Relationship Between Whole Grain Intake and Risk of Coronary Heart Disease

Food Standards Australia New Zealand
Diet-disease Relationship Review

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1.0 INTRODUCTION

Coronary heart disease (CHD) is a significant cause of morbidity and mortality in Australia, New Zealand and many affluent and developing countries. It is a much-studied subject with a voluminous body of literature describing the disease process, the genetic and environmental factors involved in increasing and decreasing risk and the routes to prevention and treatment. Coronary events are the key outcomes of the condition and include myocardial infarction (MI), ischaemia and (sudden) cardiac death as the major outcomes for the disease. Atherosclerosis is the underlying process for CHD and involves the occlusion of the coronary arteries through the accumulation of lipids in the intima. Ischaemia results from a loss of tissue perfusion leading to inadequate oxygenation and nutrient supply. MI is a major loss of blood flow resulting from arterial occlusion while sudden cardiac death can result from instability of cardiac contraction (arrhythmia). CHD has a complex multifactorial aetiology and there is an inherited element in risk (e.g. apolipoprotein phenotype) and also those which cannot be changed (e.g. age). There is also a strong modifiable component including lifestyle factors. Factors which contribute to increased risk include high blood pressure (hypertension), obesity, diabetes, cigarette smoking and lack of exercise. Obesity (especially abdominal obesity) is an independent risk factor but also predisposes to diabetes, another independent risk factor. However, there is an interaction between these two and hypertension leading to the so-called “metabolic syndrome” which predisposes to early-onset CHD.

Plasma lipids are extremely important contributors to CHD risk through atherosclerosis. Raised plasma total and low density lipoprotein (LDL) cholesterol are positive risk factors. The significance of LDL can be understood readily as cholesterol is a significant component of intimal atherosclerotic plaques. Plasma high density lipoprotein (HDL) is a negative risk factor and raised concentrations appear to confer protection through promoting cholesterol efflux from tissues. There is a general negative relationship between plasma HDL and triacylglycerols (TAG) and raised plasma TAG may increase risk through this mechanism and also independently.

It has been established quite convincingly that drug therapy to lower plasma cholesterol lowers CHD risk to the point where a statin is available as an over the counter item in British pharmacies for that purpose (Anon, 2005). However, diet and lifestyle changes to modify risk factors remain the first line of attack in primary prevention strategies (Kendall & Jekins, 2004). Recommendations to lower risk involve a portfolio of changes including limitations in the intakes of saturated and trans (unsaturated) fatty acids, both of which raise LDL cholesterol. n-6 Polyunsaturated fatty acids (PUFA) lower LDL cholesterol but long chain n-3 PUFA do not. The latter appear to lower CHD risk by promoting myocardial function and altering blood clotting parameters. As will be discussed in this
review, some dietary fibre components lower plasma cholesterol and so could lower risk. Other dietary components also appear to protect against CHD but through other mechanisms which remain to be defined. Folate is one such factor. Raised plasma homocysteine is correlated with increased risk of CHD and concentrations are lowered by increased folate intake (Shai et al., 2004). However, the mechanisms whereby homocysteine acts remains unknown but may involve changes in arterial endothelial function, possibly through inflammatory mediators. Folate is found in whole grain foods while soluble fibre is also found in a limited number of cereals (principally oats and barley) and it is thought that these might contribute to lowered risk. However, whole grains in general are believed to protect against CHD and it is the purpose of this review to assess the strength of the evidence of the relationship between their intake and lowered risk of CHD.

2.0 Definitions

Much of the key literature on whole grains and lowered risk of CHD is from observational studies. Thus it is important to define the terminology used, particularly as whole grains are not a single chemical entity and are consumed in a variety of states. As yet there is no clear evidence that one component is responsible for any benefit of this diverse group of plant foods. The definitions used in this review are those permitted in the current food regulations.

Wholegrain

“wholegrain is the intact grain or the dehulled, ground, milled, cracked or flaked grain where the constituents – endosperm, germ and bran – are present in such proportions that represent the typical ratio of those fractions occurring in the whole cereal, and includes wholemeal”

In intact (unmilled) grains, the fraction described generally as bran includes the pericarp-seed coat and aleurone layer. The former is high in insoluble fibre while the aleurone consists of cells containing protein, fats, micronutrients and some fibre.

Wholemeal

“wholemeal means the product containing all of the milled constituents of the grain in such proportions that it represents the typical ratio of those fractions occurring in the whole cereal”

Dietary fibre

“dietary fibre means that fraction of the edible part of plants or their extracts or synthetic analogues that –

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(a) are resistant to digestion and absorption in the small intestine, usually with complete or partial fermentation in the large intestine; and

(b) promote one of the following beneficial effects –

(i) laxation

(ii) reduction in blood cholesterol

(iii) modulation of blood glucose

and, includes polysaccharides, oligosaccharides (degree of polymerisation >2) and lignins.

An excellent source of whole grains is defined by the US FDA as any food providing a minimum of 16 g of a whole grain containing all of the portions of the kernel per serving. A whole grain food qualifies as such on its whole grain content and is defined below.

Whole grain food – for purposes of bearing a USFDA wholegrain health claim

“a whole grain food shall consist of not less than 51% of whole grain or wholemeal”.

Resistant starch (RS; Asp, 1992)

“All starch and starch degradation products which resist small intestinal digestion and enter the large bowel in normal humans”

Non-starch polysaccharides (NSP)

There is no universally accepted definition of NSP which are the major components of dietary fibre but they may be described conveniently as

“Dietary polysaccharides of plant origin which resist human small intestinal digestion and are the major constituents of dietary fibre”

3.0 SCOPE OF THE REVIEW

This review will provide

- An appraisal of the Health Canada documentation to determine its suitability as a basis for assessing the relationship between whole grain and bran intake and coronary heart disease.
- A review of the evidence released since the time of the Health Canada review.
- Relevance of the relationship to Australia and New Zealand.
- Relationship of whole grain intakes to relevant biomarkers of disease outcome.
4.0 THE HEALTH CANADA EXTERNAL REVIEW PAPERS

4.1 Scope of the appraisal

The documents provided report examinations of scientific studies published up to 2000 which evaluate a relationship between fruits, vegetables and grain products containing fibre (particularly soluble fibre) and coronary heart disease and also soluble fibre from certain foods (oats, psyllium) and coronary heart disease. At the direction of FSANZ, only Health Canada’s Scientific Survey (Cvitovich, Heshka and Johnston, 2003) was evaluated under three headings.

- The selection and assessment of evidence in the review.
- Re-analysis of pivotal studies cited in the review.
- Consideration of the validity of the review’s conclusions.

The peer-reviewed studies used to formulate the Health Canada Scientific Survey were all published before 2000.
The primary source document for this evaluation is the FDA report (Food and Drug Administration, 1993) (which was read in conjunction with determination for oat products Food and Drug Administration, 1997). The former states “The association between dietary patterns rich in fibre-containing foods and lower levels of serum cholesterol is the theoretical basis for consideration of the appropriateness of a health claim for dietary fibre and reduced risk of developing CHD”. In other words if whole grains were to lower risk of CHD, then it would be through modifying this major risk factor. At the time of the FDA determination, plasma lipoprotein total and low density lipoprotein (LDL) cholesterol were considered to be the benchmark modifiable biomarkers for CHD. The validity of these biomarkers has not diminished but other (e.g. circulating homocysteine levels) have emerged (Mensink et al., 2003). Not surprisingly, most material submitted to or considered by the FDA was in relation to lowering of plasma cholesterol by fibre-rich foods or fibre concentrates or isolates. Many of these studies were rather short term (a few weeks) and generally in small populations. Leaving aside specific issues of design (choice of subjects, fibre intakes etc), a general conclusion of the US FDA was that consumption of soluble fibre preparations was associated with lowering of plasma cholesterol. However, the FDA determined that while it was prudent to increase consumption of whole grain foods and cereal products and vegetables and fruits, evidence of a role of dietary fibre in lowering the risk of CHD was inconclusive. This is not surprising as dietary studies with soluble fibre preparations such as oat bran (e.g. Kestin et al., 1990) often include a control arm containing insoluble fibre as wheat bran to maintain parity of intake. The balance of the evidence is that wheat bran does not affect plasma cholesterol (Truswell, 2002) so that the relationship between total cereal fibre intake and cholesterol control may be clouded by this potential confounder. It is important also to emphasise that cereal brans enriched in the pericarp-seed coat are likely to have little or no effect on plasma cholesterol as this fraction is generally low in soluble NSP.

The Health Canada survey builds on this base and the authors have maintained a generally similar format (extensive discussion of experimental studies plus a more restricted examination of observational studies). However, there does appear to have been a temporal shift in emphasis from the FDA source (which is not surprising, given the time difference). The documentation from the US FDA considers isolated fibre components of foods in greater detail while the Health Canada Scientific Survey is concerned rather more with foods themselves. This is not surprising when one considers the role of dietary fibre in plasma cholesterol control and the developing understanding of risk factors working through mechanisms other than plasma cholesterol (Mensink et al., 2003).

The authors evaluated 24 reports on the effects of consumption of whole grains and brans on plasma lipids in human experimental studies and judged 19 to be of appropriate quality. Generally, these studies were of relatively short duration but many showed a significant lipid-lowering effect of bran consumption. The most consistent effect when the subjects consumed diets high in soluble...
fibre as barley, (especially) oats or wheat bakery products. This assessment is sound as is their conclusion that many whole grains and brans have the capacity to lower circulating lipid levels in both healthy and hypercholesterolaemic or hyperlipidaemic subjects. However, this property seems to reside in foods high in soluble NSP and neither wheat nor rice nor other brans which are high in insoluble fibre lower plasma cholesterol consistently. Of the brans tested widely, oat bran appears to have this property and it is not possible to extrapolate to other products.

The authors examined 4 prospective cohort studies published in 7 reports. 1 study failed to find a significant relationship between whole grain consumption and CHD risk using a definition of a whole grain foods as containing >25% of whole grain in the product. The other studies found significant reductions in CHD risk with consumption of whole grains with overall reductions in risk of up to 25% in persons consuming the highest amounts of whole grain products. This relationship persisted when controlled for other risk factors and behaviours. The limited scope of these cohort studies makes it rather difficult to extrapolate to the populations of Australia and New Zealand but they support the proposition that whole grain foods lower the risk of CHD.

The authors of the Health Canada Scientific Survey generally appear to have interpreted the findings of the original US review correctly and have built on it appropriately at the time of writing. However, they have tended to give excessive weight to the experimental studies and have not discriminated between the two major types of NSP (soluble and insoluble) and their differential effects on plasma cholesterol.

4.2.2 Re-analysis of pivotal studies cited in the review

These studies were selected for the insights they give into the key aspects of the Health Canada survey and are reviewed briefly.


Background Several mechanisms were proposed for the effects of soluble NSP in oats on plasma cholesterol including:

- altered fat absorption;
- inhibition of hepatic cholesterol synthesis by a specific short-chain fatty acid (SCFA) (propionate) produced through large bowel microbial fermentation of NSP; and
- enhanced faecal excretion of bile acids and neutral sterols.

The last mechanism was supported by animal studies (e.g. Illman & Topping, 1985) which suggested that soluble NSP enhanced faecal steroid excretion through altering gut digesta viscosity
so as to slow reabsorption. This led to a depletion of the body bile acid pool with compensation through enhanced hepatic conversion of cholesterol to bile acids leading to a lowering of plasma LDL cholesterol.

**Study design** The authors tested that hypothesis by examining steroid excretion in young men after labelling of the body bile acid pool with $^{13}$C cholate and chenodeoxycholate. These are the major endogenous bile acids in normal humans. The volunteers consumed a low fibre (15 g/d) control diet and then a diet high in fibre (32 g/d) as oat bran for a further 28 days.

**Outcomes** Plasma cholesterol fell on the low fibre diet and fell further when oat bran was incorporated into the diet with accelerated bile acid turnover, synthesis and excretion as measured by changes in plasma and faecal $^{13}$C bile acid turnover and excretion, respectively. The data were evaluated statistically and the effects were significant. The hypothesis was confirmed and provides a working mechanism to explain the effects of soluble NSP on plasma lipids.

**Conclusion** This technically demanding study provided other valuable insights.

- *The fall in plasma cholesterol with a low fibre diet.* As yet, there is no explanation for this effect. However, the data suggest that studies could be compromised if the effects of dietary fibre on plasma lipids were studied in groups of unequal fibre intake. Diets should be matched for their fibre content.

- *General applicability of the methodology.* The designs could be applied to examining effects of whole grains on cholesterol homoeostasis independent of any change in plasma cholesterol concentrations.


**Background** The study was carried out to compare the effects of three cereal brans (oats, wheat and rice) on plasma cholesterol in mildly hypercholesterolaemic men. The study was the first to compare three cereal products available in Australia under carefully controlled conditions. The oat bran was high in soluble NSP but wheat bran and rice bran were not.

**Study design** The study was a double blind crossover trial with 24 mildly hypercholesterolaemic men (mean plasma cholesterol 6.34 mmol/L at baseline). They consumed 11.8 g of dietary fibre/d as oat, wheat or rice bran for 4 weeks (measured as NSP). The brans were incorporated into bread and muffins and diets were matched for fibre and macronutrient intake.

**Outcomes** Blood pressure was unaffected by any dietary treatment. Oat bran lowered plasma total and LDL cholesterol relative to wheat and rice bran. Total cholesterol was lowered by 5.5%. Compared with wheat bran, both oat and rice bran raised the ratio HDL: total cholesterol. Indirectly,
the study suggests that wheat bran had no effect on total plasma cholesterol and that the same might be true for rice bran. The study was important and timely as it demonstrated that an Australian oat product was effective in lowering plasma cholesterol.

**Conclusions** The study was well-designed and controlled and macronutrient and fibre intakes appear to have been well-matched and confirms a lipid lowering by oat bran against wheat bran. There were no differences in potential confounders (e.g. body weight). Plasma cholesterol was lowered only with a soluble fibre source and, taken with the previous study, the data go some way to explaining the lack of consistent relationship between cereal fibre and CHD risk and biomarkers seen in population studies. The study also underscores the need for careful control of diet in assessing the effects of soluble fibre on plasma lipids. This is relevant in view of the fact that similar trials in New Zealand failed to find a similar reduction (reviewed in Truswell, 2002) even though they used oat bran from the company that provided it to other trials in which cholesterol reduction was shown (Kestin et al., 1990; Whyte et al., 1992).


**Background** The study was performed to determine the effects of dietary fibre intake on CHD using sound survey methodology.

**Study design** The study was a follow up to the ATBC Cancer prevention study which was a double blind placebo controlled primary prevention trial to determine effects of supplementation with \( \alpha \) tocopherol (AT) and/or \( \beta \) carotene (BC) on incidence of lung cancer in male smokers. There was no change in incidence after 5-8 years of supplementation. Diet was assessed satisfactorily in 27,111 (93%) of participants and, after exclusion of those with prior diagnosis of CHD or symptoms, 21,930 men remained. Fibre was determined as NSP (see Section 6.1). Initial assessment was by questionnaire and as food records during the trial. Correlations between the two were 0.62 for fibre, 0.65 for soluble fibre and 0.67 for insoluble fibre. These correlations were unaffected by correction for energy intake. Coronary events were recorded as deaths (581) or major events (1399) including non-fatal events (818).

**Outcomes** Individuals with a higher intake of dietary fibre (median 34.8 g/d) had a RR which was lower at 0.69 (95%CI 0.54-0.88, \( P<0.001 \)) compared with those in the lowest quintile (median 16.1 g of fibre/d). Water soluble fibre was associated with lowered risk slightly more than insoluble fibre. This study is important because the dietary methodology was measured in two ways and it seems to have been the first to use a specific analysis for dietary fibre that measured the components as NSP and not total dietary fibre (TDF).

**Conclusion** The study demonstrated that even in a population of male smokers (where risk is greatly increased over non-smokers) greater fibre intake was protective against CHD. The data are
convincing for a protective effect of fibre but the linkage to whole grains is indirect. The fact that protection was shown with smokers is an important issue as population studies show that participants with higher whole grain intakes have ‘healthier’ lifestyles i.e. they tend to smoke less, exercise more, be less obese etc.

4.3 Consideration of the validity of the review’s conclusions

The shift away from plasma lipid control (through dietary fibre) as the major (even the sole) mechanism for the effects of whole grains on CHD risk is one of the most obvious differences between the Health Canada report and current knowledge. Drug therapies had shown their effectiveness in patients with high plasma cholesterol. It was thought, not unreasonably, that dietary fibre should lower cholesterol too. This was based on the long-standing historical precedents of the observational studies of Burkett and colleagues who showed that native African populations consuming diets low in fat and high in unprocessed plant foods had low risk of non-infectious disease (Burkitt, 1973). These people also had low plasma cholesterol and were not prone to CHD. From these observations, it was assumed that they also had high intakes of dietary fibre and that this was the protective agent. However, it appears that this may not have been the case and that their fibre intakes were low compared with high risk populations (Topping & Clifton, 2001). Their staples were unprocessed starchy foods, a feature addressed obliquely by the US FDA (1993) who noted that such populations at low risk consumed very large amounts of unrefined starch, probably >70% of energy.

In this light, the emphasis given to plasma lipid control in the scientific survey is quite understandable. The experimental studies in humans (supported by a considerable body of animal work) have shown clearly that foods high in soluble non-starch polysaccharides (NSP) and NSP isolates lower plasma cholesterol. This has been accepted to the point that there are two health claims permitted in the USA:

- Soluble fibre and heart disease.
- Whole oats, psyllium and heart disease.

A further petition under consideration for soluble fibre (as β−glucan) in barley foods and heart disease was granted recently by the FDA (December 2005) (found at [http://www.cfsan.fda.gov/~lrd/fr051223.html](http://www.cfsan.fda.gov/~lrd/fr051223.html)). The relationships addressed in the Health Canada survey relate really to plasma lipid lowering and not to CHD risk itself. Indeed, there seems to be relatively little epidemiological evidence that cholesterol reduction by soluble fibre (especially as products with permitted health claims) translates to lowered risk of CHD. There have been no randomised controlled trials for soluble fibre intake and primary prevention of CHD events and only one secondary prevention trial with dietary fibre (Burr et al., 1989). This trial in over 2000 men with previous myocardial infarction to show any beneficial effect of greater cereal fibre intake on re-
infarction and has been criticised for several aspects of its design and execution including lack of ensuring of compliance and uncertainty around the measures of fibre intake. The value of this trial has been discounted (Truswell, 2002).

In view of the US FDA rulings, the Health Canada Survey report places special emphasis on oats and plasma cholesterol and the authors conclude, quite justifiably, that most studies support a lipid lowering by oats and oat products. Importantly, the mechanism of action of oat products in humans (Marlett et al., 1994) seems to be the same as that in animal studies (Illman & Topping, 1985) i.e. increased cholesterol efflux from the body through greater bile acid excretion. The deficit is made good by a lowering of the body bile acid pool with a fall in plasma LDL. This effect is thought to be due to changes in intestinal digesta flow due to the physico-chemical properties of the NSP (Fernanadez, 2001). The lowering is not due to binding of bile acids by fibre components, a proposed mechanism of action of insoluble fibre products (such as wheat bran). This hypothesis was based on in vitro data showing bile acid binding by insoluble fibre preparations but was shown to be a potential artefact of the isolation procedure (Topping & Oakenfull, 1981).

The Health Canada authors seem to have overlooked the difference between cereal brans and whole grains, especially in relation to the design of nutritional experiments. Most bran products are concentrates of the pericarp-seed coat (including the aleurone layer) and are quite unlike the whole grain, being much higher in insoluble fibre. Products containing insoluble fibre are probably neutral with respect to plasma cholesterol control and in some experimental studies showing effects of soluble fibre on plasma cholesterol (e.g. Kestin et al., 1990) the reference diet contained wheat bran to ensure balanced intakes. It follows that for plasma cholesterol, brans in general would be ineffective. Oat bran is an exception, being much closer to whole grain in composition (Illman & Topping, 1985) and contains most of the pericarp-seed carp, aleurone, germ and starchy endosperm unless specifically enriched in the outer layers by processing (Mackay & Ball, 1992).

The Health Canada survey is balanced in its recognition of potential adverse effects of experimental dietary studies. In terms of CHD risk they seem to be relatively slight, the only one of note being a rise in plasma triacylglycerols with flaxseed meal. Other side effects are those expected from greater fibre consumption – loose stools, flatulence etc. These are to be expected in populations (such as North Americans) unaccustomed to eating dietary fibre.

For the time the Canadian report was convincing but now would be seen to have substantial gaps:

- Lack of consistency in defining serve sizes of whole grain products.
- Absence of any validation of whole grain content of foods.
- Excessive emphasis on experimental studies on plasma cholesterol reduction.
- Lack of clarity about the differences between cereal brans and their NSP content.
Commercial - In Confidence

- Overemphasis on the contribution of cereal fibre to CHD risk.
- Insufficient consideration to other mechanisms of whole grain action on CHD risk besides plasma lipids (e.g. improved blood glucose control, less obesity etc).
- Limited evidence from population studies.

In my view, the Health Canada Scientific Survey was an accurate and comprehensive summary of the evidence available at the time of its completion but the interpretation of the evidence is somewhat limited. Thus, the evidence for an effect of soluble fibre on plasma cholesterol was convincing at the time, but not for whole grains. The subject has developed considerably since then and the documentation is probably not a suitable starting position for the substantiation of a relationship between whole grain and bran intake and coronary heart disease.

5.0 UPDATE OF EVIDENCE SINCE THE CANADIAN REVIEW WAS PUBLISHED

5.1 Overview

Since the publication of the Health Canada Scientific Survey a significant body of literature reporting a strong relationship between whole grain consumption and CHD risk in prospective population studies has been published in high impact, peer-reviewed journals. A number of critical review papers which have examined whole grain intakes and CHD risk have also been published (Anderson, 2003; Jacobs & Gallaher, 2004; McBurney, 2001; Richardson, 2003; Truswell, 2002). A meta analysis of population studies has also been published within one of the reviews (Anderson, 2003). Other research reports have linked whole grain consumption to lowered risk of diabetes (Meyer et al., 2000) and obesity in men (Koh Banerjee et al., 2004) and women (Liu et al., 2003a). Both diabetes and overweight are risk factors for early-onset CHD and there is the possibility that modifying their risk could mediate some of the protective effects of whole grains (Jacobs & Gallaher, 2004). Short-term interventions with whole grain foods have examined their impact on plasma cholesterol and other indicators of health status but included measures of glycaemic control (Mclntosh et al., 2003) and mediators of lowered CHD risk including blood pressure (Jang et al., 2001) which could relate to CHD risk in the longer term.

5.2 Literature Collection

Databases in use at CSIRO (National Library of Medicine (entrezPubMed), Food Science and Technology Abstracts, Biomed Central, Cochrane Library, ISI Web of Knowledge) were interrogated for published information using keyword strings to extract information on whole grains.
and whole grain foods, cereal fibre and CHD and CHD biomarkers. The results are shown in Appendix 1.

5.3 Assessment

No randomised controlled trials of the effects of whole grain foods on CHD risk as measured by the number of coronary deaths or events could be found in the databases examined. Published reports are population studies, structured reviews and short-term interventions. There are also animal studies on aspects of whole grains and biomarkers of CHD risk.

5.3.1. Experimental studies

As noted, there have been no intervention studies in humans with whole grain foods with CHD events as the outcome. Given the costs involved, it appears unlikely that this will change in the foreseeable future. Interventions in humans have been focussed on changes in surrogate biomarkers, especially plasma total and lipoprotein cholesterol (Table 1). These studies have built on the information used in the Health Canada documentation and largely support a lowering of plasma cholesterol by whole grains or isolates high in soluble fibre. Six papers published since 2000 have reported the effects of cereals on plasma lipids in volunteers. In large part, these have confirmed the lowering of plasma cholesterol by foods containing soluble fibre as whole oats. Lowering of plasma total and LDL cholesterol has been shown in male and female Hispanic Americans (Karmally et al., 2005). Davy et al (2002) did not show a significant fall in total or LDL cholesterol but did demonstrate a lowering of small, dense LDL particles by oat bran relative to wheat cereal in sedentary, overweight American men. These particles are considered to be relatively more atherogenic than larger, less dense particles. Interestingly, wheat bran provoked a rise in these particles. There have also been studies showing that foods containing barley lowered plasma total and LDL cholesterol in American men (Behall et al., 2004) and young Japanese women (Li et al., 2003). Behall et al (2004) showed that the reduction in LDL was in terms of particle number. All of the studies appear to have been well executed from the standpoint of compliance and dietary monitoring and also physical measurements and statistical analysis. Within the constraints of managing interventions in free-living populations, the studies appear to have sufficient power to give valid outcomes. The exception seems to be the study of Li et al. (2003) which was carried out with only 10 young Japanese women. This group is likely to be at very low risk of CHD as reflected by their very low plasma cholesterol concentrations. Even so, a reduction in plasma cholesterol was seen. The anomalous results found in the Finnish study by Leinonen et al (2000) are worth noting. This short four-week crossover intervention of 40 free-living adults found a significant lowering of total cholesterol and insignificant lowering of LDL cholesterol in males consuming rye bread but not wheat bread. During the rye bread intervention, men doubled
their total daily fibre intake from 15 g to 31 g/day, while the total daily fibre intake of women only increased from 12 g to 15 g/day with rye bread. It is far from clear whether the additional fibre had any effect on the outcomes observed with males and whether matching would have produced a different outcome. Aside from the small study by Li et al (2003) and the short rye study by Leinonen et al (2000) taken together, these data are convincing for a beneficial effect of oat foods on plasma total and LDL cholesterol. However, there remains the issue of balancing dietary composition. In the study of Davy et al (2002), the total intake of dietary fibre was matched in the control and groups. In contrast, in the remaining studies with foods containing oats or barley the intake of total and soluble fibre was greater than with the comparator foods. The impact of this difference is not clear and it is not certain whether it modified the plasma cholesterol responses or not. Given the observations of Marlett et al. (1994), showing that low fibre diets lowered cholesterol, it is possible that the difference was less than might have been expected. This may have been a contributor to the failure of Keogh et al. (2003) to show an effect of isolated barley glucan on plasma cholesterol. The metabolic ward study by Keogh et al (2003) involved 18 men on a four week experimental diet containing an additional 6.7 g of soluble fibre per day from enriched barley supplements added to foods. The crossover control was a glucose substitute. The imabalance in fibre intakes in this otherwise well-controlled study may explain why no significant diet effects on plasma lipids were observed.

5.3.2 Observational studies

The most significant development post the Health Canada report has been the appearance of six large prospective population studies since 2000 (Table 2). These studies were carried out over extensive periods of time with substantial numbers of volunteers representing accrued information of many person years. All of the studies published to date have shown a significant reduction of CHD risk with greater whole grain consumption. The range of reported whole grain consumptions is wide, going from virtually zero to many serves/d.

In the first study in chronological order, Jacobs et al. (2001) described a study in Norway to ascertain the relationship between wholegrain bread intake and CHD outcome. This study was well-designed and had the added advantage that the respondents also had plasma cholesterol screened at entry. The instrument was a semi-quantitative food frequency questionnaire with detailed information being sought for shop-bought and home-baked bread in terms of whole and refined grain content. The weight that can be attached to the study is limited as only one source of whole grains was measured. Whole grain content was categorised into <25, 25-50 and >50% whole grain flour. A subset of people was asked to give the same information by 24 h recall. Generally similar data were obtained by both means. Of particular interest was the estimate of whole grain intake which was determined by multiplying the whole grain content of breads by the number of slices eaten. Total deaths declined with greater whole grain consumption with a hazard
risk rate (i.e. RR) of 0.66 relative to the lowest quintile of intake. (P<0.001 for linear trend). Cardiovascular disease (CVD) deaths showed a similar trend and multivariate analyses showed that RR = 0.76 when controlling for other known risk factors in the highest quintile of intake (P<0.04 for linear trend). Whole grain consumption was 4 times higher than in the US but the protective effect remained. Strikingly, plasma cholesterol at entry correlated negatively with whole grain intake, despite the apparent lack of effect of the principal grains consumed on plasma cholesterol in experimental studies.

Steffen et al (2003) posed an interesting question – was greater consumption of refined grains associated with greater risk? The paper by Steffen et al was based on the US Atherosclerosis Risk in Communities (ARIC) Study. The ARIC study was a cohort of 15,792 45-64 year olds at baseline followed-up over an 11 year period. After exclusions and dropouts, the analysis consisted of 11,940 middle-aged adults recruited between 1987-1989. The study design assessed dietary intakes using a 66 item semiquantitative food frequency questionnaire and the food items that were classified as whole grain were dark bread and whole grain cold breakfast cereal. This design feature is an important limitation of the study, because the questionnaire was not designed to differentiate whole grain food items from refined grain food items in the food list. Wholegrain consumption may potentially have been misclassified as refined grain consumption. The median intake of whole grain foods in the subjects was 1 serving per day (similar to that in the US population as a whole) and those who consumed more whole grains completed more years of education and engaged in healthier behaviours. After adjustment for age, sex, race and total energy intake, inverse dose-response relations for incident coronary artery disease were observed across quintiles of whole grain intake, though results were not significant. For the men and women in the quintile with a mean intake of 3 servings of whole grain per day, a 28% lower risk of incident coronary artery disease was observed, compared with those in the quintile with a mean intake of 0.5 servings per day. The main conclusion drawn by Steffen et al was that the observational findings suggest a beneficial effect of whole-grain on the risks of incident coronary artery disease.

Liu et al (2003a) carried out an analysis of the Physicians’ Health Study data using dietary habit data collected in 1982. Breakfast cereal intake was assessed as to their whole and refined grain content and the study was strong through its large size. However, the study did have the drawback that the study group (although compliant) might not be representative of the general US population. Additionally, the relatively long time span between dietary recall and analysis could lead to uncertainty about compositional changes. Although the paper sought to address all cause mortality, there is considerable emphasis on whole grain consumption and CVD risk (including infarction and stroke). All of these mortalities declined with greater whole grain breakfast cereal consumption. For CVD, RR was 0.80 (adjusted for all risk factors) when >1 serving/d was
consumed compared 1 serving/wk. Because breakfast cereals represent only a fraction of whole grain consumption (the others including bakery products and whole grain foods such as pasta), these data probably underestimate the impact of whole grains on risk.

Mozaffarian et al. (2003) reported a multicenter examination of food intakes of 3588 US elderly citizens using a pictographic version of a food frequency questionnaire with intakes ranging from 5 times per year to 5 times per week. Fibre was calculated from USDA data and foods were included if they provided more than 5% of total recommended dietary fibre intake. Dietary assessment validity was tested in a subset of 79 participants and shown to be robust. Cardiovascular events were classified by centralised committees. The whole grain component was assessed by post hoc analysis of “dark” i.e. non-white breads. This study was strengthened by the fact that the study population was at high risk of CVD and it confirmed the finding that increased fibre consumption was associated with healthier lifestyle indicators. Cereal fibre consumption (including whole grain and bran) gave a lower risk of CVD. The post hoc analysis showed that people consuming dark breads (pumpernickel, whole wheat, rye) had hazard ratios (i.e. RR) of 0.76 (95% CI, 0.64-0.94) and were protected against incident CVD.

Bazzano et al. (2003) reported a study seeking to ascertain the specific protective effect of soluble fibre in a population survey (NHANES1). The 9776 people who were recruited to NHANES1 formed the study group for this evaluation. These volunteers met the appropriate exclusion criteria (absence of CHD, no medication or symptoms in the past 6 months etc). Dietary assessment was by 24 recall using databases of foods generated for NHANES1. Soluble fibre intakes were not available at the time of NHANES1 but were calculated from a food processing database. A post hoc analysis was carried out to determine the relationship of whole grain breads (as dark breads) to risk. In common with all other studies of this type, higher intakes of fibre were associated with markers of a “healthier lifestyle”. Even so, statistical analysis to correct for these co-variates showed a significant protective effect of total fibre for CHD events but not death. In contrast, soluble fibre showed a highly significant protective effect against CHD and CVD incidence and mortality. These data support a role of soluble fibre (but not TDF) in lowering risk of CHD morbidity and mortality. This applies to CVD also but apparently not to stroke.

Jensen et al (2004) sought to identify the contribution of added bran and germ to the effectiveness of whole grains, using new quantitative measures. They established whole-grain, bran, and germ intakes through a food frequency questionnaire completed by male health professionals. Good exclusion criteria were applied and the whole grain intakes were assessed using the FDA classification. The follow up period lasted over 14 years (from 1986) and they recorded 1818 CHD cases. Controlling for cardiovascular disease risk factors and the intakes of bran and germ added to foods, they found the (anticipated) reduction in risk with greater whole grain intake. They found that added bran lowered risk but that wheat germ did not.
5.3.3 Systematic reviews

Five reviews of the scientific literature examining the relationship between whole grain intake and the risk of coronary heart disease have been published since 2000 (Table 3). Each of these has concluded that there is a protective effect of whole grain foods against CHD risk. In each review, the case was built on the large prospective studies which were published before and during the period in question (see Section 5.3.2). Notably, all reviews have identified that risk reduction is greater with more whole grain consumption. Equally importantly, every reviewer has reached the same conclusion i.e. that the effect remains after correction for the fact that eating more whole grain foods is associated with “healthier” lifestyles and personal attributes. As noted in Section 5.3.2, persons in the higher echelons of consumption are better educated, smoke less, exercise more and are less obese than those in the lower ones. They also consume less total and saturated fat and alcohol. Even so, each reviewer has concluded that the correction for these differences by multivariate analyses does not account for the difference in risk and that there is an attribute (or attributes) of whole grains that confers additional protection. McBurney (2001) examined the potential of diet to lower the risk of cardiovascular disease with a special emphasis on whole grains. As discussed elsewhere (Section 8.3), the potential of whole grains to lower risk through less obesity (itself a factor in cholesterol reduction) was considered to be an important issue. The exact agency for the risk reduction was not identified conclusively and several candidates were proposed – fibre, antioxidants and vitamins. Of these, McBurney concluded that cereal fibre was strongly related to lowered risk of coronary disease.

The second review, in chronological order, was that of Truswell (2002) who examined the relationship between cereals, cereal fibre and CHD risk systematically. In keeping with other reviewers, he put the published literature in the historical context of early population data linking a lowering of CHD risk associated with greater consumption of cereal fibre. The reviewer made a clear distinction between cereals high in soluble fibre and other cereal fibre sources such as wheat. Analysis of the effects of oat bran on plasma cholesterol showed a significant reduction in most published reports. Of particular relevance to Australia and New Zealand was the fact that the four trials conducted in New Zealand before 2000 failed to show a significant reduction in cholesterol by oat bran (see Sections 5.3.1 and 7.2). Truswell concluded that the health claim for oat bran and lowering of plasma cholesterol was justified. A potential for barley to lower cholesterol was also noted although this is not a food consumed commonly in most Western countries. He was also firmly of the view that the health claim for whole grains and CHD risk reduction was justified based on the large number of person-years of observation in the published prospective studies that had been published. Evaluation of these data showed that the reduction was observed after multivariate analyses and correction for energy intake. The latter correction is applied to ensure that the respondents are not taking in more protective nutrients. As in other reports, Truswell
(2002) could not identify a single protective agency in whole grains but did draw attention to the fact that whole grains are of low glycaemic index (GI). Low GI is thought to lower risk of CHD through lowering insulin demand.

Richardson (2003) reviewed the totality of the evidence from four prospective cohort studies published during 1998-2001. He noted that the United Kingdom Joint Health Claims Initiative stated that the evidence was strong enough to support an association but not to demonstrate cause and effect. He concluded that 3 serves/day could confer significant protection but the validity of this conclusion is uncertain. Anderson (2003) drew a similar conclusion in respect of atherosclerotic cardiovascular disease and his review also contained a meta-analysis of prospective studies. Within the limitations of such dietary studies, Anderson (2003) concluded that risk reduction from the lowest to highest levels of intake was 29% after correction for potential confounders. Cereal fibre did not confer any protection but total fibre had a significant effect that equalled that of whole grains. The review considered the mechanisms whereby whole grains could confer protection but no single agency was identified.

The latest review published within the specified time frame was that of Jacobs & Gallaher (2004). They examined 13 published reports of prospective studies of whole grain food intake and atherosclerotic cardiovascular disease. The tabulated data show the strength of the data with hundreds of thousands of accumulated person-years of observations and a substantial number of coronary events as end points. Not surprisingly, the authors concluded that greater consumption of whole grains lowered CHD risk by 20-40% from the lowest to the highest strata of intake. This is one of the few reviews to factor in the likely errors in estimates of whole grain consumption and the problems of correcting for confounding factors. The authors concluded that the balance of probabilities was that the methodological errors cancelled each other out i.e. the effects of whole grain intakes were likely to be underestimated but so were the effects of potential confounders. This suggestion cannot be tested. They discounted the role of fibre per se and suggested that phytochemicals could be the effective agents, acting systemically. However, they also reviewed the data from prospective epidemiological studies linking whole-grain foods to lowered risk of incident diabetes. Risk reductions of a similar order to those for CHD were recorded in all four reports. Diabetes is a risk factor for CHD and Jacobs & Gallaher (2004) linked risk reduction for this condition to lowered risk of atherosclerotic vascular disease. Feeding studies with whole grains and refined grain foods showing greater insulin sensitivity with the former showing support for this relationship.

5.4 Overall conclusions
The experimental studies support a role for whole grains (especially oats) in lowering plasma cholesterol. The published reports of prospective epidemiological studies support a protective effect of whole grain foods against CHD. These studies are large, in diverse populations and of long duration with firm clinical end-points. All of the systematic reviews published in the period have reached the same conclusion. In a sense, this is not a surprise, given that they have examined the same body of evidence from the prospective studies which form their basis. Nevertheless, the consensus is strong as to the relationship but not the causative agency. Cereal fibre was discounted as a candidate mediator of the effect (acting via plasma cholesterol reduction) and water-soluble fibre intake has been shown to lower risk. Bran was identified as a protective agent in one prospective study but its mechanism of action is uncertain. Attention was drawn by reviewers and investigators to the fact that whole grain food consumption lowered the risk of diabetes and obesity, both risk factors for CHD so that the protection could be indirect. There are no randomised controlled trials of the effects of whole grain consumption on CHD events. However, it is concluded that the large body of prospective data provide convincing evidence for a protective effect of whole grains against CHD.

6.0. Determining the relationship between reported whole grain intakes and CHD risk

The heavy emphasis on population survey data means that valid measures of the whole grain content of foods and which foods qualify as “whole grain” are essential. Consumer understanding of the concepts of whole grains and whole grain foods are equally important. There seem unresolved issues in this important aspect of the whole grain research.

6.1 Analytical methodologies

At present, there appears to be no accepted method for monitoring the whole grain content of foods or for estimating intakes. In the USA, the dietary fibre content of a food is used to measure the level of incorporation of whole grains. The standard analytical procedure, also used in Australia, is the Total Dietary Fibre (TDF) method of the Association of Official Analytical Chemists [Section 985.29 of the publication *Official Methods of Analysis of the Association of Official Analytical Chemists* (AOAC) 15th edition (1990)]. Reference values range from 1.7 g of TDF/35 g of recommended amount customarily consumed (RACC) to 3.0 g of TDF /55 g of RACC. There are two important corollaries to the use TDF as a standard. Firstly, there is no means of assessing the presence of other grain components in a food and these may have been altered by processing or by agronomic practice. Thus, it could be possible to take ingredients from different sources (e.g. wheat bran,
starch and germ) and mix them in appropriate proportions and claim that the result is “whole meal flour”. However, as noted by Saxelby and Venn-Brown (1980), NH&MRC declined to allow this as long ago as 1975 stating that “mixtures of white flour and bran are not deemed wholemeal flour”. There seems to be no reason to change this view, especially as standard (wheat) milling makes recombination from the same parent easy. There is also the emerging issue of decolourised whole grains in the US which has apparently unknown consequences for nutrient efficacy.

A second major issue is the fact that analytical methodologies for dietary fibre have changed substantially with time. The fibre hypothesis, linking dietary fibre intake to improved health status, developed during the 1960s and 1970s. The then-current analytical procedures for dietary fibre emphasised the measurement of insoluble plant cell wall materials which were the major energy source for ruminant animals of agricultural importance. These methods were quite destructive for important fibre components which were underestimated or not measured at all. These constituents included the soluble NSP now accepted as the mediators of plasma cholesterol reduction. Analytical methods have evolved considerably since then and development has followed two routes – NSP and TDF. In the former procedure, fibre polysaccharides are isolated and analysed chromatographically as their constituent monosaccharides after hydrolysis. The method is quite specific and excludes lignin (a minor fibre component) and other carbohydrates, including starch (Englyst et al., 1994). NSP analysis is a complex and expensive procedure and is not used widely for food analysis, certainly not for most of the population surveys and interventions which have been published. It has been used to provide a fibre measure for a few published population and experimental studies. It could be argued that reporting “fibre” as NSP is optimal as it excludes other indigestible components. The TDF method is an enzymic-gravimetric procedure in which digestible (starch, fat and protein) components are removed by enzymic hydrolysis and/or extraction. After precipitation, the residue is dried and weighed and gives the dietary fibre content of a food.

There is substantial difference between the TDF and NSP methods in that the former includes a component of starch which is difficult to remove (McCleary, 2003). This portion is a fraction of resistant starch (RS) which is included in the dietary fibre value. Given that RS could contribute to lowering of CHD risk by whole grains, measurement of this component in foods is highly desirable but there is, as yet, no generally accepted method available. This deficiency may hamper research and the development of an understanding of how whole grains lower CHD risk. It is not clear which of the fibre methods (NSP or TDF) is optimal for measuring whole grain intakes in food. However, it is noteworthy that Anderson (2003) concluded that cereal fibre did not correlate to reduction of CHD risk but that total fibre did. This suggests that TDF could be the more useful measure but this needs to be established.
6.2 Cereals and cereal foods which qualify for whole grain status

The definitions used overseas are quite specific and limit the range of commonly eaten foods which can be described as whole grains (Marquart, 2003). It follows that cereal fractions (such as wheat bran or rice bran) are not whole grain, despite their high fibre content. White rice is also not a whole grain despite the endosperm being consumed as a polished, intact morsel. Heat stabilised brown rice is a whole grain as is popped corn. Even though it is not a cereal, buckwheat (a relative of rhubarb) also qualifies as a whole grain when consumed in its usual form. However, “brown or dark breads” are not necessarily whole grain as they may be coloured non-whole grain products (unless specified). Such a rye product exists in Australia with less than 50% of the ingredient mix as wholemeal rye flour. If a whole grain health claim were to be permitted, it would be necessary for the manufacturer to demonstrate that their food meets the criteria. A further important point emerges from this discussion – the possible lack of clarity around the classification of foods as “wholegrain” and community understanding of the term.

6.3 Robustness of self-reported intakes of whole grain foods and the importance of semantics

The observational data on self-reported intakes of whole grain foods and lowered CHD risk are convincing across a number of populations. The CHD endpoint data are strong but estimating individual dietary intakes by questionnaire is intrinsically more problematic. Dietary data have been gathered using different instruments and quantification scales. For example, some studies have used “number of serves” of breads or cereals over defined periods. On the other hand, Jacobs et al (2000) have used a 66 item food frequency questionnaire with a whole grain bread score. This score was a product of the estimated whole grain content of bread and the number of slices, giving a measure of actual whole grain consumed. However, it may be limited by the respondents’ understanding of “whole grains” and the foods to which the term applies. Jacobs (2001) addressed this linguistic issue and the potential for the term to be applied solely to whole kernels. He noted also that Americans, Norwegians and Australians might have totally different perceptions of the same product. Australians (and probably, New Zealanders) might consider whole grains to be “kernels” while Americans would not. Norwegians (the subject of one of the prospective studies) have a specific term (sammalt) for grains milled as a whole. The closest word in England is “wholemeal” and in the US is “wholegrain”. Sammalt cereal is reported in the Norwegian Food Disappearance tables and the use of the terminology adds confidence to the survey data from that country. These data give additional support to the findings from other populations. More recently, Jensen et al. (2004) have applied more stringent criteria to the assessment of whole grain intakes,
using the FDA definition of whole grain. Within the limits of terminology, the relationships between whole grain intake and CHD risk reduction remain in all prospective studies. The lack of a validation method (other than TDF) for the whole grain content of foods, the lack of exact terminology for whole grains and whole grain foods raises the possibility for the weakening of population survey strength and points to a need for consumer and industry education. This is particularly important given the launch in the US of decolourised whole grain breads and bakery products. The long-term health benefits of these products seem to be unknown.

7.0 RELEVANCE TO AUSTRALIA AND NEW ZEALAND

7.1 Whole grains and general dietary recommendations
Dietary recommendations and guidelines by governments and health authorities give particular emphasise to whole grains as the foundation of healthy eating patterns for the long term maintenance of health. Examples of websites are

- mypyramid.gov (usa)
- eatwell.gov.uk (uk)

In Australia and New Zealand, sites include

- nutritionaustralia.org/Nutrition_for_All_Ages/Children
- http://www.moh.govt.nz (Food and Nutrition Guidelines for Healthy Adults)

All of these dietary recommendations support substantial consumption of plant-based foods for long term health maintenance. They emphasise consumption of whole grains foods (usually as part of a healthy diet, low in total and saturated fat).

7.2 Whole grains, dietary fibre and starch in Australia and New Zealand
Dietary recommendations and guidelines by governments and health authorities give particular emphasise to whole grains as the foundation of healthy eating patterns for the long term maintenance of health. Fewer than 30% of Australians and New Zealanders are believed to meet the recommended targets for whole grain consumption. Fibre consumption in Australia is high by international standards with average estimated intakes of approximately 27 g of TDF/person/d in both men and women (Baghurst et al., 1996). Average intakes would seem to be similar in New Zealand allowing for the fact that the data are reported as NSP and not TDF (Ministry of Health, 2003). Whole grain foods are higher in NSP and TDF than refined products so any promotion of consumption would be of general benefit. Foods which meet the whole grain criteria (described
above) are low in fat. This might be of particular value in New Zealand where total and saturated fat consumption and rates of CHD are rather higher than in Australia (Nestel et al., 2005). While there is generally uniform agreement as to the benefits of whole grains in lowering CHD risk, a Melbourne prospective study failed to show a clear-cut effect of whole grain bread on Type 2 diabetes risk (Hodge et al., 2004). However, the authors did conclude that lowering GI was an effective means of lowering risk of diabetes, a risk factor for CHD.

It has to be recognised that all of the observational studies have been conducted overseas. Nevertheless, there is no reason to suppose that the data (and their interpretation) would not be applicable to Australia and New Zealand. The size of the study groups and the fact that the populations are diverse gives confidence of the relevance of the outcomes. This is the same conclusion as that of Truswell (2002).

One area needing resolution concerns a potential difference between plasma cholesterol responses to oats in New Zealand and elsewhere. Four studies prior to 2000 failed to show a significant reduction in plasma cholesterol using study designs that were apparently similar to those used elsewhere (Truswell, 2002). The reason for these findings is uncertain, especially as it appears that the same company supplied products which had been shown to be effective in Australia (Kestin et al., 1990; Whyte et al., 1992). A recent nutritional study with isolated barley β-glucan also failed to show cholesterol lowering in a group of New Zealand volunteers (Keogh et al., 2003). The reasons for this may lie in the comparisons which were made (See Section 5.3.1). However, the data do raise unresolved issues as to the apparent lack of effectiveness of cereal soluble fibre in New Zealand.

8.0 RELATIONSHIP OF WHOLE GRAIN INTAKES WITH RELEVANT BIOMARKERS OF DISEASE OUTCOME

8.1 Criteria
In recommending an altered lifestyle activity (such as whole grain consumption) through a specific health claim, there are three major issues:

- Linking increased whole grain consumption to a specific, dose dependent, lowering of risk.
- That increasing whole grain consumption is protective for the general population.
- That there are valid biomarkers which can be used to monitor improved health status.

At present, the observational evidence appears to be convincing that whole grains are protective against CHD in proportion to the amounts consumed. There is insufficient evidence to set an effective level of intake but multivariate analysis suggests relative risk reductions of ~30% at the highest intakes relative to the lowest strata. Richardson (2003) suggested that significant benefit
could accrue at consumption levels of 3 serves/d. There is, as yet, no evidence that increasing whole grain consumption is protective for the general population but the number of large prospective studies suggests that the odds are very favourable. These data build on a long history of an association between whole grain food intake and lowered CHD risk, stretching over many years (Jacobs & Gallaher, 2004). Further, there is strong supporting evidence that whole grain consumption leads to improved blood glucose control and less obesity. Both of these are risk factors for CHD. All of these points support the possibility that the relationship between whole grain consumption and lowered CHD risk is cause and effect and not merely an association. The central issue remains that of valid biomarkers to show cause and effects and for which the evidence seems to be conflicting, absent or presumptive.

8.1 Whole grains and other health outcomes relevant to CHD

One of the most interesting aspects of whole grain foods and health is the relationship between their consumption and other conditions which are themselves risk factors for CHD. As noted, prospective studies have reported a range of improved health indices with greater whole grain intake. This generalised effect of whole grains has been encapsulated into the “whole grain story”, suggesting that there is a general benefit from the consumption of whole grains as a package. However, it must be recognised that high consumers of whole grain products tend to be more active and fitter, smoke less, and consume less saturated fat and alcohol than people in the lowest strata of intake. Even so, controlling for as many of these factors, as far as practicable, the prospective studies show convincingly that whole grain consumption protects against CHD in a dose dependent manner with overall reductions of 20-30%. Thus, the data are convincing and justify a health claim for whole grains offering protection against CHD. The evidence for a cholesterol-lowering effect of soluble fibre in grains is convincing.

8.2 Whole grain consumption and biomarkers

There are a number of candidate biomarkers but, as yet, none can be linked specifically to whole grain consumption.

8.2.1 Plasma cholesterol The most consistent finding is that whole grain foods and other foods high in soluble NSP lower plasma total and LDL cholesterol. This case is strongest for oat products but evidence has accumulated for a similar effect for barley to the point that a health claim has been authorised in the United States. However, it must be remembered that oat bran is not really a bran in the conventional sense (i.e. a pericarp-seed coat fraction) but is closer to a whole meal.
Jacobs et al. (2000) reported that multivariate analysis of a prospective survey showed that plasma cholesterol was inversely and significantly related to whole grain consumption. However, the data to provide mechanistic support for this relationship are sparse and inconsistent. The lack of effect of insoluble NSP on cholesterol metabolism makes it unlikely that enhanced steroid excretion is responsible. Further, there is a study from Finland showing that consumption of whole grain rye lowered plasma cholesterol relative to wheat (Leinonen et al., 2000). This study seems to be anomalous in that rye is not a recognised source of soluble fibre. Coupled with the large number of trials which show no effect of whole grains other than those high in soluble NSP, it appears unlikely that whole grains in general do not lower plasma cholesterol but specific ones do (Truswell, 2002).

8.2.2 Plasma triacylglycerols Experimental and prospective studies have not provided a clear indicator of the value of this biomarker. However, a cross-sectional analysis of the Framingham Offspring study showed lower fasting concentrations associated with greater whole grain intake (McKeown et al., 2002).

8.2.3 Other biomarkers There is a report that adaptation to a diet containing whole grains and legume powder lowered insulin demand, plasma homocysteine and urinary prostanoid excretion (Jang et al., 2001). These changes occurred independently of any change in BMI. All of these are potential biomarkers for whole grain consumption but they could also be altered by consumption of other foods. The change in plasma homocysteine is consistent with greater folate intake with whole grains. The effects resemble some of those reported by McIntosh et al. (2003). There are reports of a blood pressure lowering effect of whole grains (e.g. Keenan et al., 2000). However, all of these studies are small and need to be replicated before any judgement can be made. Strong evidence for effects of other whole grain components (e.g. minerals) appears to be absent. There have been reports that consumption of rye can increase the plasma concentrations of enterolactones relative to wheat (McIntosh et al., 2003). These bioactive compounds are derived from grain lignans and have been postulated to mediate some of the cardioprotective effects of whole grains (Hallmans et al., 2003). As yet, there are no data of sufficient strength to justify this proposition.

8.3 Whole grain starch digestibility

There seems to be a tendency to regard whole grain consumption as a default measure of dietary fibre intake. This does not seem to be valid as cereal fibre in general is not protective against CHD. As long ago as 1996, Rimm et al. said that it appeared the effect could not be ascribed to known components and that some unidentified factor mediated the effects of whole grains. Whole grains appear to have properties which are more than just fibre + starch+ phytochemicals but there is no single mechanism whereby whole grains lower CHD risk (Jacobs & Gallaher, 2004). The only specific effect is the lowering of plasma cholesterol by soluble NSP found in oats and barley.
Moreover, whole grain consumption has been linked strongly to lowered risk of a diverse range of morbidities including obesity and diabetes. Two plausible hypotheses can be proposed for this broad range of benefits. The first is that whole grains contain such a complete portfolio of protective agents (phytochemicals, micronutrients, fats, fibre etc) (Jacobs & Gallaher, 2004) that they can be protective against multiple targets. The alternative is that whole grains possess a general characteristic which offers comprehensive protection. Both suggestions have merit but the latter has yet to be examined in detail. It is possible that the limited small intestinal digestibility of whole grains (compared with highly refined foods) is the unifying factor.

Refined cereal foods are of high digestibility and have low RS and high GI. In contrast, whole grain foods are known to contain more RS and to have lower ileal digestibility than refined products. This is classified as RS$_1$ (physically inaccessible) in the current convention (Brown et al., 1995). Studies with ileostomists have shown that starch excretion is higher when whole grain foods are consumed compared with low RS foods (Birkett et al., 2000). A similar trial with barley showed that 17% of starch resisted small intestinal digestion when the cereal was consumed as a flake compared with starch excretion of 2% when the same grain was eaten as a finely milled flour (Livesey et al., 1995). Studies with intact humans have shown greater faecal output of short chain fatty acids with wholemeal foods compared with refined products (McIntosh et al., 2003). These data are consistent with greater loss of carbohydrate from the small intestine. RS has an intrinsically lower energy value than readily digested starch (Livesey, 1990) and also seems to trigger greater fat oxidation in humans consuming it in relatively small quantities (Higgins et al., 2004). An exact value for the energy value of whole grains cannot be given as it would be expected to vary with the product. However, the energy yield of RS is at least 50% lower than that of the starch absorbed as glucose in the small intestine (Livesey, 1990).

Lowered small intestinal starch digestibility would also give a lowered glycaemic response. This is particularly important in the context of the physical state of the grain in a product. Jenkins et al. (1988) showed that for both bulgur and barley, glycaemic index was related to the degree of milling i.e. the less disrupted the kernel, the lower the GI. Nevertheless, the in vitro release of glucose was still significantly lower from wholemeal barley than from refined (white) bread. Thus it is possible that the digestibility of even wholemeal flours is lowered sufficiently to lower insulin demand and, hence, CHD risk. Both Truswell (2002) and Jacobs & Gallaher (2004) have drawn attention to this possibility and that the physical state of whole grains is important. Intact kernels might be of greatest benefit through low GI but this could have adverse effects on the bioavailability of other nutrients. Data on this issue are sparse but it has been shown in human feeding trials that the bioavailability of folate in the isolated and milled aleurone layer of wheat was increased considerably over the intact bran (Fenech et al., 2004). This was associated with a lowering of plasma homocysteine in the aleurone consumption phase. Homocysteine is a risk factor for CHD.
The study by Jang et al (2001) supports a potential role for milled grains in CHD risk reduction through lowering this agent.

Multivariate analyses of the data from prospective human studies have shown that the protective effect of whole grains against CHD risk remains after correction for known lifestyle and personal confounders. These elements include obesity and energy intake. However, it is possible that the metabolisable energy and insulin demand of whole grains is sufficiently lower than that of refined cereals to reduce CHD risk in the long term.

If RS (and lowered GI) were to be a major contributor to the health effects of whole grains it has a number of implications. Firstly, it adds to the indices which can be used to monitor the effectiveness of whole grains. This would also allow more rigorous testing of whether the association of whole grain consumption with CHD risk is cause and effect or not. Secondly, it may be necessary to evaluate products on their individual characteristics rather than on whole grain content alone. Finally, it supports the view that a mixture of bran and starch will not duplicate the effects of whole grain.

9.0 FUTURE ISSUES

Consumer interest in whole grains continues to grow in Europe, North America and in parts of Asia. This interest is likely to be fuelled further by health claims. At present, three emerging issues can be discerned which are likely to pose challenges for the research community, industry and regulators.

- Markers – At present, there is no clear biomarker for the health effects of whole grain. There is a pressing need to find suitable ones.
- Product integrity – The absence of a validation measure for the integrity of whole grain foods is not helpful to consumers.
- New products – In the US, new whole grain products (e.g. decolourised breads) are being produced with no clear substantiation of their long-term health benefits.

10.0 REFERENCES


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**Potential Conflict of Interest Declaration**

I declare that, as an internationally recognised authority in research in dietary grains and carbohydrates and health, I have an interest in the implementation of research findings for public benefit through increased consumption of foods which lower disease risk. I declare also my involvement in CSIRO research leading to the development of whole grain cultivars with lowered glycaemic index and higher resistant starch content.
Appendix 1

Search Results (from 2000)

Search strings included key words: whole grains, prevention, CHD, humans, fibre, plasma lipids, grains, cereals. Citations included in the text or those with no clear relevance have been excluded.


