

Evidence Paper 2018

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WHOLE GRAINS AND THE HEART

This paper summarises the evidence which forms the basis of the Heart Foundation's position on whole grains and heart health.

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BACKGROUND

This evidence paper is an umbrella review of research on whole grains and heart health. It gives an overview of the evidence considered when formulating recommendations on whole grains and sits within the context of Heart Foundation evidence papers on dietary patterns, sugar, fats and fatty acids.

Whole grains are traditionally considered a heart-healthy food and are one of the sources of carbohydrate and fibre in the diet, along with fruits, vegetables, and legumes. They began to form a larger part of the human diet around 10,000 years ago, during the agricultural revolution. Refined grains have become more prominent in the past 100 years.¹ Current recommendations for heart-healthy eating focus on choosing whole grain and high-fibre foods instead of refined grains and added sugars.

Whole grains are recommended in dietary guidelines around the world. In New Zealand, it is recommended to “enjoy a variety of nutritious foods every day, including ... grain foods, mostly whole grain and those naturally high in fibre”.²

REVIEW METHODOLOGY

This umbrella review assesses the links between whole grain intake and heart health. It focuses on recent systematic reviews and meta-analyses and studies published since those reviews. A summary of included meta-analyses and systematic reviews is in the Evidence Table in Appendix 1. Other reviews and papers are included where they provide useful context. The search strategy, inclusion and exclusion criteria are listed in Appendix 2 and a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement in Appendix 3.

EXECUTIVE SUMMARY

Overall, observational data found whole grains were protective against heart disease, but this was only partially backed by intervention studies on risk factors. Both types of research had methodological limitations hindering their interpretation. No meta-analyses or reviews suggested a negative impact of whole grains on heart health.

Heart disease

Higher whole grain and bran intakes are consistently associated with a 16-30% lower risk of cardiovascular and coronary heart disease in observational studies. Dose-response analysis shows the biggest incremental risk reduction at up to three serves per day. Interpretation of the data is limited by inconsistent and unclear definitions of whole grain, however the fibre or bran component seem an important contributor to their beneficial effect.

Lipids

Whole grains have a small effect on reducing total and low density lipoprotein (LDL) cholesterol by 1-2% when compared to refined grains, and within the context of an energy-restricted diet or healthy dietary pattern. Oats and barley have a greater beneficial effect on total and LDL cholesterol (3-8% reduction), especially in people with raised lipid levels, due to their soluble fibre content.

Body weight

Observational evidence suggests an association between whole grain intake and slightly lower body weight, but this may be due to the fibre component or added bran. Intervention studies have found little effect of whole grains on body weight or body composition.

Blood pressure

Observational evidence supports a beneficial effect of whole grains on blood pressure, but there is little evidence for an independent effect of whole grains on blood pressure from intervention studies.

Glycaemic control

Observational studies have found whole grains are associated with reduced risk of type 2 diabetes by 20-32%. Studies suggest a potential small improvement in insulin sensitivity.

Intact grains and fibre structure seem to create less of a glycaemic response than wholegrain products where the structure of the grain has been ground down or milled.

Inflammation

Evidence is not strong enough to support any independent beneficial effect of whole grains on inflammation.

Summary

On average, three servings of whole grains per day provides heart health benefits and there are likely to be additional benefits with higher intakes.

Whole grains may be useful for people needing to lower their cholesterol levels to reduce cardiovascular risk, as randomised controlled trials (RCT) showed small reductions. There could potentially be small improvements in glycaemic control and reduced risk of type 2 diabetes.

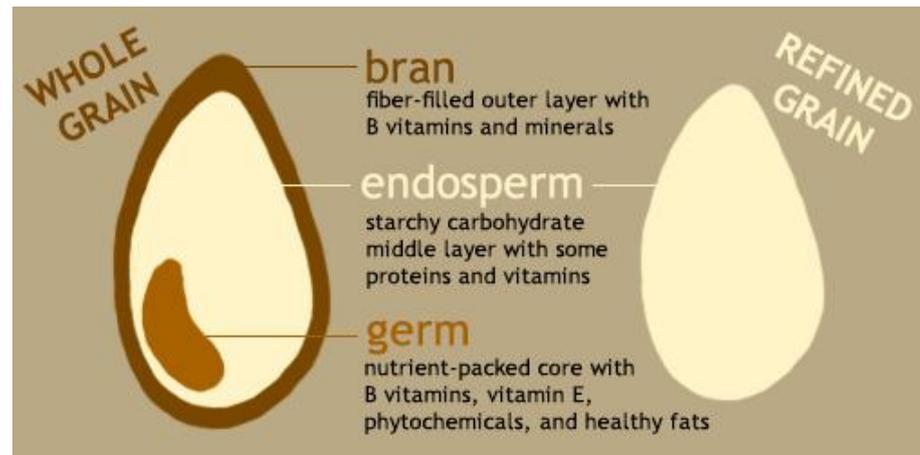
Whole grains are likely best consumed in a minimally-refined form – naturally high in fibre – in place of refined grains, within a dietary pattern that also contains fibre from fruit, vegetables, legumes and nuts.

WHOLE GRAINS

What is a 'whole grain'?

A whole grain is a grain that contains all its naturally occurring parts. There are three main parts of a whole grain: the germ, endosperm and bran (Figure 1). Fibre, vitamins and minerals in the germ and bran are removed when grains are refined, leaving just the endosperm.

FIGURE 1: DIAGRAM OF A WHOLE GRAIN



Source: <https://www.hsph.harvard.edu/nutritionsource/whole-grains/>

In New Zealand, the term whole grain is defined by Food Standards Australia New Zealand in Food Standards Code [Standard 2.1.1](#). To claim a food is whole grain, it must consist of, or contain, an ingredient with "every part of the grain including the outer layers, bran and germ".³ The whole grain can be in one piece, milled into smaller pieces, or the parts can be separated during processing and reconstituted.³ Thus, 'whole' refers to containing all constituent parts, rather than intactness of the grain. Whole grains are now most commonly eaten as reconstituted grains.⁴

Prior to 2005, whole grain was defined as "the unmilled products of a single cereal or mixture of cereals", requiring the grain to be intact.⁵ This change in definition was at the request of the cereal industry, but brought it in line with other common definitions around the world, including the US Food and Drug Administration (FDA) definition. They define whole grain as "the intact, ground, cracked, or flaked fruit of the grains whose principal components - the starchy endosperm, germ, and bran - are present in the same relative proportions as they exist in the intact grain".⁶

The latest definition of whole grain is from the European Union HEALTHGRAIN consortium. It allows the processing of grains in a way that ensures the natural proportions of bran, germ and endosperm remain: "Whole grains shall consist of the intact, ground, cracked or flaked kernel after the removal of inedible parts such as the hull and husk. The principal anatomical components – the starchy endosperm, germ and bran – are present in the same relative proportions as they exist in the intact kernel...".⁷ It allows for 2% of the grain or 10% of the bran to be removed during processing. This reduces any mycotoxin or agrochemical contaminants which concentrate in the very outer layer of the grain.⁷

Some countries require a food product to be at least 51% whole grain to classify itself as such (so it can be a mix of whole and refined grain). Only a small number of studies have applied this definition.⁶ The few studies that have applied this

definition have not provided sufficient evidence to support a health claim for cardiovascular disease (CVD) and whole grains, whereas use of broader definitions do provide support.⁶

Whole grain-rich foods are a heterogeneous group, probably with different health effects, and these differences need to be considered when interpreting the evidence.⁸ There is a lack of consistent definition of what foods are classified as whole grain between studies,⁹ and often inadequate definition of what foods are being investigated. However, most studies have been based largely on whole grain products that have used processed and reconstituted whole grain components.⁷ Earlier study definitions of whole grain included products containing >25% whole grain or bran by weight, and some included added germ and bran.^{4,10}

It is difficult to disentangle the effect of whole grains from foods high in cereal fibre and bran as they are often conflated in research.¹¹ Whole grains are an important contributor to fibre intake, and most bran comes from whole grain foods.⁹ However, it is important to differentiate between them in research as it could lead to different recommendations.⁹ For example, some whole grains such as brown rice are fairly low in fibre, whilst some non-whole grains have added fibre or bran. Further, in the US, fibre from whole grains only contributes 15% of total dietary fibre in a typical diet, whereas refined grains provide 35% because they are eaten in far higher quantities.¹² This review focuses on the effect of whole grains rather than fibre.

Nutritional value of whole grains

Whole grains contain a range of bioactive substances and nutrients such as soluble and insoluble fibre, vitamins, minerals, phytochemicals, phenols, phytoestrogens, and antioxidants.^{13,14,15,16,17,18,19} These bioactive substances not only positively influence traditional risk factors for heart disease, but there is increasing understanding of their effect on gut microbiota and subsequent health benefits.^{10,20,21} Grinding and milling remove or reduce some of these substances, and levels can be affected by other food processing such as cooking. For example, phytochemicals are reduced during bread making, in particular due to oxidation during kneading.²²

High-heat treatment or cooking can also introduce unwanted substances such as acrylamide, a potential carcinogen.²³ Bread and breakfast cereals are two of the main contributors to acrylamide intakes in New Zealand.²⁴ Of the grain foods assessed, bread and breakfast cereals each contributed 12-15% of acrylamide intakes based on dietary modelling.

Consumption of whole grains in New Zealand

The most commonly eaten grains around the world are wheat, rice, maize, oats, barley, rye, millet, sorghum and triticale.⁴ Barley and rye contain the most fibre, and rice and millet the least.²⁵

Intact whole grains (as distinct from whole grain products) are not a common feature of New Zealand diets, can take longer to prepare and some may be more expensive than refined grains. Price, taste and convenience have a major influence on food choice.²⁶⁻³⁰ Less healthy choices can seem cheaper, tastier and more convenient than healthier choices.^{31,32} Whole grain products such as breads and breakfast cereals can be easier to incorporate into the diet than intact whole grains, but many are highly processed and some can be high in salt, sugar or energy. There may also be strong cultural preference for refined grains, for example white rice compared to brown rice for Asian populations.

The biggest contributors to whole grain intake in New Zealand are breakfast cereals and bread.³³ The last national nutrition survey found that when eating bread 63% of adults reported choosing light or heavy whole grain bread.³⁴ For Māori, half of all adults reported choosing light or heavy whole grain bread.³⁵ For Pacific peoples, 32% of men and 43% of women choose light or heavy whole grain bread.³⁶ Bread choice for Asian people living in New Zealand was not reported, but the majority were eating at least one to four slices of bread per day.³⁷ These data are now 10 years old and may have changed.

CONSIDERATIONS WHEN INTERPRETING THE DATA

There are limitations with both types of studies included in this review, which need to be considered when interpreting their findings.

Prospective cohort studies/observational studies

- Cereal fibre is associated with fewer coronary events, and less coronary mortality^{25,38} and total mortality.^{39,40} Some studies on whole grains included foods with added bran, which may have had independent effects on risk. Cho *et al* attempted to determine the separate effects of bran or cereal fibre and whole grains. They found a reasonable level of evidence for an inverse association between cereal fibre or mixtures of whole grains and bran and reduced risk for type two diabetes (T2D) and CVD. However, there was less evidence, as well as less conclusive evidence, using the definition of >51% whole grains.⁴¹
- The types of foods classified as whole grain differ between studies, making it difficult to know exactly what foods are being assessed. Not all whole grain foods or products would be expected to have the same health effects.⁴²
- None of the epidemiological studies were originally set up to assess whole grain intake.⁴³
- There is the possibility, or likelihood, of residual confounding. People with higher whole grain intakes tend to have healthier eating habits and live healthier lives.⁴⁴ They tend to be more physically active, smoke less, and eat more fruit, vegetables and fibre.⁴ Even if all of these have been adjusted for in statistical analyses, there may be some residual confounding.
- If whole grain foods replace less healthy foods (rather than being added to the diet) the effect may be due to loss of harmful effects of the foods replaced rather than inclusion of whole grains.¹³
- There will be measurement error from dietary assessment methods, under-reporting, imprecise measurement of whole grain content, and imprecise food composition data. As an example, fibre intakes determined by food frequency questionnaire (FFQ) compared to a seven-day food diary had different associations with coronary heart disease (CHD) for men in the European Prospective Investigation of Cancer (EPIC)-Norfolk study (positive association versus no association). The seven-day food diary, which is less commonly used in research, was a more accurate measure.⁴⁶

RCTs/intervention studies

- Definitions and amounts of whole grain differed widely in RCTs, as they did in observational studies.⁴⁷
- There was often substantial unexplained heterogeneity between studies.⁴⁵ This also makes studies difficult to combine in meta-analyses.
- Energy intakes were often not controlled between intervention and control groups. This is important as interventions that lead to weight loss improve blood lipids and glucose levels in the long term regardless of the diet.⁴⁸ Studies often used normal diet as a control group instead of a refined grain control group, which can contribute to differences in energy intake.⁹ Composition of control group diets was not well described and there appeared to be large variations in their composition between studies.
- Whole grains may have been added to the diet rather than substituted for refined grains, increasing energy intake.^{49,50} The proportion of whole grains compared to refined grains may also be important. Cross-sectionally, a high whole grain intake has not offset the adverse association between refined grains and body composition.⁵¹ Most studies were not designed to detect differences in body composition.⁴⁷
- When participant compliance with the required dietary composition was measured, there was usually low compliance.
- Differences in care and attention between control and intervention groups.
- Due to their short time frame, RCTs tend to recruit participants with risk factors for heart disease, whereas cohort studies tend to recruit healthy participants.⁵²

EVIDENCE OVERVIEW: CARDIOVASCULAR OR CORONARY HEART DISEASE

Evidence suggests that replacing saturated fat with carbohydrate from refined grains or added sugars does not reduce cardiovascular risk, whereas replacing it with whole grain or high-fibre foods does reduce risk.⁵³ A meta-analysis by Li *et al* demonstrated this, showing that when saturated fat is substituted with refined starches and sugars there is a 10% increased risk of CHD, whereas replacing it with whole grains is linked with a 9% reduction in risk.⁵⁴ Similarly, the Heart Foundation's dietary patterns evidence paper identified improved heart health when carbohydrate is obtained from vegetables, fruit, legumes and whole grains. Thus, the type of carbohydrate eaten should be given as much emphasis as the type of fat eaten.

In relation to whole grains, Fardet *et al* pooled data from meta-analyses to identify associations between food and chronic disease. The highest intakes of whole grains tended to be protective against chronic disease. In relation to CVD, the highest versus lowest intakes of whole grains were associated with a 29% reduction in risk.⁵⁵

This is similar to other estimates from observational research which suggest highest versus lowest consumption of whole grains is associated with reduced risk of CHD/CVD events and/or mortality by between 16% to 30%.^{11,56–63} Dose response analyses show this risk reduction increases most up to three serves of whole grains per day (16g whole grains or 30g whole grain product per serve).^{56,58,63}

Overall there is moderate and consistent observational evidence for beneficial associations between whole grain intake and reduced risk of CHD/CVD. The level of evidence has been graded as probable (as it is based on cohort studies rather than RCTs).⁶⁴

EVIDENCE OVERVIEW: RISK FACTORS

LIPIDS

Five recent systematic reviews of RCTs have assessed the effects of whole grains or oats on lipids.^{62,65,66,67,68} Overall, intervention studies suggest whole grain products reduce LDL and total cholesterol in healthy adults by 1-2%, with no effect on HDL. A dose-response effect was not seen despite a wide range of intakes. Effects were less pronounced with longer study duration, and sub-group analysis only found a statistically significant effect in studies that restricted energy intake (despite minimal weight losses).⁶⁵

A separate pooled analysis found a reduction in total and LDL cholesterol with whole grains, but this effect was reduced and became statistically non-significant when studies on oats and barley were removed.⁶⁶ Interventions that included whole grains as part of a diet (rather than whole grains being the only intervention) found a greater reduction in total and LDL cholesterol.⁶² Similarly, within the context of the Step 1 diet⁶⁹ or a hypo-energetic diet,⁷⁰ inclusion of whole grains had a more beneficial effect on cardio-metabolic markers than a low fat diet without them, in individual trials.

A Cochrane review comparing the effect of whole grains with either refined grains or a low intake of whole grains found no evidence for a beneficial effect of whole grain on total cholesterol in seven low-quality RCTs ranging from 12 to 16 weeks. Only one of the included studies was on oats, with most of the remaining studies on wheat. Participants tended to be overweight or obese, and some participants had metabolic syndrome.⁶⁷

Oats have been found to be twice as effective as whole grains at reducing LDL and total cholesterol.⁶⁵ Just over half of the RCTs on oats have found statistically significant reductions of at least 3% to 8% in total cholesterol and LDL cholesterol.^{59,68,71} The majority of studies were small and underpowered. Reductions in LDL cholesterol were mostly seen in people with raised cholesterol levels.⁶⁸ Barley or barley beta-glucans were also efficacious at reducing total and LDL cholesterol, with a mean reduction in LDL of -0.27mmol/L.⁷² The effect of oats and barley on total and LDL cholesterol has been graded as convincing.⁷³ Although the effect is small, it is meaningful at a population level, and has been estimated to lower the incidence of CHD by 4%²⁵.

The effect on lipids may be dependent on fibre increasing sufficiently (>7g/day) with whole grain intake.⁷³ Fibre is fermented in the large intestine which produces short-chain fatty acids that can inhibit cholesterol synthesis.³³ Short-chain fatty acids produced by the microbiome could also alter circulating lipids. Beta-glucans, a type of soluble fibre, play an important role as they bind to bile acids^{74,75} and reduce LDL cholesterol^{73,76} at doses >3g/day from oats and barley.^{25,72,77,78} The viscosity

created by the soluble fibre seems important to its effect on cholesterol.⁷⁹ However, oat beta-glucans are affected by the level of processing, which can potentially lessen their cholesterol lowering effect^{25,80} if it alters solubility in the gut.⁸¹ Another potential mechanism is a reduced insulin response leading to lower breakdown of fatty acids in the liver.

Very high carbohydrate diets (>60% total energy) that are high in refined grains can adversely affect triglycerides, high density lipoprotein (HDL) cholesterol,⁷³ or small dense LDL.^{82,83,73} These effects are aggravated by insulin resistance.⁸⁴ To ameliorate these effects it is important to choose whole grain and high-fibre foods instead of refined grains if eating a high carbohydrate diet.⁸³

BODY WEIGHT

Four recent systematic reviews have assessed the effect of whole grains on body weight.^{11,45,47,62} Observational research has suggested an association between increased whole grains, dietary fibre or breakfast cereals and slightly lower body weight.^{21,45,62,85,86} Three servings of whole grains per day has been associated with less central adiposity and attenuation of weight gain.⁴ However, the strength of the evidence depends on whether the study is on cereal fibre, mixtures of whole grain and bran, or whole grain on its own.¹¹ The data on whole grains are hampered by inconsistent definitions and amounts. In relation to body weight, the strongest epidemiological evidence was for cereal fibre and mixtures of whole grain and bran.¹¹

The beneficial effect seen in observational epidemiological research was not supported in three meta-analyses of RCTs, which overall found little effect of whole grains on body weight or body composition.^{47,62,45} A small improvement in body fat percentage was detected with whole grains in one meta-analysis, but this was only in energy-restricted diets.⁴⁷ Further, sixteen percent of the weighting in the meta-analysis came from a Korean study on rice that had very low quality data.

Studies have tended to show a beneficial effect of whole grains on subjective satiety, but few have shown a subsequent effect on energy intake.^{4,45} Satiety could be induced more quickly by insoluble fibre stimulating an earlier release of peptide Y.⁷⁴

Fibre also influences the bacterial profile in our gut,⁸⁷⁻⁸⁹ and increased fibre appears to support growth of beneficial bacteria.^{4,90}

BLOOD PRESSURE

Observational studies have shown a link between higher whole grain intake and reduced risk of hypertension.¹³ Three recent systematic reviews of randomised controlled trials have assessed the effect of whole grains on blood pressure in a mix of people with normal and high blood pressure.^{66,67,68} These intervention studies have not generally supported the finding from observational studies. A recent meta-analysis pooled data from eight RCTs, and found no evidence for an effect on diastolic or systolic blood pressure.⁶⁶ Similarly, a Cochrane review did not identify an effect on blood pressure.⁶⁷ However, when whole grains are included as part of a heart-healthy dietary pattern there can be a meaningful reduction in systolic and diastolic blood pressure.⁹¹ It may also be that the effect becomes evident over a longer time period than study time frames. Interventions may also be more likely to see an effect if the study population had high rather than normal blood pressure.

There is little evidence for an effect of oats on blood pressure, with the majority of studies not finding any statistically significant effect. Only three out of 25 RCTs

found a statistically significant reduction in blood pressure with oat intake.⁶⁸ Studies were underpowered, and most did not assess blood pressure accurately. This is in contrast to a meta-analysis of 28 intervention studies on fibre, which found a beneficial effect of beta-glucans from oats and barley on blood pressure.⁹²

GLYCAEMIC CONTROL

McRae's umbrella review identified four meta-analyses on whole grains and type 2 diabetes.⁶⁰ All four meta-analyses found correlations between whole grain intake and a statistically significant 20% to 32% reduction in risk of type 2 diabetes in observational studies.^{62,93,94} A review for the Nordic nutrition guidelines found moderately strong evidence that whole grains were associated with lower risk of type 2 diabetes.⁶⁴ Similarly, dietary fibre has been associated with reduced risk of type 2 diabetes.⁹⁵

Observational studies have also found a small, but statistically and biologically significant, reduction in glucose and insulin levels with higher compared to lower whole grain intake.^{60,62} Intervention studies suggest the effect of whole grains may be through improved insulin sensitivity rather than improved glucose levels.^{42,64} Studies have tended to compare diets that include whole grains as one component, rather than whole grains being the only intervention. However, a study by Giacco *et al* directly compared whole grain products with a refined grain control. In 61 participants with metabolic syndrome, postprandial insulin response reduced by 29% compared to control, with no difference in glycaemic response.⁹⁶

A systematic review by Thies *et al* did not find statistically significant changes in glucose levels or insulin concentrations in the majority of RCTs on oats.⁶⁸ In the few studies that did see changes in glucose levels, on average, some went up and some went down. In contrast, Bao's meta-analysis found a statistically significant reduction in fasting insulin concentrations.⁹⁷ A few small and heterogeneous studies in the meta-analysis assessed Homeostatic model assessment of insulin resistance (HOMA-IR) and HbA_{1c} but they did not change significantly.⁹⁷ Hou *et al* found oats reduced fasting blood glucose and HbA_{1c} in people with type 2 diabetes, but half of the weight in their meta-analysis was from the only individual study that found a statistically significant reduction.⁷¹ Thus, the effect of oats on glycaemic control is not clear.

The intactness of the grain structure influences glycaemic response.⁸⁰ Digestion rates and glucose and insulin response have been shown to differ *in vitro* by level of processing of wheat and maize, but not for oats*.¹⁰² In humans, larger particle size has been found to reduce glycaemic and insulin responses of whole grain wheat.^{102,103} Similarly, a randomised controlled trial found glycaemic control and blood lipids were significantly better with an intact, rather than disrupted, starch structure.¹⁰⁴

Higher versus lower intakes of both total dietary fibre and cereal fibre have been associated with reduced risk of type 2 diabetes. The dose-response was linear for cereal fibre, whereas for total dietary fibre an intake of at least 25g/day was associated with reduced risk.¹⁰⁵ These findings from epidemiological studies have been supported in RCTs where fibre supplementation reduced fasting blood

* Oats are usually kept intact during initial processing as they are softer and it is more difficult to separate out the constituent parts.¹¹⁶ They might then be further processed into products like instant oats, oat flour or oat bran.

glucose and HbA_{1c}.¹⁰⁶ Fibre improves glycaemic response^{21,107} by delaying intestinal absorption of glucose, fructose and fat, giving a slower rise in blood glucose levels⁷⁴ and reducing insulin response.²¹

INFLAMMATION

Three recent systematic reviews have assessed the effect of whole grains on inflammation.^{68,108,109} Whole grains could potentially reduce chronic inflammation through the action of fibre, beneficial gut microflora,⁸⁸ bioactive compounds, or by slowing the glycaemic response.¹⁰⁸

Most observational studies have found that higher whole grain intake is associated with lower levels of inflammatory markers.¹⁰⁸ Conversely, the majority of intervention studies have found no statistically significant effect on inflammatory markers either for whole grains or oats.^{68,108,109} The effect in observational studies seems largely due to confounding factors; but conversely, intervention studies were short term, in overweight participants, and did not have inflammation as a primary outcome.^{108,109} Since these reviews, an eight-week RCT, that substituted refined wheat with whole wheat, found improved inflammatory markers with whole wheat.

Taken together, and despite limitations in both study types and widely varying definitions of whole grains, currently the evidence is not strong enough to support an independent beneficial effect of whole grains on inflammation. No studies found an adverse effect.

DISCUSSION

Most observational research suggests benefits for whole grains in relation to both cardiovascular disease and its risk factors. Observational studies are better positioned to assess accumulation of risk over a lifetime, but cannot prove cause and effect relationships. Observational evidence is ideally backed by data from RCTs. However, other than for lipid levels and glycaemia, results are inconsistent and there is discrepancy between observational data and RCTs.^{110,111}

While RCTs are usually considered a stronger level of evidence than observational studies, they need to be well designed, of sufficient duration, at low risk of bias and adequately powered to answer the question. They also need to be similar enough for data to be combined through meta-analysis. Few of the studies have met these criteria. Observational studies also had limitations, with widely varying definitions of whole grain, inaccurate assessment of dietary intakes and whole grain composition, and likely residual confounding.

As currently defined, not all whole grains are equal. Evidence on the glycaemic response in relation to level of processing suggests minimally processed/unrefined whole grains with the natural fibre structure intact are preferable. The influence of grain structure is lost in much of the research, as it does not generally differentiate between intact whole grains and whole grain products. Despite the lack of differentiation, observational research still suggests heart health benefits from whole grains and/or whole grain products. Studies that have looked at individual foods have found evidence of heart health benefits for oats and barley in particular, which are high in viscous fibre and tend to be less processed.

From the evidence in this paper, observational research suggests three serves of whole grains per day are associated with heart health benefits, and there are likely to be additional benefits with higher intakes. Intervention studies on risk factors are less compelling but show most consistent evidence of benefits for a small reduction

in total and LDL cholesterol, especially in relation to oats and barley, and possibly improved glycaemic control.

CONCLUSION

Whole grains are associated with reduced risk of heart disease. They may be most useful for people needing to lower their cholesterol levels to reduce cardiovascular risk, as this is where RCTs found a small beneficial effect.

Whole grains are likely best consumed in a minimally refined form, naturally high in fibre, within a dietary pattern that also contains fibre from fruit, vegetables, legumes and nuts. They will be most beneficial if eaten in place of refined grains.

IMPLICATIONS FOR PRACTICE

- If eating grains, use whole grains or high-fibre whole grain products instead of refined grains.
- Choose intact whole grains such as whole oats, barley, or cracked wheat whenever possible.
- On average, aim for at least three serves of whole grains per day for heart health benefits.

ACKNOWLEDGEMENTS

The Heart Foundation would like to thank Dr Andrew Reynolds, Otago University, for his peer review of this paper.

GLOSSARY

Bran	The outer protective layer of a grain kernel. It is high in fibre.
Cereal	Cereal or cereal grain is another name for grain.
Endosperm	The food store inside the grain kernel that feeds the plant once it germinates.
Fibre	Fibre is the indigestible part of plant foods, including grains.
Germ	The germ is the embryo of the grain kernel that can sprout into a new plant.
Intact grain	A grain that hasn't been ground or milled.
Refined grain	A grain where the bran, germ or endosperm have been removed.
Whole grain	Contains the bran, germ, and endosperm in the same proportions as the intact grain kernel.
Whole grain product	A whole grain product is more than half whole grain. ¹¹²

EVIDENCE TABLE: META-ANALYSES ON WHOLE GRAINS

Study author and design	Population and duration	Intervention and comparator	CVD and CHD outcomes	Notes
Aune (2016) ⁵⁶ Dose-response meta-analysis of prospective studies	Seven cohort studies on CHD with 7068 cases and 316 491 participants. Ten cohort studies on CVD with 26 243 cases and 704 317 participants. 45 cohort studies conducted in Europe (20), US (16), and Asia (9).	Intervention: whole grain intake Comparator: high vs low intake Whole grain definition: defined in individual studies Whole grain amount: 90g/day (3 serves) for whole grain products; 195g/day for brown rice for dose response [†]	Coronary heart disease incidence or mortality: High versus low intake RR 0.79 (95% CI 0.73, 0.86) ($I^2=0$) Per 90g/day dose RR 0.81 (95% CI 0.75, 0.87) ($I^2=9$) Slightly steeper reduction in risk up to 3 serves/day, but further reductions in risk up to 210g/day. Whole grain bread, whole grain breakfast cereals, and added bran were inversely associated with coronary heart disease, but no association for germ, refined grains, white bread, refined grain breakfast cereals, total rice, or total grains. Rye was only inversely associated in high versus low analysis and not in the dose-response analysis. Cardiovascular disease incidence or mortality: High versus low intake RR 0.84 (95% CI 0.80, 0.87) ($I^2=0$) Per 90g/day RR 0.78 (95% CI 0.73, 0.85) ($I^2=40$) Stronger reduction in risk from no intake up to 50 g/day than with higher intakes.	Definition of whole grain likely to have varied between studies. No information provided on individual study definitions other than food type. Individual studies adjusted for varying confounders, and the adjusted models were used in the meta-analysis. No evidence of publication bias. Small number of studies for individual analyses. No discussion of methods of dietary assessment in individual studies. Sub-group analysis conducted on validated dietary assessment. Study quality assessed with Newcastle-Ottawa Scale. Mean score of 8 out of a possible 9 (high quality). There was little evidence of heterogeneity for CHD or CVD by length of follow up, type of outcome, location, number of cases or deaths, or adjustment for confounding factors.
Benisi (2016) ¹¹³ Meta-analysis of prospective cohort studies	11 cohort studies on CVD mortality with 757,966 participants and 25,595 cases.	Intervention: intake of total whole grain Comparator: high versus low intake or 90g/day dose response	Six studies reached an inverse association and 4 found no association. One study found an inverse association in women but not in men.	Study quality assessed with the Newcastle-Ottawa Scale. Median score 6 out of a possible 9. Authors reported they could not clearly

[†] The standard serve is 30g for a whole grain product, e.g. whole grain bread and 16g for intact whole grain, e.g. oats

Whole grains and the heart

Study author and design	Population and duration	Intervention and comparator	CVD and CHD outcomes	Notes
	<p>Six cohort studies included in the dose-response analysis with 141,968 participants and 2,720 cases.</p> <p>Most studies on men and women, but one was women only and two were men only.</p> <p>Studies conducted in US (6), Europe (4), and China (1).</p>	<p>Whole grain definition: studies defined them as whole-wheat bread, whole-meal bread, whole-grain bread, whole-grain cereals, whole-grain breakfast cereals, breakfast cereals, rye bread, and rye product</p> <p>Whole grain amount: 90g day whole grain product (3 serves) for dose-response analyses</p>	<p>Cardiovascular mortality</p> <p>Highest vs lowest intake RR 0.84 (95% CI: 0.78, 0.89) ($I^2=34$)</p> <p>Dose-response per 90g/day (three serves) RR 0.75 (95% CI: 0.68, 0.83)</p>	<p>assess risk of bias in studies because of incomplete reporting.</p> <p>No evidence of heterogeneity. No single study influenced the overall association.</p> <p>Most studies used a FFQ to assess dietary intake, but one used a short questionnaire and another dietary record.</p> <p>Studies had varying definitions of whole grain and some did not define it. Some assessed whole grain foods as opposed to whole grain intake.</p> <p>All whole grain foods grouped due to the low number of studies, which may obscure benefits or harms of an individual food.</p> <p>Most studies adjusted for age, BMI, smoking, and alcohol. Some also adjusted for dietary factors and physical activity.</p>
<p>Buyken (2014)²⁰⁸</p> <p>Systematic review of observational and intervention studies</p>	<p>14 studies in adults with no inflammatory diseases.</p> <p>Seven were observational studies with 11,295 (259–5,496) participants aged 27–62 years with a BMI of 24–31.</p> <p>Seven studies were RCT or crossover trials lasting 3–16 weeks with 742 (15–166) aged 46–60 years with a BMI of 27–36.</p>	<p>Intervention: whole grain intake</p> <p>Comparator: high vs low intake</p> <p>Whole grain definition: not defined, varied between studies</p>	<p>Observational outcomes:</p> <p>Five studies found a statistically significant association between higher whole grain intake and lower inflammatory markers (IL-6 and CRP). In three studies, whole grain intake was not related to inflammatory markers.</p> <p>Intervention outcomes:</p> <p>Five studies found no statistically significant effect of whole grains on CRP or IL-6.</p> <p>Two studies found positive effects of whole grains on CRP or IL-6 compared to no whole grains or control diet, but in one study this was only seen in patients not using statins.</p>	<p>Six observational studies used a FFQ to assess diet, but definition and assessment of whole grain intake varied widely between studies.</p> <p>Differences in whole grain intakes in highest and lowest quintiles in observational studies was much larger than differences between treatment groups in intervention studies.</p> <p>Most intervention studies were small and did not have low-grade inflammation as a primary outcome.</p> <p>Evidence was stronger in observational studies than intervention studies, which may have been due to residual confounding in observational studies or lack of power to detect smaller effects in intervention studies.</p>

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Chen (2016) ⁵⁸ Meta-analysis of prospective cohort studies	12 cohort studies with 26,352 deaths.	Intervention: whole grain intake Comparator: high vs low whole grain Whole grain definition: three studies reported on whole grain intake and the remainder on whole grain products Whole grain amount: dose-response 50g/day whole grains (3 x 16g whole grain serves)	Cardiovascular mortality CVD mortality high compared with low intake RR 0.82 (95% CI 0.78, 0.85) (<i>I</i> ² =0) CVD mortality dose-response per 50g/day whole grain (not whole grain product) RR 0.70 (95% CI 0.61, 0.79) (<i>I</i> ² =64.8) IHD mortality high compared with low intake RR 0.82 (95% CI 0.79, 0.85) (<i>I</i> ² =0) IHD mortality dose-response per 50g/day whole grain RR 0.68 (95% CI 0.55, 0.84) Evidence of non-linear associations between whole grain intake and CVD mortality with additional but more moderate reductions in risk after the intake of 35 g whole grain/d.	Study quality assessed with Newcastle-Ottawa Scale (individual scores ranged from 6-9). Fully adjusted risk estimates were used from individual studies. Most studies only assessed dietary intake at baseline and by self-administered FFQ. Studies had differing definitions of whole grain.
Cho et al (2013) ¹¹ Systematic review of prospective cohort and cross-sectional studies	22 prospective cohort studies. 10 assessing cereal fibre, 10 assessing whole grains and bran, and three assessing whole grain only.	Intervention: foods that contain >51% whole grain ingredients Comparator: mixtures of whole grain and bran, or cereals high in fibre Whole grain definition: whole grain only, not bran-enriched foods or high cereal fibre	Cardiovascular outcomes: Cereal fibre: risk reduction of 14–26% for CVD mortality and 22–43% for stroke. Inconsistent results on CVD events and MI. No adverse results. Whole grains plus >25% bran: risk reduction of 7–52% for CVD mortality, CVD events, and heart failure. Whole grain only: after full adjustment, non-significant risk reductions in CHD or CVD mortality of 30% to 6% (hypertension).	Varying definitions of whole grain between studies limit conclusions that can be drawn e.g. two studies included brown bread and wheat germ; and studies in the 1990s included foods with >25% whole grains and bran, and high-fibre bran cereals. Most studies investigated mixtures of whole grains and ≥25% bran rather than whole grains alone. No RCTs identified lasting >1 year. In many of the studies, inverse associations were attenuated by cereal fibre or bran, indicating that much of the benefit of whole grain may be from those components.
Fardet (2014) ⁵⁵ Review of meta-analyses and systematic reviews	304 reviews or meta-analyses on 170 associations between foods and chronic diseases. From this, there were 17 references on CVD,	Intervention: whole grain cereals and refined cereals	CVD and chronic disease: Highest intakes of whole grain cereal tended to be protective against (15 references) or not	Due to the large scale of the review there was limited detail on individual food category or disease definitions or on methodology or

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	16 on whole grain, and six on refined grains.		<p>associated with (10 references) chronic disease risk.</p> <p>Highest intakes of refined cereal tended to be not associated with (one reference) or to have a deleterious effect on (six references) chronic disease risk.</p> <p>Based on meta-analyses only, the highest level of whole grain cereal consumption may significantly reduce risk of CVD by up to 29%.</p>	limitations of individual meta-analyses or reviews.
Holloender (2015) ⁶⁵ Meta-analysis of RCTs	24 RCTs in healthy adults (n=2275) over 2-16 weeks.	<p>Intervention: whole grain foods 28g-213g/day</p> <p>Comparator: non-whole grain or refined grain foods</p> <p>Whole grain definition: varied between studies: whole grain products, oats, whole grain wheat or rye, or brown rice</p>	<p>LDL cholesterol:</p> <p>Weighted difference -0.09 mmol/L (95% CI -0.15, -0.03)</p> <p>Oats: weighted difference of -0.17 mmol/L (95% CI: -0.10, -0.25). Difference removed when studies on oats excluded.</p> <p>Energy restriction: mean difference was only statistically significant in studies that also applied energy restriction.</p> <p>Other lipids:</p> <p>TC: weighted difference -0.12 mmol/L (95% CI: -0.19, -0.05) compared with the control. Difference non-significant when oats (half of the studies) removed from analysis.</p> <p>HDL: no effect.</p> <p>TG: non-significant effect except for oats (weighted difference: -0.14 mmol/L (95% CI: -0.22 to -0.05).</p> <p>Dose-response: no dose-response effect despite wide range of intakes.</p>	<p>Few studies had objective measures of dietary compliance (e.g. biomarkers).</p> <p>Low to moderate heterogeneity.</p>
Kelly (2017) ⁶⁷	Nine RCTs of 12-16 weeks duration with 1,414 healthy adults, and	Intervention: whole grain foods (mostly whole grain wheat)	Total cholesterol (six studies, n=722):	<p>Studies had an unclear or high risk of bias. Lipids = low quality evidence.</p>

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Cochrane review of RCTs on whole grain cereals	mean age 45-59 years for primary prevention of CVD.	Comparator: refined grains or usual diet Whole grain definition: individual study authors' definition	Mean difference 0.07 (95% CI: -0.07, 0.21) LDL cholesterol (seven studies, n=770): Mean difference 0.06 (95% CI: -0.05, 0.16) HDL cholesterol (seven studies, n=772): Mean difference -0.02 (95% CI: -0.05, 0.01) Triglycerides (seven studies, n=771): Mean difference 0.03 (95%CI: -0.08, 0.13) Systolic blood pressure (seven studies, n=768): Mean difference 0.04 (95% CI: -1.67, 1.75) Diastolic blood pressure (seven studies, n=768): Mean difference 0.16 (95% CI: -0.89,1.21)	Five studies received funding from the cereal industry. Low heterogeneity. Short trials, small samples sizes, and many trials had a large number of dropouts.
Kromhout (2015) ^{59,114} Review of meta-analyses and systematic reviews to develop the Dutch dietary guidelines	Adults and children.		Coronary heart disease: 90g/day whole grain products associated with -25% risk 7g/day cereal fibre associated with -15% risk 7g/day total fibre associated with -10% risk Stroke: High vs low intake associated with -15% risk Blood pressure: Additional 10g/day total fibre lead to -1 to -2mmHg Lipids: 30-60g/day oats reduced LDL cholesterol by -0.20mmol/L 1g/day beta-glucan reduced LDL cholesterol by -0.05mmol/L	Background evidence papers are in Dutch. Summary paper reviewed only.

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Study author and design	Population and duration	Intervention and comparator	CVD and CHD outcomes	Notes
Lefevre (2012) ¹⁰⁹ Systematic review; of prospective cohort studies, cross-sectional studies or interventions	Four cohort studies and five intervention trials.	<p>Intervention: whole grain or whole grain products (not fibre or bran)</p> <p>Comparator: cohort studies: high versus low intake; intervention studies: refined grain</p> <p>Whole grain definition: varied widely between observational studies:</p> <ul style="list-style-type: none"> • Dark bread, high fibre bran or granola cereal, shredded wheat, cooked cereal • Cold cereal >3g fibre/100g, oatmeal, dark wholegrain breads or cereals, bran muffins, brown or wild rice • Food product in which whole-grain ingredient is the first ingredient on the product label • Dark bread, breakfast cereal >25% whole grain or bran, brown rice, popcorn, wheat germ, bran, oatmeal, other grains • Foods than contain any of (or their flours) whole wheat, oats, whole cornmeal, brown rice, whole barley, whole rye, bulgur, buckwheat, popcorn, amaranth, psyllium <p>Whole grain amount: varied between studies from participant-identified medium-sized serve compared to what others eat; 16g or ½ cup of whole grain food; and commonly used serving size</p>	<p>Dietary patterns:</p> <p>Dietary patterns high in whole grains associated with 10-29% reduction in CRP. Less consistent associations with IL-6. No association with fibrinogen.</p> <p>Cohort studies of whole grains:</p> <p>No statistically significant effect on high versus low intake of whole grains on CRP, IL-6 or fibrinogen in fully adjusted models.</p> <p>Dose response:</p> <p>Each 16g/day serve of whole grains associated with 7% reduction in CRP adjusted for dietary factors. Further adjustment for adiposity and/or insulin resistance reduces the effect by ~40%.</p> <p>Intervention studies:</p> <p>Only one out of five studies found a positive effect of whole grains on inflammatory markers and this was in obese subjects on a reduced energy diet, although decreases in CRP were independent of weight loss.</p>	<p>People with higher whole grain intake tend to have healthier lifestyles (less smoking, lower body weight, increased physical activity, increased fruit and vegetable intake, and lower alcohol, saturated fat and/or meat intake). Adjusting for these factors reduced or removed associations between whole grains and CRP or IL-6 in cohort studies.</p> <p>Cohort studies were small (n=249 to 5,496).</p> <p>In the intervention studies, no diets were completely controlled. As an example, in the largest study, WHOLEheart, the intervention group added whole grains instead of substituting them (increasing energy intake) and decreased fruit.</p> <p>All intervention studies were in overweight or obese participants, short term and generally small. WHOLEheart was the largest study with 316 participants.</p>
McRae (2017) ⁶⁰ Umbrella review of meta-analyses	21 meta-analyses on type 2 diabetes (four meta-analyses), CVD (four meta-analyses), cancer and obesity (two meta-analyses).	<p>Intervention: whole grain intake</p> <p>Comparator: high vs low intake or ~30g whole grain (two serves)</p>	<p>Cardiovascular disease:</p> <p>CVD (n=4) RR 0.63 to 0.79, all statistically significant</p>	<p>CVD studies had no significant heterogeneity but two of the meta-analyses identified significant publication bias.</p>

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Study author and design	Population and duration	Intervention and comparator	CVD and CHD outcomes	Notes
		<p>Whole grain definition: varied between studies, most common was >25% whole grain.</p>	<p>CVD mortality (n=2) RR 0.81 to 0.82, all statistically significant</p> <p>Stroke (n=2) RR 0.86 to 0.92 (NS)</p> <p>Type 2 diabetes:</p> <p>Glucose -0.02 mmol/L, P<.0001</p> <p>Insulin -0.02 pmol/L, P<.0001</p> <p>Type 2 Diabetes (n=4) RR 0.68 to 0.80, all statistically significant</p> <p>Body composition (n=2):</p> <p>BMI -0.63 kg/m², P<.0001</p> <p>Waist circumference -1.2 to -2.7 cm, both NS</p> <p>Body weight -0.06 kg, NS</p> <p>Body fat -0.48%, P=.04</p>	<p>Quality assessment not conducted in all studies and unclear how quality incorporated into findings in others.</p>
Pol (2013) ⁴⁷ Meta-analysis of RCTs	<p>26 RCTs in healthy adults (n=2060), all <16 weeks duration (most four-six weeks). Seven studies were also energy-restricted.</p> <p>Majority of studies in white and Western populations.</p>	<p>Intervention: whole grain foods or diets high in whole grain</p> <p>Comparator: same diet but non-whole grains</p> <p>Whole grain definition: mixed whole grains, oats, whole wheat, barley, rye, or rice</p> <p>Whole grain amount: 18.2g/day to 150g/day</p>	<p>Body weight:</p> <p>Weighted difference: 0.06 kg (95% CI: -0.09, 0.20)</p> <p>Body fat:</p> <p>Weighted difference: -0.48% (95% CI: -0.95, -0.01). The effect of whole grains was greater in energy-restricted diets, and attenuated in non-energy restricted diets.</p> <p>Waist circumference:</p> <p>Weighted difference: -0.10 cm (95% CI -0.25, 0.0)</p>	<p>The amount of whole grains provided in individual studies was unable to be determined in eight studies.</p> <p>No dose-response effect seen.</p> <p>One of the energy-restricted diets had abnormal results (260kJ/day diet) and used a low-dose of powdered whole grain rice as a meal replacement for Korean women. It strongly influenced body fat and body weight analyses.</p> <p>Most studies did not have body composition as a primary outcome.</p> <p>Actual intakes not measured in most studies, amounts reflect those provided for consumption.</p>

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Study author and design	Population and duration	Intervention and comparator	CVD and CHD outcomes	Notes
Schwingshackl (2017) ¹¹⁵ Meta-analysis of prospective cohort studies	19 prospective studies on whole grains with 121,141 mortality cases and four on refined grains in healthy adults.	Intervention: Comparator: highest vs lowest intake and dose-response Whole grain definition: not defined Whole grain amount: 30g whole grains or cereals/day; range 0-110g/day	All-cause mortality: Whole grains dose-response RR: 0.92 (95% CI: 0.89, 0.95). Risk of mortality decreased by 25% up to 100g/day. Whole grains high vs low intake RR: 0.88 (95% CI: 0.84, 0.92) No associations with refined grains for any analyses.	High heterogeneity seen in high vs low intake analyses. Inverse association not seen in European, Asian, Australian, or short-term studies. Inverse association seen only for studies using validated dietary assessment methods. Nutri-Grade meta-evidence rating high for whole grains and low for refined grains.
Tang (2015) ⁶¹ Meta-analysis of observational studies	15 cohort studies and three case-control studies with 14,427 CHD cases. Studies conducted in US (12) and Europe (3).	Intervention: Comparator: high vs low intake Whole grain definition: not defined Whole grain amount: individual studies used a mix of grams and serves per day or week	CHD: RR 0.79 (95% CI 0.74, 0.83)	11 studies inverse association, 7 no association. No heterogeneity. No association in case-control studies. Significant associations in US and European studies. Five of the studies were conducted on two cohorts.
Thielecke (2014) ⁴⁵ Systematic review of observational and intervention studies	28 epidemiological studies: eight prospective and 20 cross-sectional studies in adults. 37 intervention studies: 21 acute satiety studies, 15 long-term weight loss studies, and one was a combination.	Intervention: whole grains Comparator: non-whole grains Whole grain definition: varied between studies	Body weight: Observational studies: all apart from 1 cross-sectional study show a beneficial association between higher whole grain consumption and body weight. No association between refined grain intake and body weight or composition. Intervention studies: 10/15 studies showed an effect on body weight as part of a reduced-energy diet, but does not appear to lead to greater weight loss. Limited evidence for a small improvement in body composition over the short term. Satiety: Most intervention studies (16/21) showed improvements in subjective satiety, but few showed a subsequent impact on energy intake.	Inconsistent definition of whole grain between studies. Use of self-reported dietary assessment and body weight measures. Most observational studies are from the US in white populations. Residual confounding likely. Considerable heterogeneity between intervention studies.

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Thies (2014) ⁶⁸ Systematic review of long-term RCTs	69 studies ranging from two weeks to six months duration. Studies conducted mostly in the US (54%).	Intervention: addition or substitution of oat products Comparator: wide range, including refined wheat, whole-wheat products, rice bran, psyllium, farina, fruit or no control Whole grain definition: oats, oat cereal, oat milk or oat bran	Fasting lipids: TC: 58% of studies found reductions in TC of -2 to -19% LDL-cholesterol: 53% of studies found reductions of -4 to -23%, mostly in hypercholesterolaemic participants Studies n>60: more studies found a positive effect on TC and LDL but the effect was smaller (-3 to -8%) Most studies that looked at HDL or TG found no significant effects. Blood pressure: 22 out of 25 studies found no significant effect on blood pressure. The remainder found a beneficial effect on SBP of -4 to -6% Glucose and insulin: No significant blood glucose change in 16 out of 21 studies. The remaining studies found increases or decreases in blood glucose. 15 out of 16 studies found no significant effect on insulin levels. Inflammation: No studies (n=6) found a significant effect on inflammatory markers.	Majority of studies were small (n<30 in oat group) and underpowered. Only 11 studies had more than 60 participants. Only 30% of studies had carried out a sample size or power calculation. Using the Jadad scale, 46 studies (61%) had a low quality of reporting, and 30 articles (39%) had a high quality of reporting. Studies assessing blood pressure were underpowered to assess this outcome, and used inadequate blood pressure measurement methods. One study measured blood pressure accurately and found a reduction over 12 weeks. Studies were too heterogeneous for meta-analysis. Outcomes reported inconsistently between studies. Appropriateness of control group not considered in this review.
Ye (2012) ⁶² Meta-analysis of prospective cohort studies and randomised controlled trials	Six PCS on T2D (US and one Finnish), 10 PCS on CVD (all US), 3 PCS on weight gain, and 21 RCTs in healthy adults (4-16 weeks duration).	Intervention: whole grain Comparator: high vs low intake Whole grain definition: not defined Whole grain amount: In PCS, median whole grain intake = 44.4 g/d (2.75 serving/d)	CVD: RR=0.79 (95% CI: 0.74, 0.85) Type 2 diabetes: RR=0.74 (95% CI: 0.69, 0.80) Weight gain:	RCTs were interventions that included whole grains, therefore it may not have been the only intervention or the main focus. Possible publication bias for CVD. Similar risk reductions seen for total dietary fibre and cereal fibre and CVD in PCS.

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		<p>Fibre amount: median fibre intake = 25.4 g/d in PCS</p>	<p>PCS: Unable to pool data. Indicated an inverse association between whole grain and dietary fibre intakes and weight gain over time.</p> <p>RCT: -0.18kg (95% CI -0.54, 0.18)</p> <p>Risk factors:</p> <p>Fasting glucose -0.93 mmol/L (95% CI: -1.65, -0.21)</p> <p>TC -0.83 mmol/L (95% CI: -1.24, -0.42)</p> <p>LDL-c -0.72 mmol/L (95% CI: -1.34, -0.11)</p> <p>SBP -0.06mmHg (95% CI -0.21, 0.10)</p> <p>DBP -0.05mmHg (95% CI -0.21, 0.11)</p>	<p>Heterogeneity across RCTs, remained significant after stratification for duration, study quality, and health status.</p>
<p>Zong (2016)⁶³ Meta-analysis of prospective cohort studies</p>	<p>14 data sets with 786 076 participants, 97 867 total deaths (n=12), and 23 957 CVD deaths (n=11).</p> <p>Studies conducted in the US (10), Scandinavia (3) and UK (1), with follow-up from 6 to 28 years.</p>	<p>Intervention: whole grain</p> <p>Comparator: dose-response</p> <p>Whole grain definition: ranged from a single item (e.g. whole grain bread, dark bread, or whole grain cereals) in FFQs to a comprehensive list of grain-based foods available from 24-hour diet recall</p> <p>Whole grain amount: 16g/day dry weight for dose response analysis</p>	<p>CVD mortality:</p> <p>High vs low RR 0.82 (95% CI: 0.79, 0.85)</p> <p>Dose response RR 0.91 (95% CI: 0.90, 0.93)</p> <p>All-cause mortality:</p> <p>High vs low RR 0.84 (95% CI: 0.80, 0.88)</p> <p>Dose response RR 0.93 (95% CI: 0.92, 0.94)</p> <p>Population attributable fraction 11.6% for CVD mortality.</p>	<p>Study quality assessed using Newcastle-Ottawa scale, scores ranged from 6 to 9 (highest possible score), with nine studies scoring ≥8.</p> <p>Seven studies only used a baseline FFQ.</p> <p>No heterogeneity for CVD analyses, and no indication of publication bias. Significant heterogeneity for all-cause mortality, which was not explained.</p> <p>Dose response effect seen up to 50g/day.</p> <p>Different foods included as whole grain between studies.</p>

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APPENDIX 1: SEARCH STRATEGY

Research question:

In adults with or without coronary heart disease or cardiovascular disease (heart disease), what effect does consumption of whole grains have on risk of heart disease events or mortality, or risk factors for heart disease such as lipids, blood pressure, and body weight?

PubMed title/abstract free-text search terms (modified for Scopus):

- Wholegrain OR whole grain OR cereal OR oats OR rye OR barley OR wheat OR non-starch polysaccharide AND mortality OR coronary OR heart OR cardiovascular OR atherosclerosis OR myocardial OR blood pressure OR hypertension OR lipid OR \$cholesterol\$ OR triglyceride OR lipoprotein OR obesity OR overweight OR body fat OR body weight OR inflammation
- Reviews published in the past five years in humans and published in English

Inclusion criteria:

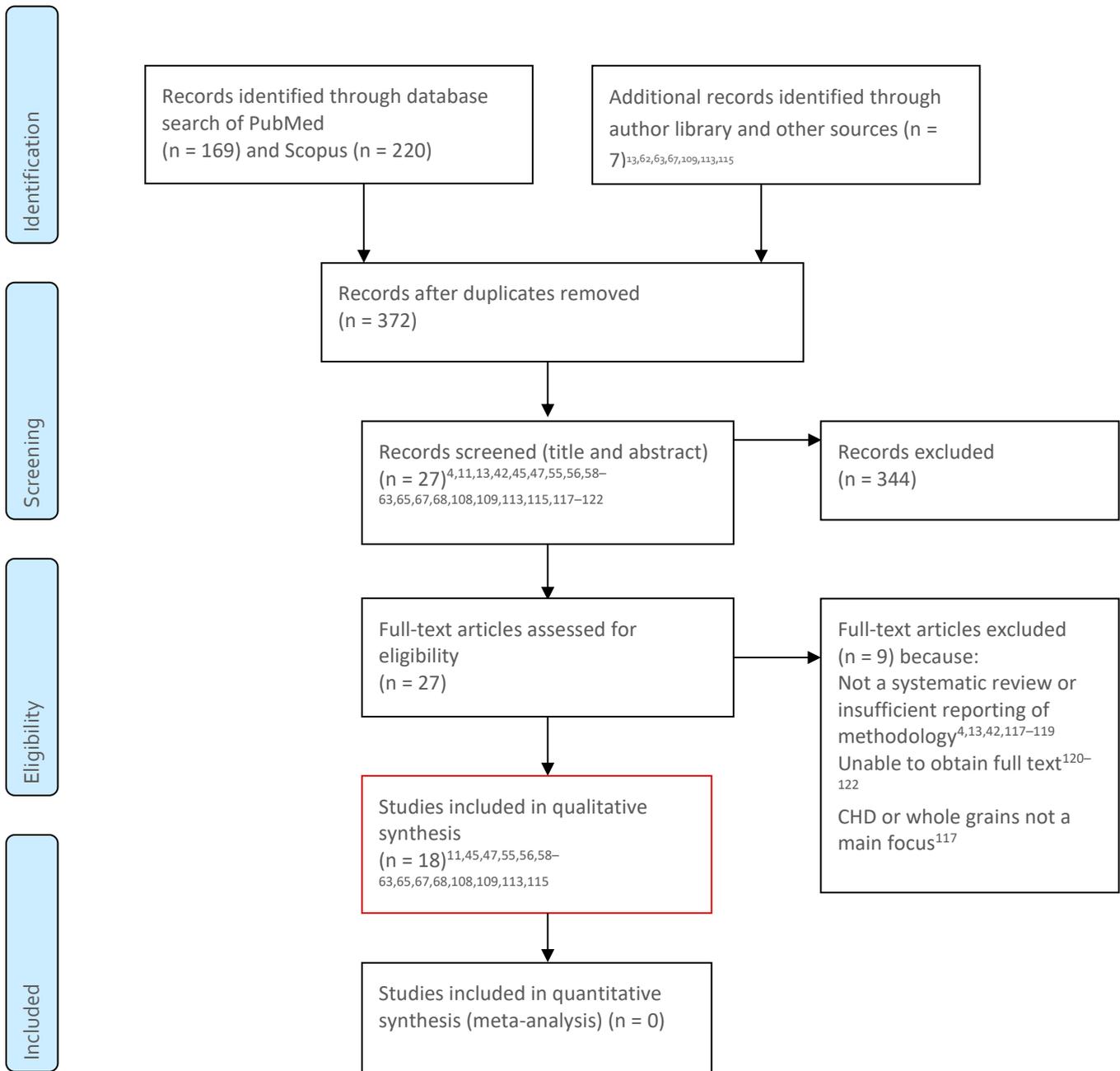
- Systematically conducted reviews of randomised controlled trials or prospective cohort studies
- Published July 2012 to July 2017
- Human subjects
- English language
- Healthy adults or people at risk or with heart disease
- Appropriate definition of whole grains (*this was difficult to apply*)
- Heart disease related outcomes

Exclusion criteria:

- Animal studies
- In vitro studies
- Non-systematic reviews or systematic reviews that did not provide sufficient methodological data or results
- Cross-sectional, case control or retrospective studies
- Not published in an academic journal
- Full-text article not obtainable
- Whole grains not main focus
- Grain that is not common in New Zealand
- Focused primarily on fibre, glycaemic index, glycaemic load, sugar or bioactive components
- Related specifically to breakfast cereals, drug development, sports nutrition, dietary patterns, or vegetarian diets
- Reviewed studies that were shorter than 8 weeks duration

Some studies that fit within the exclusion criteria are discussed but were not part of the main body of evidence summarised in Appendix 1.

APPENDIX 2: PRISMA FLOW DIAGRAM FOR REVIEWS INCLUDED IN EVIDENCE TABLE



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097