 g of the 580 kDa β -glucan was calculated to be -0.88 mmol/L using the summary numeric data rise (Table 3 in Kwong et al. 2013b) and that calculated from the corresponding graphical data (Figure 2B in Kwong et al. 2013b) was -0.61 mmol/L. Similarly, there was a mismatch between the effect sizes that were calculated using numeric and graphical data (Kwong et al. 2013a) for the stratum in which the subjects received the intervention as a 130 mL beverage. The mean difference in the peak post-prandial glucose concentration based on the numeric data was calculated to be -1.42 mmol/L and that calculated from the corresponding graphical data was -1.10 mmol/L.

The discordant mean differences are likely to have arisen because of the authors' definition of peak blood glucose concentration. FSANZ understands this to mean the rise from $t = 0$ to the maximum recorded point on the blood glucose concentration-time curve. However, it appears that the authors' definition is based on the maximum peak on the control blood glucose concentration-time curve and a time-matched point on the intervention glucose concentration-time curve. Because FSANZ used the peak-to-peak mean glucose concentration difference between the groups as the effect size, the mismatches were not problematic for the meta-analysis. Furthermore, the peak glucose concentrations were extracted from the graphs because those points were clearly discernible in the blood glucose concentration-time curves. In any case, the meta-analytic summary effect size was -1.15 mmol/L when the authors' summary numeric data was used in the meta-analysis and -0.96 when graphical data was used.

No studies were identified that used purified β -glucan derived from barley.

2.2.2 Quality assessment of studies and strata

Both of the included studies had clearly stated their hypothesis and purpose of testing β -glucan from oats and measured the health outcome of interest, i.e. changes in postprandial blood glucose concentration, and reported peak concentrations for each of the treatments.

Adequate control for confounders in the included strata was achieved by designing the studies as crossover RCTs.

Although the trials were short-term and the subjects were fasted before the intervention, it is unclear whether the subjects were given any instructions regarding exercise or background diet prior to each test and if the subject complied with these instructions.

Despite that the health outcome has been assessed by a well-defined analytical method, using blood samples obtained from finger pricks to measure glucose concentrations is subject to bias because of so-called milking. Applying pressure to a pricked finger to produce a drop of blood can produce negatively biased results by dilution of whole blood with tissue fluids, which in effect reduces the concentration of glucose in the blood sample. The risk of detection bias in the included strata was assessed to be unclear because the study authors' did not state that the outcome assessor(s) was (were) adequately blinded to avoid this type of measurement bias.

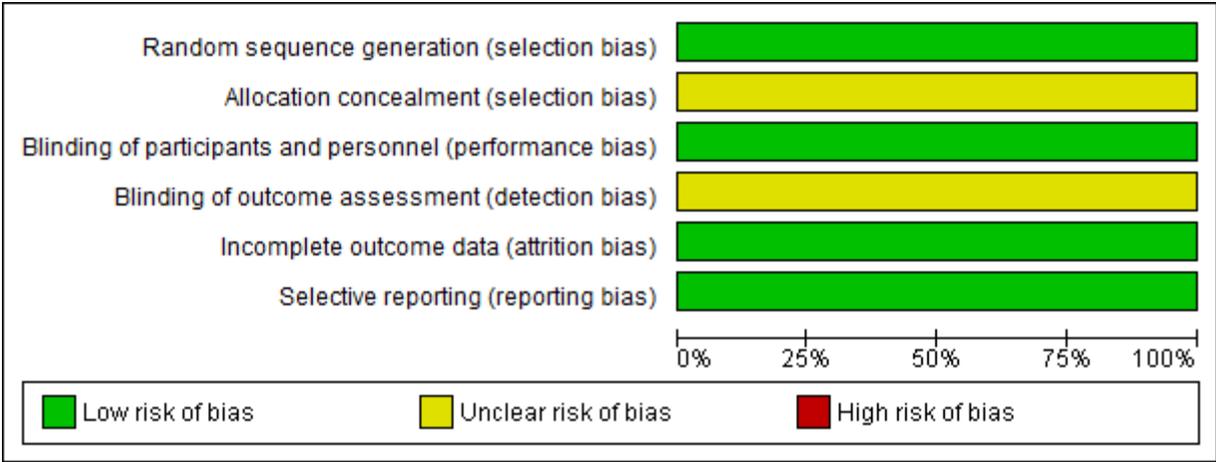


Figure 2. Risk of bias summary for included strata

Because the three included strata from the two Kwong et al. articles all followed the same protocol, there was little variation in the risk of bias assessment (Figure 2 and Appendices 4 and 5). Overall, there was a moderate risk of bias in the included strata which has seriously affected the quality assessment of the body of evidence (Appendix 6).

The outcome was measured at different time intervals within 2 hours following the intervention which is a sufficient duration to assess changes in postprandial blood glucose concentration. A follow-up on measuring the health outcome is not required due to the short-term effect of the intervention and the changes in the health outcome of interest. The results were analysed by the same statistical method between each time point using repeated measures ANOVA.

2.3 Summary of evidence

2.3.1 β-glucan from oats or barley and peak postprandial blood glucose

The literature search did not identify any article reporting a study that used sufficiently pure β-glucan derived from barley. However, two studies, from which three strata involving a “high molecular weight” oat-derived β-glucan fragment that was dissolved in beverages containing 50 g glucose have been used for the purpose of a meta-analysis. Four grams of the β-glucan was used in the three strata and a scatterplot of the changes in mean difference for peak postprandial blood glucose between the intervention and the control is provided in Figure 3.

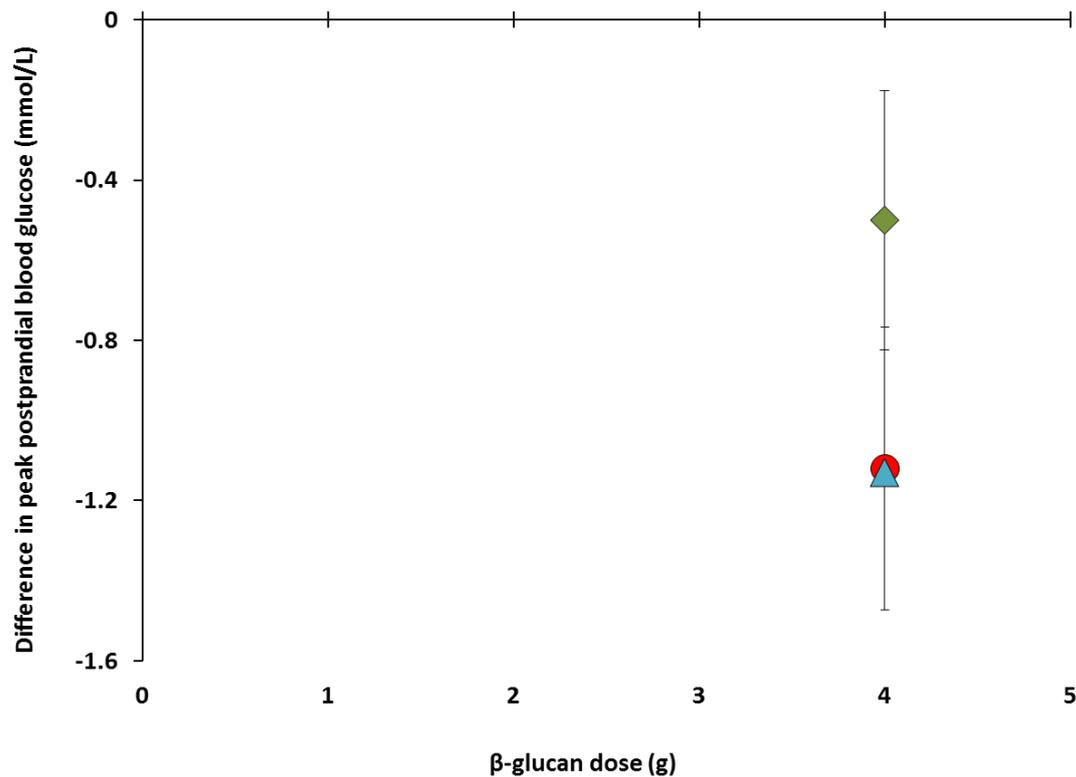


Figure 3. Differences (mean \pm SEM) between the intervention and control groups in the peak postprandial blood glucose following the consumption of β -glucan from oats.

The overall effect on peak postprandial blood glucose concentration was a difference of -0.96 mmol/L [95% CI: $-1.34, -0.58$], which was significant ($P < 0.00001$) with low heterogeneity among strata ($I^2 = 15\%$, $P = 0.31$) (Figure 4).

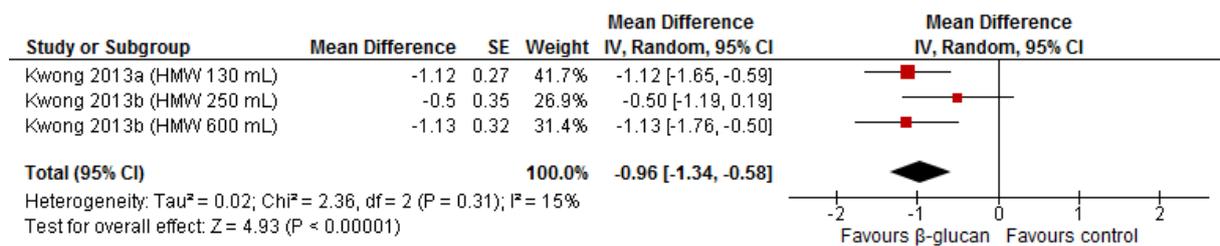


Figure 4. Forest plot of studies measuring peak blood glucose concentration

2.3.2 Publication bias

Publication bias could not be assessed because three strata (from two articles) are insufficient to allow for the examination of a funnel plot for asymmetry.

3. Weight of evidence

Three strata from two studies reported in two separate articles were included in the current systematic review, the conclusion from which was an overall significant reduction in the peak postprandial blood glucose concentration. Low and non-significant heterogeneity was detected. The effect size was estimated based on interventions that used similar experimental methods and materials; commercially available β -glucan purified from oats and enzymatically modified to obtain low and high molecular weight β -glucan fragments. The three strata included in the systematic review used 4 g of the higher molecular weight fragment dissolved in beverages containing 50 g of glucose, which were tested in a total population of 15 healthy subjects.

3.1 Assessment of body of evidence

3.1.1 Consistency

The three strata were all conducted on the same 15 subjects using the same quantities of β -glucan and glucose in beverages. Therefore, it is not surprising that there is consistency of effect across the strata (Appendix 6).

3.1.2 Causality

The included strata were from a crossover RCT, which is a strong design for inferring causality. However, the β -glucan used in the intervention had been enzymatically processed to modify its molecular weight and, therefore, its rheological relevance to the naturally occurring β -glucans in oats is uncertain, because humans are unable to digest the β -glucan present in food to these fractions. Hence, the evidence has been down-rated one level for indirectness (Appendix 6) as it is not clear how the results could be extrapolated to other food matrices.

Only 15 subjects have been tested, and the work was done by the same research group. Therefore, the research findings cannot be regarded as having been replicated. Although the results are statistically significant, the evidence has been down-rated one level for imprecision (Appendix 6).

The relationship was further down-rated because the authors did not describe whether or not subjects were given instructions about diet and exercise to adhere to in the days prior to each testing phase. Variations in diet and exercise can affect the responses seen in blood glucose tests and this so consistency in this area is important as the trials were not blind.

Along with the imprecision due to the low number of participants, a dose-response relationship could not be established because a single dose of 4 g was used in the three included strata. Therefore, a causal relationship for an amount that is more likely to be achieved in a single serving of food cannot be established by extrapolation.

3.1.3 Plausibility

β -glucan purified from oats and dissolved in glucose-containing beverages, containing no fat or protein, significantly reduced peak postprandial glucose concentration (Kwong et al. 2013a; Kwong et al. 2013b). A similar effect has not been investigated for β -glucan purified from oats or barley and taken as part of a usual meal containing different amounts of macronutrients and micronutrients.

Different hypotheses suggest several mechanisms by which β -glucan derived from oats or barley may affect postprandial blood glucose concentration (reviewed in Tosh 2013). Oat and barley β -glucans are polysaccharides of very high molecular weight that exhibit high viscosities at low concentrations (Ren et al. 2003). Consumption of such polysaccharides increases the viscosity of the meal bolus in the stomach which reduces mixing of the food with digestive enzymes and delays gastric emptying (Würsch and Pi-Sunyer 1997; Marciani et al. 2001). Increased viscosity has also been suggested to reduce the absorption of glucose (Braaten et al. 1991; Panahi et al. 2007). Regand et al. (2011) demonstrated that the *in vitro* digestibility of available starch in oat foods was reduced as the *in vitro* viscosity increased.

3.2 Applicability to Australia and New Zealand

3.2.1 Intake required for the effect

Because the relationship relates to peak postprandial glucose concentration, the β -glucan would need to be present in a single serving of the food. The available studies all tested a single intake: 4 g of an enzymatically-modified oat-derived β -glucan within glucose-based beverages. As oats contain approximately, 2-3 g of β -glucans per 100 g (dry weight) it is unlikely that a food would contain 4 g of β -glucan in a single serving. The available data do not allow extrapolation to this lower amount of intake. Furthermore, the test vehicles contained 50 g glucose and this quantity is not likely to be present in a single serving of many foods. There are no studies testing lesser quantities of glucose or equivalent glycaemic carbohydrates in food.

Naturally-occurring β -glucans in oats have a higher average molecular weight compared with the one referred to as “high” in the included strata. Humans do not have the enzymes required to digest β -glucans and, therefore, β -glucans are not hydrolysed during their passage through the upper small intestine of humans (Mälkki and Virtanen 2001) where glucose absorption takes place (Kellett et al. 2008), (Englyst and Cummings 1985; Lia et al. 1996). Therefore, the extent to which the 580 kDa semi-synthetic β -glucan reduces postprandial blood glucose compared with that of the naturally occurring β -glucans in oats, which have a higher molecular weight, is uncertain.

3.2.2 Target population

The included strata were taken from studies conducted in North America on healthy adult subjects.

3.2.3 Extrapolation from supplements

Not assessed due to the absence of evidence.

3.2.4 Adverse effects

No adverse effects have been noted in the included studies. In particular, changes in serum insulin were not described.

4. Conclusion

FSANZ concludes that there is a very low degree of certainty in the relationship between the intake of β -glucan from oats and the reduction in peak postprandial blood glucose concentration. The available evidence relates to a quantity of β -glucan that is unlikely to be present in a single serving of food, findings from one research group, and interventions that used enzymatically modified β -glucans and contained no fat and which were all tested in a small group of the same 15 subjects.

FSANZ concludes that the relationship between the intake of β -glucan from barley and the reduction in peak postprandial blood glucose concentration is not assessable because no RCT measured the effect of pure β -glucan from barley. All studies, including those which investigated extracted/concentrated barley, included other fibres and food components in addition to β -glucan.

5. Acknowledgment

We acknowledge the permission from The Cochrane Collaboration to use the Review Manager software.

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Appendix 1: Database search strategy

Medline - PubMed: on 08th January 2016

Search	Query	Items found
#1	beta glucans[MeSH Terms]	7914
#2	((postprandial hyperglycemia[MeSH Terms]) OR postprandial hyperglycemias[MeSH Terms]) OR blood glucose[MeSH Terms]	153474
#3	(((((beta glucan[Text Word]) OR beta glucans[Text Word]) OR glucose[Text Word]) OR postprandial glucose[Text Word]) OR postprandial blood glucose[Text Word]) OR postprandial hyperglycemia*[Text Word]	471659
#4	#2 or #3	478809
#5	#1 and #4	3087
#6	#1 and #4 Filters: Clinical Conference; Clinical Trial; Clinical Trial, Phase I; Clinical Trial, Phase II; Clinical Trial, Phase III; Clinical Trial, Phase IV; Congresses; Controlled Clinical Trial; Journal Article; Randomized Controlled Trial; Humans	1101

Cochrane trials (CENTRAL): on 08th January 2016

ID	Search	Hits
#1	MeSH descriptor: [beta-Glucans] explode all trees	155
#2	MeSH descriptor: [Hyperglycemia] explode all trees	1447
#3	MeSH descriptor: [Blood Glucose] explode all trees	11505
#4	#2 or #3	12100
#5	beta glucan or "glucose" or "postprandial glucose" or "postprandial hypoglycaemia" or "postprandial hypoglycaemias" (Word variations have been searched)	32315
#6	beta glucans (Word variations have been searched)	117
#7	#5 or #6	32360
#8	#4 or #7	32495
#9	#1 and #8 in Trials	88

Embase® (OVID): on 15th January 2016

- 1 beta glucans/ or (beta-glucan* or beta glucan*).mp. or oat*.mp. or barley.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (30909)
- 2 glucose/ or glucose metabolism disorders/ or glucose intolerance/ or blood glucose/ or plasma glucose/ or glycosylation/ or hemoglobin a, glycosylated/ or diabetes mellitus/ or prediabetes/ or insulin/ or insulin, regular,human/ or insulin resistance/ or metabolic syndrome x/ or hyperglycemia/ or hypoglycemia/ or glucose tolerance test/ or (glucose or "glucose metabolism disorders" or "glucose intolerance" or "blood glucose" or "plasma glucose" or glycosylation or haemoglobin a, glycosylated or hemoglobin a, glycosylated or "diabetes mellitus" or prediabetes or insulin or insulin, regular, human or insulin resistance or "metabolic syndrome x" or hyperglycemia or hyperglycaemia or hypoglycemia or hypoglycaemia or "glucose tolerance test").tw. (1113073)
- 3 ("randomized controlled trial" or "controlled clinical trial").pt. or randomi*ed.ti,ab. or placebo.ti,ab. or randomly.ti,ab. or trial.ti,ab. or groups.ti,ab. (2447282)
- 4 humans/ (14675059)
- 5 exp "disorders of carbohydrate metabolism"/ (734241)
- 6 exp glucose intolerance/ (11195)
- 7 exp glucose blood level/ (164600)
- 8 exp glycosylated hemoglobin/ (14550)
- 9 exp diabetes mellitus/ (594098)
- 10 exp impaired glucose tolerance/ (18252)
- 11 exp insulin/ (248860)
- 12 exp human insulin/ (3877)
- 13 exp hyperglycemia/ or exp hypoglycemia/ (107343)
- 14 (glycosylated hemoglobin or glycosylated haemoglobin).tw. (8468)
- 15 human insulin.tw. (6348)
- 16 1 and 2 and 3 and 4 (206)
- 17 or/5-15 (884725)
- 18 1 and 3 and 17 (269)
- 19 limit 18 to human (190)
- 20 19 not 16 (9)

Appendix 2: Studies excluded at full text review

	Study	Reason for Exclusion
1.	(Akyol et al. 2014)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
2.	(Aldughpassi et al. 2012)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
3.	(Alminger and Eklund-Jonsson 2008)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
4.	(Ames et al. 2015)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
5.	(Aoe et al. 2014)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
6.	(Beck et al. 2009)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
7.	(Beck et al. 2010)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
8.	(Behall et al. 2006)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
9.	(Biörklund et al. 2005)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
10.	(Biörklund et al. 2008)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
11.	(Braaten et al. 1991)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
12.	(Braaten et al. 1994)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
13.	(Casiraghi et al. 2006)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
14.	(Cavallero et al. 2002)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
15.	(Chillo et al. 2011)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
16.	(Cugnet-Anceau et al. 2010)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.

	Study	Reason for Exclusion
17.	(De Natale et al. 2012)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
18.	(Frank et al. 2004)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
19.	(Fukuhara et al. 2013)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
20.	(Granfeldt et al. 2008)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
21.	(Hallfrisch et al. 1995)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
22.	(Hallfrisch et al. 2003)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
23.	(Hlebowicz et al. 2008)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
24.	(Jenkins et al. 2002)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
25.	(Juntunen et al. 2002)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
26.	(Kabir et al. 2002)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
27.	(Kim et al. 2009)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
28.	(Langella et al. 2015)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
29.	(Lan-Pidhainy et al. 2007)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
30.	(Liatis et al. 2009)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
31.	(Mäkeläinen et al. 2007)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
32.	(Maki et al. 2007)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
33.	(Nakao et al. 2010)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.

	Study	Reason for Exclusion
34.	(Nazare et al. 2009)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
35.	(Panahi et al. 2007)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
36.	(Panahi et al. 2014)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
37.	(Poppitt et al. 2007)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
38.	(Rami et al. 2001)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
39.	(Rondanelli et al. 2011)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
40.	(Tapola et al. 2005)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
41.	(Tappy et al. 1996)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
42.	(Thondre and Henry 2009)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
43.	(Thondre et al. 2013)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
44.	(Tosh et al. 2008)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
45.	(Wang and Ellis 2014)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.
46.	(Yokoyama et al. 1997)	Dietary fibres other than β -glucan were present in different amounts in the dietary interventions.

Appendix 3: Characteristics of included strata

	Study	Study design	Objectives	Participants & sample size	Interventions	Methods	Confounders	Results	Notes
1.	(Kwong et al. 2013a)	Cross-over. Subjects served as their own control.	To determine the effects of oat β -glucan of high or low molecular weight dissolved in solutions or gels on glycaemic response.	Fifteen healthy subjects (7 males, 8 females) average age 37.2 years.	Test beverages containing 50 g of glucose and orange flavour made up to 130 mL volume and with 4 g of purified either oat β -glucan of either low or high molecular weight. Control beverages without β -glucan were provided. Dietary interventions were provided with 250 mL of a beverage of choice (water, tea or coffee with milk and/or the artificial sweetener aspartame)	Fasting blood sample taken in the morning then test meals taken. Multiple finger-prick postprandial blood samples collected within 2 h. YSL 2300 Stat auto-analyser measured glucose by glucose oxidase. Peak postprandial blood glucose and the incremental area under the curve were measured and compared by ANOVA.	Minimised by the cross-over design and fasting subjects overnight.	Significant reduction in peak postprandial blood glucose concentration achieved by the high molecular weight β -glucan.	One stratum (HMW 130mL) has been used in the meta-analysis: drink with high molecular weight β -glucan.
2.	(Kwong et al. 2013b)		To determine whether the effects of oat β -glucan solutions on glycaemic response is due to the viscosity <i>per se</i> .		Test beverages containing 50 g of glucose and orange flavour made up to either 250 mL or 600 mL volume with 4 g of purified oat β -glucan of either low or high molecular weight. Control beverages without β -glucan were provided. Test beverages were provided with 250 mL of a beverage of choice (water, tea or coffee with milk and/or the artificial sweetener aspartame)				Two strata have been used in the meta-analysis: 250 mL drink with high molecular weight β -glucan (HMW 250 mL) and 600 mL drink with high molecular weight β -glucan (HMW 600 mL)

Appendix 4: Summary of risk of bias for the included strata

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)
Kwong 2013a (HMW 130 mL)	+	?	+	?	+	+
Kwong 2013b (HMW 250 mL)	+	?	+	?	+	+
Kwong 2013b (HMW 600 mL)	+	?	+	?	+	+

Appendix 5: Risk of bias of strata included in the systematic review

Study	Strata	Random sequence generation (selection bias)		Allocation concealment (selection bias)		Blinding of participants and personnel (performance bias)		Blinding of outcome assessors (detection bias)		Incomplete outcome data (attrition bias)		Selective reporting (reporting bias)	
		Risk	Description	Risk	Description	Risk	Description	Risk	Description	Risk	Description	Risk	Description
(Kwong et al. 2013a)	HMW 130 mL	Low	Stated randomisation design with repeated measures. The author confirmed similar random sequence generation as in the other study (Kwong et al. 2013b).	Unclear	Same amount of flavour and colouring were added into different treatments. Randomisation of allocation is not clearly stated.	Low	Short time between the intervention and measuring the health outcome makes performance bias unlikely..	Unclear	Samples tested by autoanalyser. However, no sufficient details given on the finger prick bleeding procedure.	Low	No attrition	Low	All relevant results from performed analyses were reported.
(Kwong et al. 2013b)	HMW 250 mL	Low	Stated randomisation controlled block design with repeated measures.	Unclear	Same amount of flavour and colouring were added into different treatments. Randomisation of allocation is not clearly stated.	Low	Short time between the intervention and measuring the health outcome makes performance bias unlikely.	Unclear	Samples tested by autoanalyser. However, no sufficient details given on the finger prick bleeding procedure.	Low	No attrition	Low	All relevant results from performed analyses were reported.
	HMW 600 mL												

Appendix 6: GRADE summary of findings tables

Question: *Does the dietary intake of β -glucan from oats or barley reduce peak postprandial blood glucose concentration?*

Source: FSANZ systematic review of evidence

Quality assessment of body of evidence							Participant numbers		Quality (degree of certainty in relationship)	Mean difference mmol/L [95% CI]
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Considerations	Parallel	Cross-over		
Changes in peak postprandial blood glucose concentration are related to consuming β-glucan from oats										
2 studies (3 strata)	RCT	Serious ¹	None	Serious ²	Serious ³	Some ⁴	0	15x3 subjects	⊕ Very Low	-0.96 [-1.34, -0.58]
Changes in peak postprandial blood glucose concentration are related to consuming β-glucan from barley										
0	NA	NA	NA	NA	NA	NA	0	0	Not assessable	NA

¹ Moderate risk of bias has been assessed for the overall evidence.

² Humans cannot digest the naturally-occurring β -glucans from oats down to the molecular weight used in the included strata. The molecular weight of the tested oat β -glucan has been modified and does not resemble the molecular weight of β -glucan naturally-occurring oats.

³ Small size of the overall population sample.

⁴ Unclear whether the subjects were given dietary and exercise instructions to follow prior to each testing phase and whether they complied with these instructions.