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Whole grain and health: new evidence

II World Congress of Public Health Nutrition – Porto (Portugal), September 23-25, 2010

Contents

Summary

The HEALTHGRAIN definition of whole grain was developed with consideration of modern industrial practice:
"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. Small losses of components - *i.e.* less than 2% of the grain/10% of the bran - that occur through processing methods consistent with safety and quality are allowed."

Nutritional recommendations for consumption of whole grain foods vary across countries but increasingly stress the importance of choosing whole grain foods as key components of cereal intake.
However, actual consumption of whole grain is invariably lower than the recommendations in all countries. Consumer research has produced some clues as to how the barriers to eating whole grain can be overcome but this requires further investigation if successful public health strategies are to be developed.

There is good evidence for beneficial relationships between whole grain intake and several chronic diseases; the strongest is for cardiovascular disease but good evidence also exists for type 2 diabetes, some cancers and gastrointestinal health.
Currently evidence from observational studies is stronger than that from intervention studies but this could reflect the long term nature of the benefits of whole grain.
The main bioactive components, including fibre and other bioactive compounds, are found in the bran and germ fractions of the grain. Possible cellular mechanisms through which these components may exert their effects include effects via inflammatory status, vascular function and improved insulin sensitivity.

Editorial

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Kraft Foods Europe – Biscuits R&D, in conjunction with the HEALTHGRAIN EU research project, organised a symposium within the II World Congress of Public Health Nutrition, held in Porto, Portugal in September 2010. It was entitled "Whole grain and health: new evidence". The symposium was chaired by Dr Jan Willem van der Kamp. Other planned speakers were Professor Chris Seal and Professor Jan Delcour. Dr van der Kamp and Professor Delcour were both participants in the HEALTHGRAIN project. This booklet is a summary of the presentation of Dr Jan Willem van der Kamp and Professor Chris Seal at that symposium [1].

Cereals have been a staple food across the globe for many years but exciting evidence is continuing to mount that whole grain cereals can have superior beneficial health effects compared with refined cereals.

The HEALTHGRAIN Integrated Project (see www.healthgrain.org) was funded for a five year period (2005 to 2010) as part of the EC 6th framework food research programme. It aimed to improve the well-being and to reduce the risk of metabolic syndrome related diseases in the European population by providing a scientific basis for increasing the intake of protective compounds in grains or their fractions as part of processed foods. HEALTHGRAIN was an integrated, multi-disciplinary effort establishing the variation, process-induced changes and human metabolism of bioactive compounds in the major European bread grains wheat and rye.

In this booklet, Dr van der Kamp discusses the definition of whole grain, dietary recommendations for their intake, and current consumption levels in various countries. Barriers to whole grain consumption, along with suggestions as to how they could be overcome are also included.

Professor Seal summarises the evidence for the relationships between whole grain intake and chronic diseases and speculates on the possible bioactive components in whole grain, as well as their putative mechanisms.

Many very recent studies from the HEALTHGRAIN project are discussed in detail, making this symposium a timely overview of the state-of-the-art with the focus on the latest scientific advances in this important topic.

Details of the HEALTHGRAIN project are also included (Appendix 1).

[1] Professor Jan Delcour finally could not attend the congress.

1 WHAT IS WHOLE GRAIN AND HOW MUCH SHOULD WE BE EATING?

Dr Jan Willem van der Kamp (Senior Officer International Projects, TNO Innovation for Life, NL) presented definitions, recommendations and intakes of whole grains in Europe and provided some interesting results from the consumer research module of HEALTHGRAIN.

1.1 What is whole grain? How is it defined?

Structure of the grain and specific compounds

Cereal grain kernels consist of three main parts (Figure 1): **the germ** which contains the vital embryo (3% of total weight of the grain), **the endosperm** containing the nutritive reserves for the embryo (83%) and the **bran outer layers** which provide protection (14%).

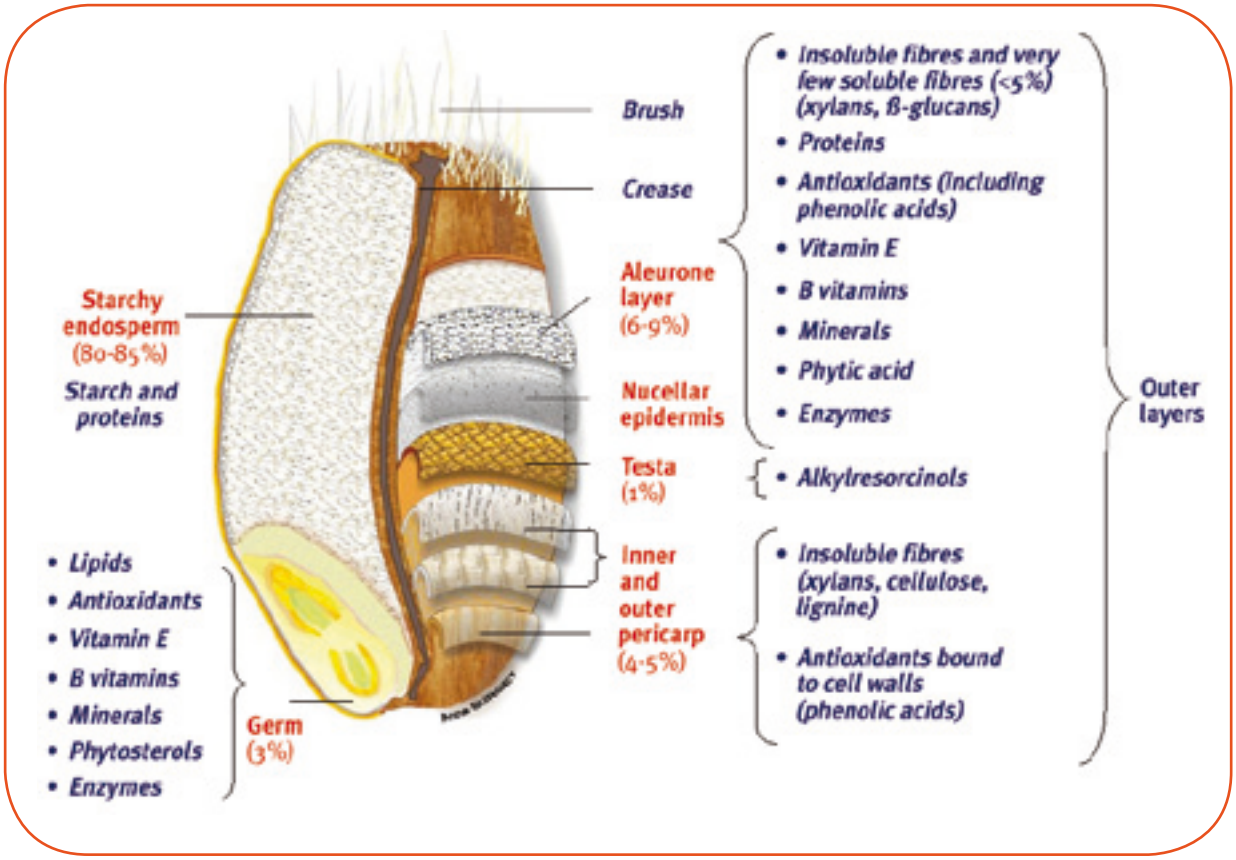

Figure 1: Wheat grain anatomy and location of some specific compounds
Source: © INRA, Anne Surget, adapted from Surget and Barron, 2005

Traditionally in Europe and elsewhere, most refined cereal products have been based on endosperm *i.e.* kernels or flour after removal of the bran and germ; ironically the two parts containing most of the dietary fibre and other bio-active components (micronutrients, phytochemicals). Levels of these substances in whole wheat flour are 2.5 to more than 5 times higher than those in refined white flour.

Whole grain definition

In the past decade, consumers have (re-)discovered the value of whole grain based products, and food producers have substantially increased their efforts to develop and introduce such products. As a result, **consumption of whole grain products is growing, both in countries with an established whole grain tradition such as in Denmark, and in countries, such as the UK, where whole grain was hardly known**. Figure 2 shows how the launches of new whole grain "products" have grown exponentially during the decade.

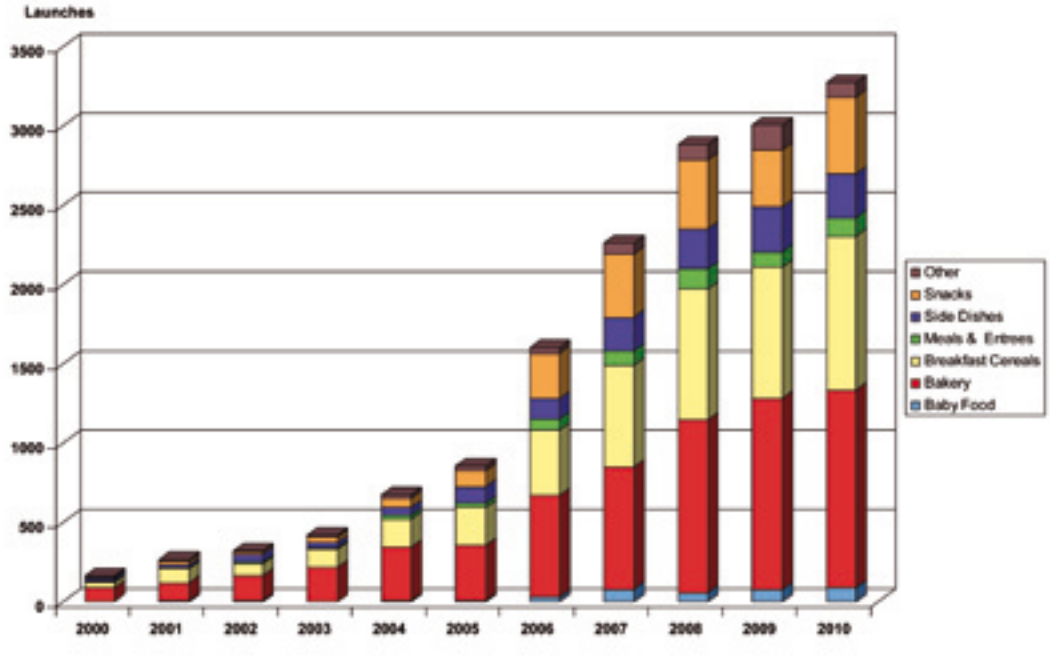

Figure 2: Global new food & drink launches with "whole grain" claim by product category (from 2000 to 2010)

Source: Adapted from data of the Whole Grains Council

In most countries there are no definitions of whole grain, while in a number of countries short definitions of whole grain have existed for a while. These tend to be along the lines of: "Whole grain products include the entire germ, endosperm and bran. Grains that have been subjected to processing such as milling are also included."
Recently more comprehensive definitions have been developed in the USA, Canada, UK, and Denmark. These definitions included items such as a positive list of the grains included and specifications of allowed processes.

In this context, the European HEALTHGRAIN consortium (Appendix 1) felt the need to develop a harmonized and comprehensive definition of whole grain in Europe which should be:
- More comprehensive than current definitions in most EU countries,
- Similar or equal to definitions outside Europe, if possible,
- Reflect current industrial practices for producing whole grain products,
- Useful in the context of nutritional guidelines and nutrition claims.

The HEALTHGRAIN definition is therefore based on modern industrial practices which have produced foods in which the benefits of whole grain have been demonstrated. The first part of the definition is very similar to the definition used in the USA *[American Association of Cereal Chemists, 1999; Food and Drug Administration, 2006].*

HEALTHGRAIN definition of whole grains (2010)

"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. Small losses of components (*i.e.* less than 2% of the grain and 10% of the bran) that occur through processing methods consistent with safety and quality are allowed."
See www.healthgrain.org/webfm_send/44 for the extended definition which includes the list of cereal grains included and milling and processing aspects.

The HEALTHGRAIN definition means that the following are therefore recognised as "whole grain":
- **Cereal flakes,**
- **Stone-ground wholemeal flour,**
- **Recombined wholemeal flour** *i.e.* recombination of the separated milling streams of flour, germ and bran to the same composition as the original grain.

In fact more than 90% of wholemeal flour is now produced by recombination because this "modern milling" process ensures a longer shelf life and constant flour quality in terms of composition and processability than with the traditional stone-ground process.

1.2 Nutritional advantages of whole grain

Eating whole grains means that **all the nutrients in the grain** are consumed, in particular those contained in the bran and the germ. This leads to increased intake of **fibre, vitamins, minerals, essential fatty acids** and **phytonutrients** (physiologically active plant components which have positive functional effects), as well as increased intake of other **bioactive nutrients.**

Whole grain products, made with flours containing virtually 100% of the grain are important sources of dietary fibre, vitamins, minerals and other components that play an important role in human health. Levels of these substances in whole wheat flour are 2.5 to more than 5 times higher than those in refined white flour.

Figure 1 shows the anatomy of wheat grain with the location of specific beneficial nutrients and other bioactive compounds highlighted *[Surget and Barron, 2005; van der Kamp, 2010]:*
- The **endosperm** is mainly made up of **starch** (60% to 70%) and **reserve proteins** (10% to 15%), but also to a lesser extent, **fibres, vitamins and minerals.**
- The **germ** is rich in **lipids** (28.5%) *[Delcour and Hoseney, 2010]*, notably **unsaturated fatty acids** (oleic and linoleic acid). The germ also contains certain **minerals, B vitamins, vitamin E** (antioxidant), and **phytosterols**, compounds responsible for a cholesterol-lowering effect *[Slavin, 2003].*
- The **bran** is rich in **fibres,** and in **insoluble fibres** in particular, which have a beneficial effect on intestinal transit. The bran also contains **proteins, vitamins from the B group** (thiamine, niacin, pyridoxine and folic acid) and **minerals** (magnesium, iron, zinc and manganese).

Whole grain bread has antioxidant activity comparable to that of fruit and vegetables. Such activity is not only related to the presence, in the germ, of vitamin E and its isomers (tocopherols and tocotrienols), but also to minerals such as selenium or to phytochemical compounds such as phytins, alkylresorcinols, and phenolic acids (lignans and ferulic acid) *[Jones, 2007]*.

1.3 How much whole grain should we be eating?

Recommended consumption level for whole grains for healthy diet

Nutritional recommendations increasingly stress the importance of choosing whole grain products for cereal intake. Table 1 shows that recommendations range from 3 to 7 servings/day if we define a serving as ~16-18 g of whole grain (dry matter), provided for example in a 30 g slice of whole grain bread.

Whole grain intake - National recommendations
Approximate range: 3 - 7 servings (serving~slice of bread)

Countries	National recommendations for the "bread, cereals, starchy food" category	National recommendations for whole grains and whole grain foods
France [www.mangerbouger.fr/]	3 portions/day (one at each meal)	Prefer cereals in whole grain form
United Kingdom [www.eatwell.gov.uk]	3 portions/day (one at each meal)	Prefer cereals in whole grain form
Switzerland [www.sge-ssn.ch]	3 portions/day (one at each meal)	When possible 2 of which in whole grain form
The Netherlands [www.voedingscentrum.nl]	For bread: 5-7 slices	Preferably whole grain
Denmark, Sweden [www.food.dtu.dk] [www.slv.se]		The equivalent of 75 g whole grains per 10 MJ (2400 kcal) equivalent to 62 g for a reference 2000 kcal diet
The United States [www.health.gov/dietaryguidelines/] [www.mypyramid.gov]	6 ounce-equivalent serving of cereals for a 2000 kcal diet per day	At least half of cereal intake to be consumed in whole grain form, equivalent to at least 3 ounce-equivalent[2] servings of whole grain foods for individuals over 9 years: "Make at least half your grains whole grains".
Australia [www.nhmrc.gov.au]	"Eat plenty of cereals"; For women 4-9 servings For men 6-12 servings	Prefer cereals in whole grain form
Canada [www.hc-sc.gc.ca]	6 to 8 servings per day	Of which half in whole grain form

[2] 1 ounce equivalent is the same as about 16 g whole grain ingredients.

Table 1: National recommendations for cereals and whole grain consumption

Recommendations in countries without a whole grain tradition, e.g. USA, UK and France, are at the bottom end of this range and make more general comments such as: "make at least half your grains whole grain" or "prefer cereals in whole grain form".
Recommendations in countries with a whole grain tradition go further and are found at the top end of the range. Denmark recently agreed on the equivalent of 4 servings of whole grain ingredients (75 g per 10 MJ equivalent to 62 g per 2000 kcal) and, in the Netherlands, the daily recommendation of ~6 slices of bread should be preferably consumed in their whole grain form, delivering about 120 g of whole grain.

Recommendations for whole grain in relation to heart health

The great majority of whole grain products are high in fibre and therefore their consumption is important for meeting recommendations for dietary fibre intake.

A fibre intake of 35 g/day is recommended for the beneficial effect for heart health by the Institute of Medicine *[Institute of Medicine, 2002]* and in the guideline for fibre intake of the Netherlands Health Council *[Health Council of the Netherlands, 2006]*. This Council recommends fibre intake via a mixed diet consisting of products - such as fruit, vegetables and whole grain products - that have not been enriched with isolated and purified dietary fibre. If 50% of this recommended fibre intake comes from whole grain, then it follows that 17.5 g/day of fibres from whole grain is recommended to get a benefit for heart health. Converting these fibre recommendations into whole grain recommendations, with whole wheat products as the key source of whole grain, results in a recommendation of ~140 g/day whole grain dry matter.

Consumption of whole grain products other than from whole wheat bread, such as breakfast cereals, biscuits and pasta, will be needed if these intakes are to be achieved. Further, all recommendations invariably advocate consumption of fruits, vegetables, whole grain products, nuts, and potatoes rather than adding isolated fibres to products.

1.4 Actual consumption of whole grain across Europe is well below recommendations. Why?

Consumption of whole grains across europe

Unfortunately, actual whole grain consumption in Europe invariably falls well below the recommendations, even in those countries, such as Denmark, which have a strong whole grain tradition (only 6% of Danes meet the Danish recommendation: 75 g/day) *[Strunge Meyer, 2010a] [Strunge Meyer, 2010b] [Danish Whole Grain campaign]*. In France, less than 50% of the population meet the French recommendation *[French Nutrition and Health Survey, 2006]*. One third of British adults never eat whole grain *[Thane et al., 2005]*.
In Germany, average consumption in children from 2 to 18 years is 20 g to 33 g per day, again below national recommendations *[Alexy et al., 2010]*. The situation is no better outside Europe. In the USA, adults consumed on average 0.7 whole grain servings/day *[O'Neil et al., 2010]*. But the situation is improving: compared to 2005, consumption in 2008 increased by 20% *[The Whole Grains Council]*.

Factors influencing the gap between recommendations and intakes

What are the barriers to increasing intake of whole grain products? The HEALTHGRAIN consortium identified these as:

- Tradition of "white" products,
- Taste and texture of whole grain products,
- Costs (wholemeal flour more expensive than white),
- Limited positive perception of nutrition and health information about whole grain,
- Consumers' mindset and reluctance to change,
- Limited availability of whole grain products with higher levels in products.

1.5 Consumers' perception of whole grain products and associated health claims

Perceived benefits of whole grain products

Part of the HEALTHGRAIN project (Appendix 1) was devoted to exploring consumer attitudes to whole grain products. **Interviews with more than 500 consumers in three different countries (UK, Finland, Italy) showed that whole grain foods are perceived as being more natural, healthier, and more nutritionally balanced than refined grain products.** However this difference was much more pronounced in Finland which has a whole grain tradition than it was in Italy which does not. The Italians (as opposed to UK and Finland) did not rate the taste higher than refined grain foods *[Arvola et al., 2007; Dean et al., 2007]*.

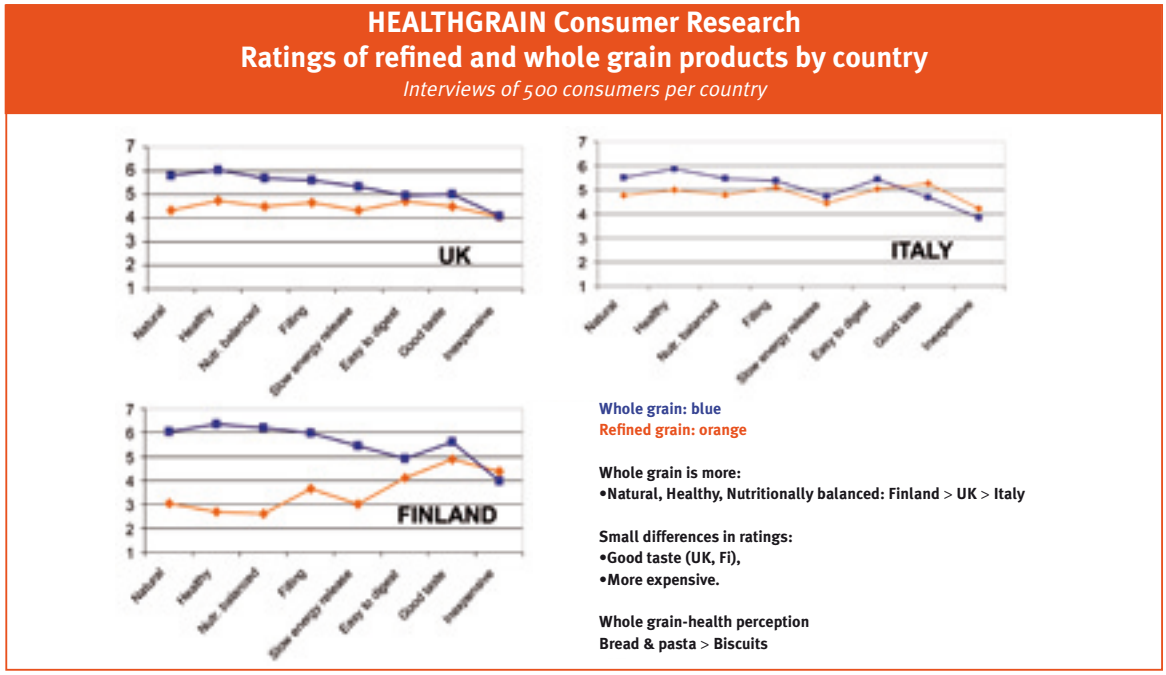

Figure 3: Perceived benefit of whole grain and refined grain products

Source: HEALTHGRAIN

The results of this survey may stimulate food producers to launch more whole grain products.

Effect of health claims on willingness to buy whole grain products

The HEALTHGRAIN project also examined consumers' perception of health statements and their impact on consumers' willingness to buy a whole grain product in four countries (Germany was added to the other three). They compared two types of statements with no statement at all:

- Strong statement: "Contains cereal-based compounds which balance the blood glucose levels and therefore lower the risk of type-2 diabetes."
- Weak statement: "Promotes regulation of blood sugar balance."

In general, consumers considered the health statement on the label to indicate the product was healthy but the impact on their likelihood of buying the product varied across countries. Finnish and German consumers were most likely to buy on the prompt of strong health statement but British consumers preferred the weak health statement. The Italians were deterred by both health statements and would prefer to buy products without any health statement about whole grain *[Saba et al., 2010]*. These results underlined the usefulness of health claims which might, or might not be, used according to consumers' attitudes within the country.

1.6 How do we get consumers to increase their intake of whole grain?

Initiatives to promote whole grain towards consumers

One of the most impressive campaigns in Europe to increase whole grain consumption was launched in 2009 in Denmark; it is a partnership between government, health partners, and commercial partners (see www.fuldkorn.dk). The Danish whole grain campaign announced its first results in March 2010 and showed that whole grain product sales had increased by 19%, whereas there had been no growth in the general market for bread, cereals, rice and pasta market.
Success factors in the campaign included the commitment of a wide range of stakeholders who put together an information campaign and ensured wider availability, namely by encouraging product innovation. The campaign also gave increased prestige to whole grain products and to the organisations supplying them (schools, employers, retailers, etc.). Other such initiatives around the world include the whole grain stamp, developed in the USA and currently applied in more than 20 countries (see www.wholegrainscouncil.com).

Healthgrain initiatives to promote whole grain

HEALTHGRAIN includes education, training and dissemination elements in order to transfer the technology and "know how" about healthy grain foods to the European grain processing industry and health professionals. This will help to increase awareness of the benefits of eating whole grains rich in micronutrients and other protective substances as part of an enjoyable and healthy diet. This will hopefully lead in Europe to their increased consumption, improved health perception and subsequent benefits.

Key Points

- Whole grains contain all 3 parts of the grain: bran, germ and endosperm, compared to refined cereals, which essentially contain the endosperm.
- Whole grains have a high nutritional density due to the presence of bran and germ, increased contents of fibre, antioxidant compounds, vitamins and minerals.
- The HEALTHGRAIN project has produced a comprehensive definition of whole grain.
- There is not yet a universal quantitative recommendation for whole grain. For a healthy diet, Denmark promotes 75 g of whole grain per 10 MJ daily need, which corresponds to 62 g/day.
- Consumption of whole grain in Europe is currently well below recommendations.
- We need to increase the range of whole grain foods and educate consumers about their benefits. The results of the HEALTHGRAIN project will help to achieve this.

2 WHAT EVIDENCE DO WE HAVE FOR RELATIONSHIPS BETWEEN WHOLE GRAIN INTAKE AND CHRONIC DISEASE?

There is general agreement that whole grains are good for you, but what do we mean by this? Good for what? How do we know? How do they do this? To try to answer these questions, Professor Chris Seal (Professor of Food & Human Nutrition, Newcastle University, UK) gave an overview of the literature on whole grains and health.

2.1 Types of evidence for whole grain and health

Hierarchy of evidence

Scientists and policy makers tend to judge the evidence according to a hierarchy of evidence. In this, consensus reports from authoritative bodies and intervention trial evidence rate highest, "observational comparison" studies come next and animal studies and other *in vitro* studies are lowest (although these are very important for establishing mechanisms).

Whole grain and health

Hierarchy of evidence for whole grains and health

- Consensus reports from National and International Expert panels and authoritative statements: yes, for CVD (and cancer).
- Human intervention studies: mixed outcome, expanding.
- Observation/Ecological studies: extensive, mostly convincing.
- Animal and *in vitro* studies: some, mechanistic value.
- Evidence of traditional and experience of use: yes.

The fact that whole grains have been eaten in traditional diets since before the industrial revolution is an important testament to their safety, but this does not feature on this hierarchy of evidence. **Most of the scientific evidence for the benefits of whole grain comes from "observational" studies which have associated its consumption in different population groups with reduced disease risk or death from the disease.** However, the obvious question follows: does this positive association only exist because whole grain consumers have healthier lifestyles? (lifestyles which relate not only to types of diet, but to drinking and smoking habits and to levels of physical activity).
Currently, there is much less supporting evidence for whole grains from intervention studies and the results are more variable. Nevertheless, the overall benefits of whole grains are difficult to argue against and several authoritative bodies have recognized a beneficial effect of whole grain consumption.

Examples of authorised statements about whole grain

"Diets rich in whole grain foods and other plant foods and low in total fat, saturated fat and cholesterol may reduce the risk of heart disease and some cancers."

(Food and Drug Administration, 1999)

"People with a healthy heart tend to eat more whole grain foods as part of a healthy lifestyle."

(Joint Health Claims Initiative, 2002)

"A healthy lifestyle and a well balanced diet rich in whole grain products reduces the risk for (coronary) heart disease. The product X is rich in whole grains (contains Y% of wholegrain)."

(Swedish Nutrition Foundation, 2004)

2.2 Cardiovascular diseases

Cardiovascular diseases, including coronary heart disease, ischaemic heart disease, stroke and peripheral vascular disease are the most common causes of death in developed countries.

Observational evidence

Some of the impressive observational studies based on prospective evidence from cohorts on whole grain in relation to CVD are summarised in Table 2. Even after allowing for the many confounding factors mentioned above, substantial positive effects are still seen for CVD and stroke.

Study	Whole grain intake comparison	Outcome
Health Professionals Follow-Up Study	Comparing 1st and 5th quintiles of whole grain intake (median intake range 3.5-42.5 g of WG/day)	18% reduction in coronary heart disease HR 0.82 (95% CI 0.70, 0.96)
Nurse's Health Study	Comparing 1st and 5th quintiles of whole grain intake (median intake range 0.13-2.70 servings of WG/day)	36% reduction in ischaemic stroke RR 0.64 (95% CI 0.47, 0.89)
Iowa Women's Health Study	Comparing 1st and 5th quintiles of whole grain intake (median intake range 1.5-22.5 servings of WG/week)	18% reduction in all cardiovascular disease deaths HR 0.82 (95% CI 0.66, 1.01)
		18% reduction in coronary heart disease deaths HR 0.82 (95% CI 0.63, 1.06)
		30% reduction in ischaemic heart disease deaths RR 0.70 (95% CI 0.50, 0.98)
Atherosclerosis Risk in Communities (ARIC) Study	Comparing 1st and 5th quintiles of whole grain intake (mean intake range 0.1-3.0 servings of WG/day)	28% reduction in incident coronary artery disease HR 0.72 (95% CI 0.53, 0.97)
		Incident ischaemic stroke significantly reduced but only for basic multivariate model HR 0.62 (95% CI 0.39, 0.99)

Only significant differences are reported. CIs are confidence intervals for the 5th quintile.
HR: Hazard Ratio; RR: Relative Risk.

Table 2: Summary of large scale observational studies showing a benefit of increase whole grain consumption on CVD risk
Source: Adapted from Seal and Brownlee, 2010

Three separate meta-analyses have been performed *[Anderson et al., 2000 ; Anderson, 2003 ; Mellen et al., 2008]* on the results of many of these observational studies and the consistency of the evidence has led one author to state "In light of this consistent evidence, policy makers, scientists and clinicians should redouble efforts to incorporate clear messages on the beneficial effects of whole grains into public health and clinical practice endeavours" *[Mellen et al., 2008]*.

Intervention studies

Two systematic reviews - Ruxton (2008) and Kelly (2007) - have summarised the evidence from intervention trials which have investigated the effect of whole grain on risk factors for CVD and have not produced such a consistent picture. The first review (restricted to studies on oats) provided evidence that regular oat consumption is an effective dietary strategy for helping to attenuate CVD risk. Despite the consistency of effects seen in trials of whole grain oats *[Ruxton and Derbyshire, 2008]*, the second review only found weak evidence for a reduction in LDL cholesterol concentrations and warned that "the positive findings should be interpreted cautiously" *[Kelly et al., 2007]*. Most trials have been conducted in "at risk" populations with small numbers of subjects. Results from larger trials are gradually being published; some support the consistent message from observational studies but some do not.

2.3 Type 2 diabetes

Many of the cohort studies mentioned above have also been used to examine the effect of whole grains on the risk of developing type 2 diabetes (T2D) *[de Munter et al., 2007]*. Figure 4 shows the forest plot for multivariate adjusted relative risk (RR) of T2D for a 2-serving per day increment in whole grain intake for individual studies and the combined effect accross all studies. The average reduction in relative risk (RR) of type 2 diabetes was about 21%.

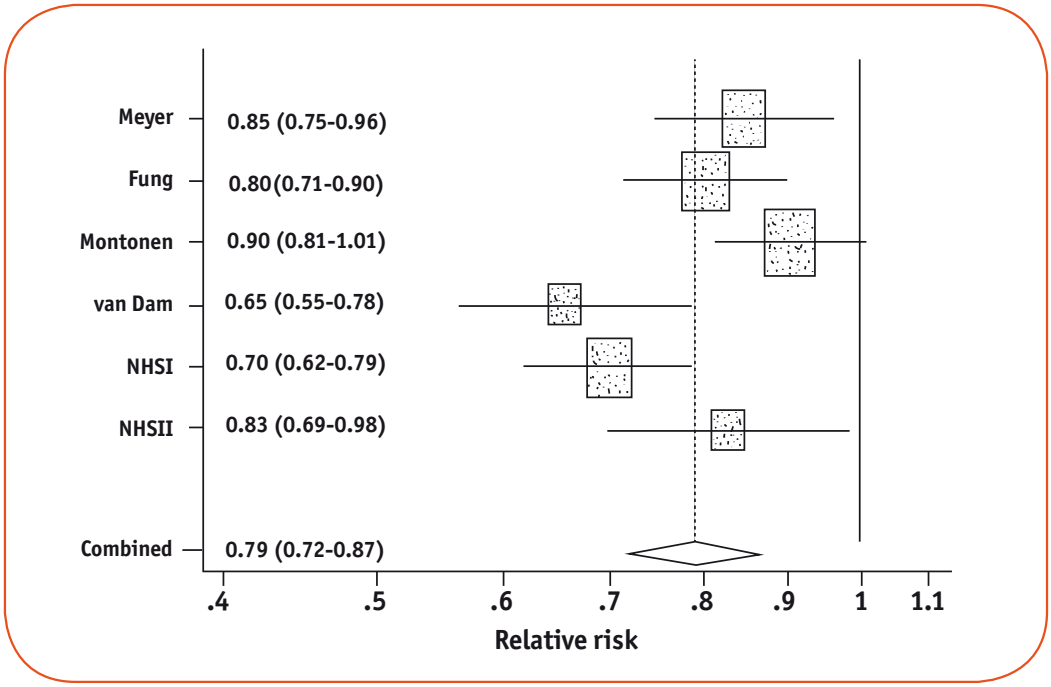

Figure 4: Forest plot showing the multivariate-adjusted RR of type 2 diabetes for a two-serving-per-day increment in whole grain intake for individual cohort studies and all studies combined.
Bars and the diamond indicate 95% CIs. The size of the squares corresponds to the weight of the study in the meta-analysis
Source: de Munter *et al.*, 2007

The evidence is generally weaker than that for the reduction of CVD risk *[Priebe et al., 2008]* but a very recent analysis on pooled data from three large US cohorts *[Sun et al., 2010]* has shown a 27% reduction in incident cases of T2D in the highest whole grain consumers. A dose response effect for the amount of brown rice consumed was also shown. In fact, replacing 50 g of white rice with brown rice was calculated to give 16% reduction in the relative risk of developing T2D and replacing it with whole grain gave a 36% reduction.

2.4 Cancers

Jacobs *et al.* conducted a meta-analysis of forty observational studies (from the US, Italy, Central Europe) published between 1984 and 1997. The pooled odds ratio (0.69) for cancer risk compared between high intake *vs.* low intake of whole grain foods was a highly significant risk reduction *[Jacobs et al., 1998]*, but additional published studies have not been evaluated further since that time. As would be expected from the body of evidence now available, the beneficial associations are strongest for cancers of the gastrointestinal tract. Two very recent studies in the USA have supported this conclusion. Schatzkin *[Schatzkin et al., 2007; Schatzkin et al., 2008]* showed that high whole grain consumers had lower risk of colorectal and intestinal cancer. However a study in Denmark has not shown a consistent effect of whole grain reducing risk of colon cancer in women, although it did in men, possibly due to the high baseline intake of whole grain in Denmark *[Egeberg et al., 2010]*. Lam *et al.* *[Lam et al., 2010]* used data on nearly half a million people from the NIH-AARP study to show that the risk of head and neck cancers was reduced with increased whole grain intake.

2.5 Body weight and fat distribution

Many cohort studies show reduced BMI with increasing whole grain intake. The decreased BMI range is between 0.5 and 1.7 kg/m^2 comparing the highest whole grain consumers with the lowest whole grain consumers *[Seal and Brownlee, 2010]*. In addition, data from some prospective studies have also suggested that weight gain over time is lower in those who consume more whole grain *[Bazzano et al., 2005]*.

Data from 15 studies were reviewed and subject to meta-analysis *[Harland and Garton, 2008]*. A modest reduction in BMI of 0.58 kg/m^2 and a reduction in waist circumference of 2.7 cm was shown with consumption of three servings of whole grain per day. These changes are relatively small and their significance is difficult to evaluate. Interestingly, not all studies showed positive benefits of whole grains.

There are plausible reasons why body weight might be lower in those consuming whole grains. Whole grain foods have a higher fibre content and may also have a lower glycemic index with a larger particle size compared with refined grain flours. As a result they may have a slower digestion, increase satiation and satiety, and reduce postprandial metabolite and hormonal responses. These factors together may result in a cumulative reduction in overall energy intake.

Abdominal obesity is acknowledged to be a greater health risk than total obesity and so it is of interest that the association of whole grain cereal consumption with reduced amounts of visceral fat has recently been shown in Framingham Heart Study participants *[McKeown et al., 2010]*. Mechanisms linking whole grain intake with a beneficial fat distribution have yet to be proposed.

2.6 Gastrointestinal health

Increased whole grain intake has been associated with various benefits to gastrointestinal health. Apart from the lower incidence of cancer at different sites along the GI tract as mentioned above, whole grain intake is associated with reduced symptoms of irritable bowel syndrome (IBS) and improved laxation.

Whole grain foods deliver various components and their effect on gastrointestinal health may be due to any or all of them:

- Dietary fibre:
  - Insoluble fibre (mainly from wheat, brown rice)/prebiotic,
  - Soluble fibre (higher concentration in oats, rye, barley)/prebiotic,
- Resistant starch (affected by processing of grain),
- Bioactive compounds associated with bran, germ and aleurone ("antioxidants", polyphenols, phytate).

Dietary fibre can cause benefits by improved water retention; altered stomach emptying and flow of digesta along the GI Tract; sequestration of nutrients affecting absorption rates; delivery of fermentable carbohydrates to large bowel; or by changing the SCFA (Short Chain Fatty Acids) profile in the colon.

Prebiotic effect

The prebiotic index is defined as the change in proportions of beneficial bacteria (bifidobacteria and lactobacilli) and those considered detrimental (clostridia and bacteroides) *[Hughes et al., 2007]*.

A cross-over design study with 31 human subjects consuming 48 g whole grain or refined grain breakfast cereal for 2 weeks (with a two week washout between treatments) showed a significant increase in faecal bifidobacteria and lactobacilli and a significant increase in stool frequency during whole grain breakfast cereal consumption *[Costabile et al., 2008]*.

2.7 How might whole grain cause these beneficial health effects?

Evidence from observational studies indicates that consumption of whole grain reduces the risk of chronic diseases as described above. One of the objectives of the nutrition module of HEALTHGRAIN was to identify mechanisms involved. HEALTHGRAIN has revealed novel insights but corresponding mechanisms remain only partially elucidated.

Possible mechanisms for beneficial whole grain effects:

- Lowered inflammatory status,
- Improved insulin response,
- Improving vascular function and blood pressure,
- Modified blood lipid profiles,
- Facilitated weight control,
- Deliver bioactive components to the gut (fibre, prebiotics, "antioxidants") and affect digestion of diet.

Figure 5 is an overview of the possible ways in which whole grain intake may exert health effects. The dietary fibre and associated components, oligosaccharides, and the resistant starch that reach the colon are fermented by intestinal microflora to SCFA which may inhibit inflammation and thus improve insulin sensitivity and blood lipid profile. Other bioactive components present in whole grain can affect colonic fermentation ("antioxidants", polyphenols and phytate) or may lower homocysteine concentrations (choline, betaine) and thus improve vascular function.

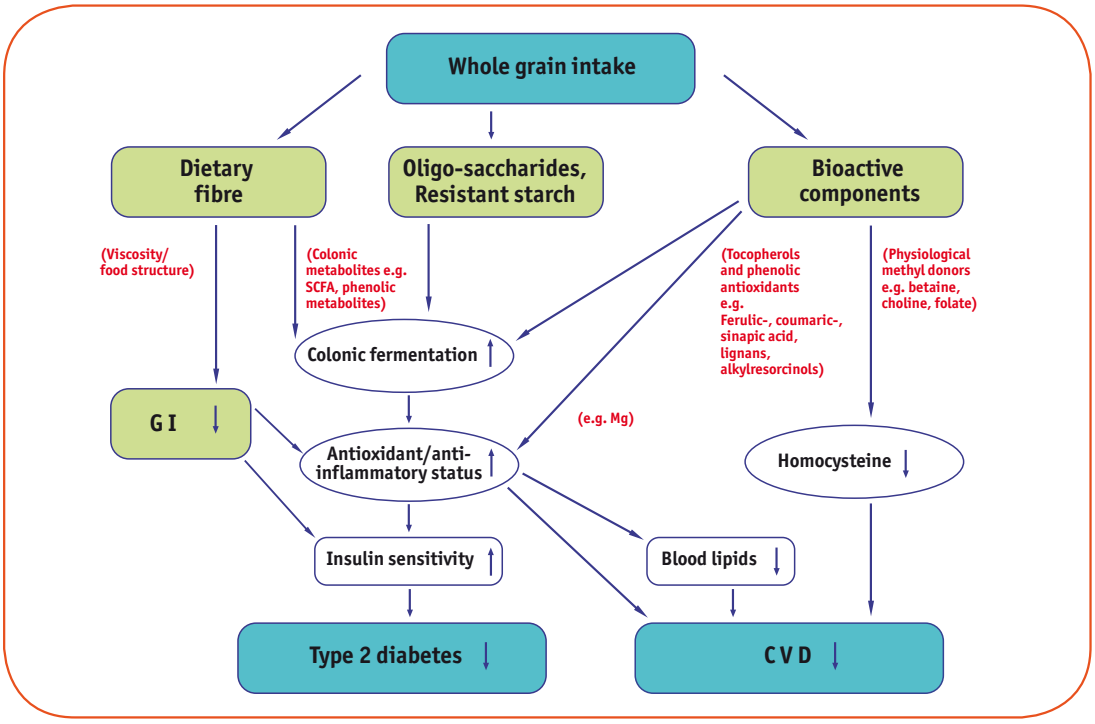

Figure 5: Some suggested mechanisms for metabolic benefits of whole grain

Source: HEALTHGRAIN

Improved inflammatory status

Evidence for this possible mechanism comes from observational studies. Data from the Insulin Resistance Atherosclerosis Study showed that high whole grain consumers had decreased concentrations of the inflammatory markers, C-Reactive Protein (CRP) and Plasminogen Activator Inhibitor-1 (PAI-1) *[Masters et al., 2010]*. Older women with T2D in the Nurses Study also showed reduced concentrations of CRP and another inflammatory marker, tumour necrosis factor receptor 2 (TNF-R2) with increase whole grain consumption *[Qi et al., 2006]*.
Gaskins showed that premenopausal women who had one, or more than one serving of whole grain per day had lower concentrations of CRP at all phases in their menstrual cycle *[Gaskins et al., 2010]*.

Improved insulin response

Lower fasting plasma glucose and insulin concentrations in hyperinsulinaemic subjects consuming increased amounts of whole grains have been demonstrated e.g. *[Pereira et al., 2002]*, but this is by no means consistent across studies *[Keenan et al., 2002]* and has rarely been replicated in intervention studies.

Data from the Multi-Ethnic Study of Atherosclerosis (MESA) (a prospective cohort study of older adults initiated in 2000) showed a significant trend for lower insulin concentrations and lower HOMA-IR (homeostatic model estimated insulin resistance) levels in the top quintile of whole grain consumption compared with the bottom quintile *[Lutsey et al., 2007]*.

The best recent study used the glycemic clamp technique to measure insulin sensitivity *[Andersson et al., 2007]*. In this randomized crossover study, 22 women and 8 men were given either whole grain or refined grain products to include in their habitual daily diet for two 6-wk periods. Peripheral insulin sensitivity did not improve significantly between the two groups at the end of the experimental period.

One of the most cited studies for a whole grain effect on insulin response *[Alminger and Eklund-Jonsson, 2008]* showed lower post-prandial glucose and insulinemic response with whole grain, high amylose high beta glucan barley, and high beta glucan tempe. However it is not clear that this is a genuine whole grain effect or an effect due to some fermentation component in the tempe.

Improved vascular function

Data from the Health Professionals Study (prospective cohort study 1986-2004), after 18 years of follow-up *[Flint et al., 2009]*, has shown that consumption of whole grain cereals reduce the risk of incident hypertension. However the intake of whole grain was particularly low in the lowest quintile of intake.

Whole grain can also reduce changes in vascular function *[Erkkilä et al., 2005]*. After 3.2 yrs follow-up in a prospective cohort study involving 229 postmenopausal women participating in the Estrogen Replacement and Atherosclerosis trial, progression in stenosis tended to be less in women with higher intake of cereal fibre ($P = 0.10$) or whole grain foods ($P = 0.09$), after adjustments for age, cardiovascular risk factors, and dietary intakes of saturated and polyunsaturated fat, cholesterol, and alcohol. Intakes of total, fruit, and vegetable fibre, and number of servings of refined grain, fruits, or vegetable were not associated with progression.

Improved lipid profile

In the Baltimore Longitudinal Study on ageing *[Newby et al., 2007]* significant changes in total and LDL cholesterol concentrations were seen with increasing whole grain intake.

2.8 Large scale intervention studies to study changes in risk factors for heart health

While the observational evidence described above is a powerful indicator of the inverse correlation between whole grain intake and CVD risk, this evidence does not demonstrate causality. Evidence from controlled dietary intervention studies with large numbers of subjects showing clear benefit of increased consumption of whole grain foods on markers of disease risk is needed. However, two such recent studies have produced conflicting results.

The WHOLEheart study *[Brownlee et al., 2010]* involved a total of 316 participants (aged 18–65 years; BMI = 25 kg/m^2) consuming 30 g WG/d who were randomly assigned to three groups: control (no dietary change), intervention 1 (60 g WG/d for 16 weeks), and intervention 2 (60 g WG/d for 8 weeks followed by 120 g WG/d for 8 weeks). Markers of CVD risk, measured at 0 (baseline), 8, and 16 weeks, were BMI, percentage body fat, waist circumference; fasting plasma lipid profile, glucose and insulin; and indicators of inflammatory, coagulation, and endothelial function. Results showed that consuming whole grains had no effect on:

- Insulin sensitivity,
- Fasting lipid profile,
- Endothelial functions,
- Anthropometric measures (no weight gain despite WG group consuming more energy during the intervention).

Explanations for the lack of effect could be that a period of 4 months may be insufficient to change the lifelong disease trajectory associated with CVD or that compliance in the high whole grain groups had not been good enough to show an effect. Any beneficial effects may also have been masked by the higher food consumption in the high whole grain consumers.

The GrainMark study *[Seal et al., unpublished]* was another intervention study over 4 weeks comparing 0, 3, and 6 servings of whole grain rye *vs.* whole grain wheat. In this study better compliance than WHOLEheart was achieved, possibly by telling subjects that the investigators were measuring markers of whole grain intake. In this study a significant dose response reduction in LDL cholesterol was seen with both types of whole grain.

Key Points

- The strongest relationships between whole grain intake and disease risk have been found for cardiovascular diseases.
- Strong relationships have been found for type 2 diabetes, symptoms of the metabolic syndrome, and several cancer types, particularly those of the gastrointestinal tract.
- Whole grain intakes are associated with improved gastrointestinal health in general.
- Possible active components are increased intake of soluble and insoluble fibre, resistant starch and prebiotic components, bio-active compounds associated with the bran and germ fractions such as plant lignans, phyto-oestrogens, phytates and phenolics.
- Possible mechanisms include lowered inflammatory status, improved insulin response, and maybe improved vascular function.
- Further research will strengthen the evidence base to develop health promotion strategies, so that whole grain intake is increased across all population groups.

Appendix 1: The HEALTHGRAIN Integrated Project

The HEALTHGRAIN Integrated Project (www.healthgrain.org) was funded for a five year period beginning mid 2005 as part of the EC 6th Framework food research programme.
It aimed to improve the well-being and to reduce the risk of metabolic syndrome related diseases in the European population by providing a scientific basis for increasing the intake of protective compounds in grains or their fractions as part of processed foods. HEALTHGRAIN was an integrated, multi-disciplinary effort establishing the variation, process-induced changes, and human metabolism of bioactive compounds in the major European bread grains wheat and rye. It revealed physiological mechanisms by which cereal foods may contribute to prevention of metabolic syndrome related diseases. The work included studies on consumer expectations and attitudes, on grain improvement, on technology and processing, and on nutrition. HEALTHGRAIN had a strong dissemination and technology transfer component, which is evident from its large network of about 120 different organisations.

Current product development of healthy cereal grain based products is focussing on whole grain and high bran products. HEALTHGRAIN also paid attention to the concentration, structure and effects relevant for health of bioactive components in sub-fractions of the bran (the inner bran layer, aleurone, and the outer layers, inner- and outer pericarp) and in the inner- and more outer parts of the endosperm. In this way a scientific basis was established for a new generation of healthy products beyond just whole grain and high bran.

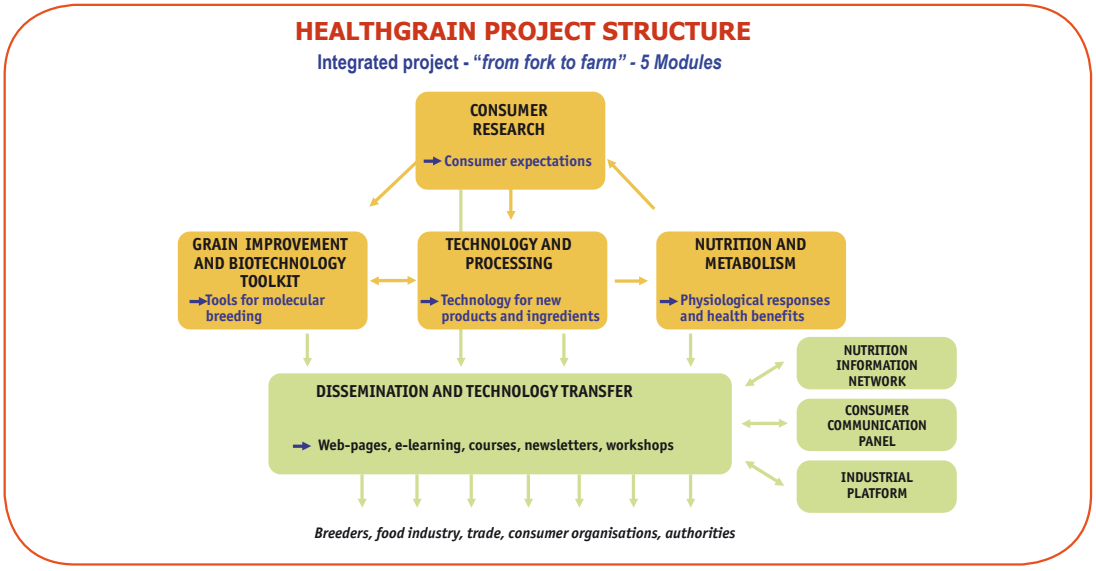

Figure 6: HEALTHGRAIN project structure
Source: HEALTHGRAIN

HEALTHGRAIN includes a comprehensive intellectual property rights, technology transfer and dissemination program with dedicated workshops, contributions to conferences and publications at international and national/regional levels. It is also responsible for an Industrial Platform of companies of different sizes and representing all parts of the cereal production chain as a core target group for technology transfer, dissemination and training. Furthermore, a Nutrition Information Network of nutrition and health professionals throughout Europe has been formed for dissemination, training and exchange of views as well as a highly interactive web page (see www.healthgrain.org), and training possibilities at the PhD and post-doc levels as well as for industrial researchers.

Appendix 2: Biographies of the speakers

Dr Jan Willem van der Kamp
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Jan Willem van der Kamp is at present Senior Officer International Projects in TNO Innovation for Life. After his graduation in chemistry at Utrecht University (1970) and a range of R&D activities in Unilever, he moved in 1985 to TNO as director of cereal and animal nutrition research.
As research manager his scope broadened, firstly in biotechnology and later on in the areas of food safety, nutrition and health and regulatory affairs. He has gained wide international experience, in the management and supervision of European projects, in scientific organisations - e.g. as President of ICC (International Association for Cereal Science and Technology) and International Director of AACC International - in the programming of international conferences all over the world and as invited speaker in such events.
He is serving on the editorial boards of the World Mycotoxin Journal and Quality Assurance and Safety of Crops & Foods.
For his contributions to cereal research he received ICC's Friedrich Schweitzer Award. Van der Kamp's recent activities related to cereal grains and -products include the management of knowledge transfer activities of the HEALTHGRAIN project and the newly established HEALTHGRAIN Forum (see www.healthgrain.org), start-up activities for a major HEALTHGRAIN Holland project and the editing of the recent book "Dietary Fibre - new frontiers for food and health"(Wageningen Academic Publishers).

Professor Chris Seal
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Chris Seal is Professor of Food & Human Nutrition at Newcastle University, where he has been working since 1983. He leads the Food Quality and Health research group in the School of Agriculture, Food & Rural Development (AFRD) and is Co-Director of the University's Human Nutrition Research Centre. He is also Research Director for AFRD.
His research interests include how to encourage, and evaluate the effects of changing diet. A particular focus is promoting the adoption of healthy diets based on increased consumption of whole grain foods, fruits and vegetables. Chris has coordinated a number of intervention studies with volunteers to test the health benefits of eating these foods, including the WHOLEheart, GrainMark (see www.grainmark.org), and VegBP (see www.vegbp.org) studies funded by the Food Standards Agency. Professor Seal works closely with colleagues from the Nafferton Ecological Farming Group investigating the effects of organic, low input and conventional production systems on the nutritional value of foods.
His work is supported by the Food Standards Agency, Research Councils, and industry. Chris sits on many national and international research advisory committees and has recently joined "the breakfast panel" to promote breakfasts as part of a healthy lifestyle. In addition to his research, Chris is heavily involved with teaching; he is Degree Programme Director of the Food & Human Nutrition BSc degree at Newcastle University and has acted as external examiner for several undergraduate and postgraduate nutrition courses across the UK.

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FRANCE - www.mangerbouger.fr/
SWEDEN - www.slv.se/sv/grupp3/Nyheter-och-press/Nyheter1/Nytt-rad-om-fullkorn-ersatter-brodrad/
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ABBREVIATIONS:

AACC: American Association of Cereal Chemists
AFRD: School of Agriculture, Food & Rural Development
ARIC STUDY: Atherosclerosis Risk in Communities study
BMI: Body Mass Index
CI: Confidence Interval
CRP: C-Reactive Protein
CHD: Coronary Heart Disease
CAD: Coronary Artery Disease
CVD: Cardiovascular diseases
DM: Dry Matter
EC: European Commission
FDA: Food and Drug Administration
GI: Glycaemic Index
HOMA-IR: Homeostatic Model Estimated Insulin Resistance
HR: Hazard Ratio
IBS: Irritable Bowel Syndrome
ICC: International Association for Cereal Science and Technology
INRA: French National Institute for Agricultural Research
LDL: Low Density Lipoprotein
MESA STUDY: Multi-Ethnic Study of Atherosclerosis study
NIH-AARP STUDY: National Institute of Health-American Association of Retired Persons study
PAI-1: Plasminogen Activator Inhibitor-1
RR: Relative Risk
SCFA: Short Chain Fatty Acids
T2D: Type 2 Diabetes
TNF-R2: Tumour Necrosis Factor Receptor 2
WG: Whole Grain

NUTRINSIGHT N°2
Whole grain and health: new evidence

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