



Summary of Recent Research On Whole Grains and Health

Compiled by The Whole Grains Council and Oldways

12/15/08 DRAFT FOR WGC MEMBERS ONLY

Since the deliberations of the last Dietary Guidelines Advisory Committee in 2003-2004 and the release of the 2005 Dietary Guidelines for Americans, a great many studies have been published that deepen our knowledge of the health benefits of whole grains.

The Whole Grains Council has compiled a summary of major research since 2004 in the area of whole grains and health, and has made it available to the new Dietary Guidelines Advisory Committee and to anyone else who can benefit from this compilation.

This summary consists of:

- a. Six tables, which depict the research at a glance. The six tables are:
 1. Summary of studies of whole grain intake and morbidity and mortality
 2. Summary of studies of whole grain intake and surrogate markers of disease
 3. Summary of clinical trials of whole grains
 4. Summary of studies comparing dietary patterns with morbidity and mortality
 5. Summary of studies comparing dietary patterns with surrogate markers of disease
 6. Summary of systematic reviews
- b. A list of references, in order of the studies in the six tables.
- c. One-page overviews of 30 of the 45 studies included in the tables – especially the most recent ones in the first three tables – making it possible to review the study in more depth. The overview pages are listed in alphabetical order by the author cited in the tables.

This compilation is designed as a companion to another excellent research review created by the Bell Institute of Health and Nutrition of General Mills, entitled “Whole Grains and Health” Get the Whole Story: A Self-Study Guide for Health Professionals.

The Whole Grains Council would like to thank Heather Katcher for her help in compiling this summary. For more information about this summary, please contact Cynthia Harriman, Director of Food and Nutrition Studies, Oldways and the Whole Grains Council. 617.896.4820 or cynthia@oldwayspt.org. We also invite you to visit www.WholeGrainsCouncil.org.

Table 1: Summary of studies of whole grain intake and morbidity and mortality

Study	Sample Size	Type of Study	Disease Studied	Difference in Risk
Nettleton et al., 2008 ¹	14,153	Prospective	Heart Failure	-7% ^a
Schatzkin et al., 2008 ²	492,321	Prospective	Small intestinal cancer	-41% ^{b,c}
Chan et al., 2007 ³	532 cases, 1701 controls	Case-control	Pancreatic cancer	-40% ^d
DeMunter et al., 2007 ⁴	161,737	Prospective	Type 2 diabetes	-27% to -30% ^b
Djoussé et al., 2007 ⁵	21,376	Prospective	Heart Failure	-29% ^e
Jacobs et al., 2007 ⁶	27,312	Prospective	Noncardiovascular, noncancer death	-34% ^b
Schatzkin et al., 2007 ⁷	489,611	Prospective	Colorectal cancer	-21% ^b
Wang et al., 2007 ⁸	28,926	Prospective	Hypertension	-11% ^b
Merchant et al., 2006 ⁹	34,160	Prospective	Periodontitis	-23% ^b
Sahyoun et al., 2006 ¹⁰	535	Prospective	Death from cardiovascular disease	-52% ^f
"	"	Cross-sectional	Metabolic syndrome	-54% ^f
Van Dam et al., 2006 ¹¹	41,186	Prospective	Type 2 diabetes	-31% ^b
Esmailzadeh et al., 2005 ¹²	827	Cross-sectional	Metabolic syndrome	-32% ^f
"	"	"	Hypertension	-16% ^f
Larsson et al., 2005 ¹³	61,433	Prospective	Colon cancer	-33% ^b
Jensen et al., 2004 ¹⁴	42,850	Prospective	Coronary heart disease	-18% ^b
Slattery et al., 2004 ¹⁵	952 cases, 1205 control	Case-control	Rectal cancer	-31% ^g

^a Per serving of whole grains

^b Highest vs. lowest quintile

^c $P = 0.06$

^d ≥ 2 servings/day vs. < 1 serving/day

^e ≥ 7 servings cereal/week vs. 0 servings

^f Highest vs. lowest quartile

^g Controls vs. cases

Table 2: Summary of studies of whole grain intake and surrogate markers of disease

Study	Sample Size	Type of Study	Endpoint(s)	Difference in Risk
Good et al., 2008 ¹⁶	2,092	Cross-sectional	BMI, waist circumference	↓
Lutsey et al., 2007 ¹⁷	5,496	Cross-sectional	BMI, homocysteine, insulin, insulin resistance (HOMA)	↓
Mellen et al., 2007 ¹⁸	1,178	Cross-sectional	Common carotid artery intima media thickness	↓
Newby et al., 2007 ¹⁹	1,516	Cross-sectional	BMI, total and LDL-C, 2-hour glucose	↓
Rose et al., 2007 ²⁰	159	Cross-sectional	BMI	↓
Van de Vijver et al., 2007 ²¹	4,237	Cross-sectional	BMI	↓
Jensen et al., 2006 ²²	938	Cross-sectional	Insulin, homocysteine, total cholesterol, c-peptide	↓
Qi et al., 2006 ²³	902	Cross-sectional	CRP, TNF-R2	↓
Sahyoun et al., 2006 ¹⁰	535	Cross-sectional	BMI, glucose	↓
Bazzano et al., 2005 ²⁴	17,881	Prospective	Body weight and weight gain	↓
Erkkilä et al., 2005 ²⁵	229	Prospective	Change in minimum coronary artery diameter	↓
Esmailzadeh et al., 2005 ^{12, 26}	827	Cross-sectional	Triglycerides, 2-hour glucose, diastolic BP, waist circumference	↓
Koh-Banerjee et al., 2004 ²⁷	27,082	Prospective	Weight gain	↓

BMI = body mass index, HOMA = homeostasis model assessment, LDL-C = low-density-lipoprotein cholesterol, CRP = c-reactive protein, TNF-R2 = tumor necrosis factor-alpha receptor-2, BP = blood pressure

Table 3: Summary of clinical trials of whole grains

Study	Sample Size	Study Type and Duration	Treatment	Results
Alminger et al., 2008 ²⁸	13	Randomized block design, 2-hour postprandial	Glucose solution vs. tempe fermented whole-grain barley and oat	↓ glucose, ↓ insulin
Costable et al., 2008 ²⁹	31	Crossover, 3 weeks per diet	Wheat bran vs. whole grain breakfast cereal	↑ bifidobacteria, ↑ lactobacilli
Hsu et al., 2008 ³⁰	11	Crossover, 6 weeks per diet	White rice vs. pre-germinated brown rice	↓ glucose ↓ total cholesterol ↓ triglycerides, ↓ fructosamine
Katcher et al., 2008 ³¹	50	Parallel-arm, 12 weeks	Reduced-calorie diet with refined grains vs. reduced-calorie diet with whole grains	↓ CRP, ↓ Abdominal fat
Lammert et al., 2008 ³²	14	Prospective, 2 days, 4-week follow-up	Standard diet vs. standard diet + oatmeal	↓ glucose, ↓ insulin, ↓ leptin, ↓ adiponectin
Andersson et al., 2007 ³³	30	Crossover, 6 weeks per diet	Habitual diet with refined grains vs. whole grains	No change in IL-6, CRP, BP, insulin sensitivity, or lipids.
Rave et al., 2007 ³⁴	31	Crossover, 4 weeks per diet	Hypocaloric diet containing meal replacements (Slim Fast) vs. whole grain double-fermented wheat	↓ insulin and insulin resistance after adjusting for weight loss
Behall et al., 2006 ³⁵	16	Latin square design, 5 weeks per diet	Step 1 diet vs. Step 1 diet with 20% of energy replaced with brown rice, whole wheat, and/or barley	↓ Systolic and diastolic BP
Panlasigui et al., 2006 ³⁶	19	Crossover, 3-hour postprandial	White rice vs. brown rice	↓ glucose
Karmally et al., 2005 ³⁷	152	Parallel-arm, 6 weeks	Corn vs. oat cereal	↓ total and LDL-C
Behall et al., 2004 ³⁸	18	Latin square design, 5 weeks per diet	Step 1 diet vs. Step 1 diet with 20% of energy replaced with brown rice, whole wheat, and/or barley	↓ total and LDL-C, ↑ HDL-C

CRP = c-reactive protein, IL-6 = interleukin-6, BP = blood pressure , LDL-C = low-density-lipoprotein cholesterol, HDL-C = high-density-lipoprotein cholesterol

Table 4: Summary of studies comparing dietary patterns with morbidity and mortality

The studies in this table include whole grains as part of a dietary pattern. While all show positive health benefits for diets that include whole grains, the effect may be due to foods other than whole grains. For each study, all patterns are listed, but only those results pertaining to whole grain are included.

Study	Sample Size	Dietary Patterns Studied	Disease Studied	Difference in Risk
Brunner et al., 2008 ³⁹	7,731	<ol style="list-style-type: none"> 1. Unhealthy (white bread, processed meat, fries, full-cream milk) 2. Sweet (white bread, biscuits, cakes, processed meat, high-fat dairy products) 3. Mediterranean-like (fruit, vegetables, rice, pasta, wine) 4. Healthy (fruit, vegetables, whole-meal bread, low-fat dairy, little alcohol) 	<p>Coronary death or nonfatal myocardial infarction</p> <p>Incident diabetes</p> <p>All-cause mortality</p>	<p>-29% for unhealthy vs. healthy dietary pattern</p> <p>-26% for unhealthy vs. healthy dietary pattern</p> <p>No association</p>
Heidemann et al., 2008 ⁴⁰	72,113	<ol style="list-style-type: none"> 1. Prudent (higher intakes of vegetables, fruit, legumes, fish, poultry, and whole grains) 2. Western (higher intakes of red meat, processed meat, refined grains, French fries, and sweets/desserts) 	<p>Cardiovascular mortality</p> <p>Cancer mortality</p> <p>All-cause mortality</p>	<p>-28% for highest vs. lowest quintile of prudent diet</p> <p>Not significant for highest vs. lowest quintile of prudent diet</p> <p>-17% for highest vs. lowest quintile of prudent diet</p>
Nettleton et al., 2008 ⁴¹	5,011	<ol style="list-style-type: none"> 1. Fats and processed meats 2. Vegetables and fish 3. Beans tomatoes, and refined grains 4. Whole grains and fruit (whole grains, fruit, nuts/seeds, green leafy vegetables, low-fat dairy) 5. Low-risk food pattern – sum intake of 10 food groups 	<p>Type 2 diabetes</p>	<p>-15% for highest vs. lowest quintile of whole grains and fruit dietary pattern</p> <p>-13% for highest vs. lowest quintile of low-risk food pattern</p>

Table 5: Summary of studies comparing dietary patterns with surrogate markers of disease

The studies in this table include whole grains as part of a dietary pattern. While all show positive health benefits for diets that include whole grains, the effect may be due to foods other than whole grains. For each study, all patterns are listed, but only those results pertaining to whole grain are included.

Study	Sample Size	Dietary Pattern Studied	Biomarkers Assessed	Difference in Risk
Nettleton et al., 2008 ⁴²	5,089	1. Comprehensive Healthy Dietary Pattern – sum of weighted categorical ranks of 36 food groups 2. Simplified Healthy Dietary Pattern – sum of weighted categorical ranks of 6 food groups	Markers of subclinical atherosclerosis, inflammation, renal disease, lipids, vascular compliance, glucose, and insulin.	↓ urinary albumin:creatinine ratio, common carotid artery intima-media thickness, triglycerides, insulin, CRP, IL-6, and homocysteine for highest vs. lowest quintiles of both patterns
Nettleton et al., 2006 ⁴³	5,089	1. Fats and processed meats 2. Vegetables and fish 3. Beans, tomatoes, and refined grains 4. Whole grains and fruit (whole-grain bread, rice, and pasta, fruit, seeds, nuts, peanut butter, green leafy vegetables, and low-fat milk)	CRP, IL-6, homocysteine, sICAM-1, and soluble E-selectin.	↓ CRP, IL-6, homocysteine and sICAM-1 with the whole grains and fruit dietary pattern
Lopez-Garcia, 2004 ⁴⁴	732	1. Prudent (higher intake of vegetables, fruit, legumes, fish, poultry, and whole grains) 2. Western (higher intakes of red and processed meats, sweets, desserts, French fries, and refined grains).	C-reactive protein, E-selectin, IL-6, sICAM-1, and sVCAM-1.	↓ CRP and E-selectin with the prudent diet

CRP = c-reactive protein, IL-6 = interleukin-6, sICAM-1 = soluble intercellular adhesion molecule-1

Table 6: Summary of systematic reviews

These two systematic reviews document positive associations between whole grains and health. We have listed them separately to make clear that they do not represent primary research.

Study	Sample Size	Endpoint Assessed	Results
Harland et al., 2008 ⁴⁵	15 observational studies (n = 119,829)	Body weight	↓ BMI (-0.6 kg/m ²), waist circumference (-2.7 cm), and waist:hip ratio (-0.023) with the highest vs. lowest intake of whole grains
Priebe et al., et al., 2008 ⁴⁶	11 prospective cohort studies and 1 randomized control trial	Type 2 diabetes	The prospective studies consistently showed a reduced risk (27% to 30%) for developing type 2 diabetes with a high intake of whole grain foods. The randomized trial reported a slight improvement in insulin sensitivity.

BMI = body mass index

REFERENCES TO SUMMARY TABLES

Those marked with an asterisk (*) also have an overview page, following.

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Alminger et al., *Eur J Nutr.*, 47: 294-300, 2008.

Whole-grain cereal products based on a high-fibre barley or oat genotype lower post-prandial glucose and insulin responses in healthy humans.

Introduction:

- The intact botanical structure of cereal grains can have a critical effect on glucose and insulin responses.
- Factors that influence the post-prandial glucose response to cereal grains include the amount of beta-glucan, the botanical origin, the amylose:amylopectin ratio, and the amount of food processing.
- The aim of this study was to evaluate the impact of fermented whole grain cereal kernels with a high content of amylose (40%) and/or beta-glucan (4.6%) on postprandial glucose and insulin responses in healthy adults.

Methods:

- Thirteen healthy volunteers age 20-75 years were given 25 g available carbohydrate portions of: (1) glucose solution, (2) tempe fermented whole-grain barley, or (3) tempe fermented whole grain oat in a randomized, block design.
- Blood samples were collected directly before the meal (fasting), and 15, 30, 45, 60, 90, and 120 minutes after the start of the meal.
- The glycemic index and insulin index of the meals were calculated for each subject according to FAO/WHO standards.

Results:

- Peak glucose was lowest after the high-amylose/high beta -glucan barley tempe meal, while the peak insulin response was lowest after the high beta -glucan oat tempe meal.
- The mean blood glucose and insulin responses for both the barley and the oat tempe meals were significantly lower than for the reference glucose load during the first 60 minutes after the meal ($P < 0.005$).
- The calculated glycemic indices for the barley and oat tempe were 30 and 63, respectively.

Discussion:

- The present study shows that consumption of fermented whole-grain barley or oat with a high amylose and/or beta -glucan content can reduce the glucose and insulin responses of healthy individuals.
- The physical form and high fiber content of fermented whole-grains, as well as the presence of organic acids (such as lactic acid), appear to work synergistically to affect digestion and absorption of carbohydrates.
- The results suggest that cereal products that beneficially influence postprandial glucose and insulin responses can be achieved by fermentation and by using grains with an increased amylose and/or beta -glucan content.

Andersson et al., *J Nutr.*, 137: 1401-1407, 2007.

Whole grain foods do not affect insulin sensitivity or markers of lipid peroxidation and inflammation in healthy, moderately overweight subjects.

Introduction:

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- Recent studies have linked whole grain foods to a reduced risk of type 2 diabetes and metabolic syndrome.
- Despite indications that whole grain foods may beneficially influence glucose and lipid metabolism, knowledge of the biological mechanisms that contribute to the health effects of whole grains remains weak.
- The aim of this study was to evaluate the health effects of a diet rich in whole grains, compared with a diet containing the same amount of refined grains.

Methods:

- Thirty-four participants (22F, 8M) were given either whole-grain or refined grain products (3 bread slices, 2 crisp bread slices, 1 portion muesli, and 1 portion pasta) to include in their habitual daily diet for two 6-week periods in a randomized, crossover design.
- The whole-grain products contained a minimum of 50% whole grain per dry substance.
- Clinical and laboratory tests were conducted before and after both 6-week test periods. A 3-day diet record was completed before and during each test period to assess nutrient intake.

Results:

- The reported intakes of dietary fiber, alpha-tocopherol, phosphorus, iron, magnesium, and zinc were, as expected, higher during the whole grain diet period than during the refined grain period.
- Otherwise, nutrient intakes did not differ between the two test periods, with the exception of slightly higher intake of calcium during the refined-grain diet period.
- The diet treatments did not affect peripheral insulin sensitivity, blood glucose, serum insulin, lipids, free fatty acids, systolic or diastolic blood pressure, or markers of lipid peroxidation, antioxidative activity, markers of inflammation, or fibrinolytic activity.

Discussion:

- Insulin resistance, lipid peroxidation, and inflammation are presumed to be central factors involved in the etiology of CHD and type 2 diabetes; however no significant effect of whole grain intake on these variables, or any other variables measured, was observed.
- The whole grain products were mostly based on milled flour with small particle size in the form of bread or pasta, which may have reduced the effects on glucose and insulin.
- More extensive and controlled dietary studies on different groups of subjects, using different forms of whole grain foods are needed.

Behall et al., *J Am Diet Assoc.*, 106: 1445-1449, 2006

Whole grain diets reduce blood pressure in mildly hypercholesterolemic men and women.

Introduction:

- Several epidemiologic studies reported that diets rich in whole grains may protect against hypertension, stroke, cardiovascular disease, and type 2 diabetes.
- Clinical studies testing the effects of whole grains high in soluble fiber have used oats or psyllium, even though barley contains as much or more soluble fiber.
- This study examines the effect of a controlled whole grain diet containing brown rice/whole wheat and/or barley on blood pressure.

Methods:

- Sixteen participants consumed a controlled step 1 diet for 2 weeks, then 20% of energy was replaced with (1) whole wheat/brown rice, (2) barley, or (3) half whole wheat-brown rice/half barley for five weeks each.
- To qualify, participants had to have a systolic blood pressure (BP) < 140 mmHg, diastolic BP < 90 mmHg and cholesterol levels between 200-240 mg/dL.
- Blood pressure was determined weekly and weight daily before breakfast.

Results:

- Consumption of all whole grain diets resulted in decreases in blood pressure (systolic BP, $P < 0.02$; diastolic BP, $P < 0.009$)
- Systolic blood pressure decreased 2.2 mmHg during the Step 1 diet (n.s.) and an additional 1.4 to 6.7 mmHg on the whole grain diets.
- Diastolic blood pressure decreased 2 mmHg (n.s.) during the Step 1 diet and an additional 2.9 to 3.7 mmHg on the whole grain diets.

Discussion:

- Replacing white rice with brown rice, white bread with whole grain bread, and low-fiber cereals with barley or whole wheat cereals lowers systolic and diastolic blood pressure in mildly hypercholesterolemic men and women.
- Because hypertension is so prevalent in the United States (> 50 million people) this modest change in an already healthful diet (i.e. Step 1) could have beneficial effects on blood pressure.

Behall et al., *J Am Coll Nutr.*, 23: 55-62, 2004.

Lipids significantly reduced by diets containing barley in moderately hypercholesterolemic men.

Introduction:

- Whole grains that are high in soluble fiber, such as oats, are effective in decreasing blood cholesterol levels.
- The majority of clinical trials on soluble fiber have used oats and psyllium, even though barley contains as much or more soluble fiber.
- The purpose of the study was to determine whether using barley as a soluble fiber source beneficially changes cardiovascular risk factors.

Methods:

- Eighteen moderately hypercholesterolemic men consumed a controlled Step 1 diet (35% fat, 55% carbohydrate, 15% protein, < 300 mg cholesterol) for 2 weeks followed by three controlled diets for 5 weeks in a Latin square design.
- The three controlled diets had ~20% of energy replaced with barley containing < 0.4 g, 3 g or 6 g soluble fiber/2800 kcal.

Results:

- Total cholesterol concentrations were significantly lower (14%, 17%, and 20%, respectively, $P < 0.001$) after the low-, medium-, and high-soluble fiber barley diets compared with baseline.
- LDL-cholesterol concentrations were also significantly lower (17%, 17%, and 24%, respectively, $P < 0.001$) after consuming the low-, medium-, and high-soluble fiber barley diets compared baseline.
- The ratio of total:HDL cholesterol was significantly lower after the three barley diets compared with baseline. The ratio was lowest after the high-soluble fiber barley diet.
- Triglyceride concentrations were 6%, 10% and 16% lower after the low- medium- and high-soluble fiber compared with baseline.

Discussion:

- Adding barley to the diet lowered total and LDL-cholesterol and triglyceride concentrations and the ratio of total to HDL-cholesterol.
- The highest soluble fiber intake had the greatest effect on total and LDL-cholesterol
- These results indicate that adding barley to a healthy diet can reduce cardiovascular disease risk.

Chan et al., *Am J Epidemiology*, 166:1174-1185, 2007.

Whole grains and risk of pancreatic cancer in a large population-based case-control study in the San Francisco Bay Area, California.

Introduction:

- Pancreatic cancer is the most fatal cancer in the United States.
- Previous studies have suggested that diets high in fiber, low in glycemic load, or high in high grains may confer benefits.
- To further explore the relations, the intake of grains and cereals within a large population-based case-control study of pancreatic cancer was examined.

Methods:

- Food intake of 532 men with adenocarcinoma of the exocrine pancreas was compared with the food intake of 1,701 age and sex matched controls.
- Participants were asked to report their frequency of intake of individual food items 1 year before cancer diagnosis (for cases) or 1 year before interview (for controls)
- Consumption of individual grain items and overall categories of whole grain, refined grains, mixed grains, and sweetened refined grains was examined.

Results:

- There was an inverse trend for total servings of whole grain products and pancreatic cancer risk in multivariate analyses adjusted for age, sex, total energy, BMI, race, education, smoking, history of diabetes, and other food groups.
- The OR was 0.60 (95% CI 0.31 to 1.2, P = 0.04) for ≥ 2 servings/day vs. < 1 serving/day.
- Total refined grains, sweetened refined grains, and mixed-grain products were not associated with risk of pancreatic cancer.
- Both crude and dietary fiber were associated with a 30-35% reduction in pancreatic cancer risk when the fourth quartile was compared with the first quartile (P = 0.009 and P = 0.02, respectively).

Discussion:

- These data provide support for the hypothesis that whole-grain foods and fiber, but not refined grains, are associated with reduced risk of pancreatic cancer.
- Plausible biologic mechanisms for the reduction in pancreatic cancer risk are via decreased levels insulin, cholesterol, and/or inflammation.

Costabile et al., *Br J Nutr.*, 99: 110-120, 2008.

Whole-grain wheat breakfast cereal has a prebiotic effect on the human gut microbiota: a double-blind, placebo-controlled study.

Introduction:

- One proposed mechanism for the protective effect of whole grains on risk of chronic diseases is their impact on gut microbiota.
- Fermentation of soluble fibers in whole grains may have a prebiotic effect by changing the composition and/or activity in the gastrointestinal microbiota.
- Bacteria that are beneficial for human health include *Bifidobacterium* and *Lactobacillus*.
- Currently no information exists on the prebiotic potential of whole grain wheat.

Methods:

- This double blind crossover study compared the efficacy of whole grain wheat with wheat bran to modulate the gastrointestinal microbiota.
- Thirty-one healthy subjects were randomized to either consume a whole grain wheat breakfast cereal (48 g/day) or wheat bran breakfast cereal (48 g/day) daily for 3 weeks. After a 2-week washout period, volunteers then consumed the other type of cereal for another 3 weeks.

Results:

- Numbers of fecal bifidobacteria and lactobacilli were significantly higher after consuming the whole grain cereal compared with the wheat bran cereal (9.3 ± 0.4 vs. 8.8 ± 0.4 \log_{10} cells/g feces, $P < 0.001$ and 8.7 ± 0.2 vs. 8.4 ± 0.2 \log_{10} cells/g feces, $P < 0.05$, respectively).
- Consuming both cereals resulted in a 2.5 fold increase in ferulic acid (an antioxidant in plant foods) concentrations in the blood compared with baseline.

Discussion:

- This is the first report that whole grains have a prebiotic effect, which may be protective against certain cancers and cardiovascular disease.
- Ingesting a whole grain breakfast cereal resulted in higher numbers of bifidobacteria and lactobacilli
- Antioxidants from whole grains, including ferulic acid, may also decrease oxidative damage and contribute to cardiovascular disease prevention.

De Munter et al., *PLoS Medicine*, 4: 1385-1395, 2007.

Whole grain, bran, and germ intake and risk of type 2 diabetes: A prospective cohort study and systematic review.

Introduction:

- Evidence is accumulating that consumption of whole grains reduces risk of chronic diseases including certain types of cancer, cardiovascular disease, and type 2 diabetes.
- In most previous studies, foods are defined as whole grains if at least 25% is whole grain by weight, which is an arbitrary cut point.
- The current study uses a recently developed food composition database containing the grams of whole grains per food to estimate each participant's whole grain intake in grams per day.

Methods:

- Twelve to eighteen year follow up of 161,737 women in the Nurses' Health Studies (NHS) I and II without history of diabetes, cardiovascular disease, or cancer at baseline.
- Dietary information was collected using a semiquantitative food frequency questionnaire that asked about average food intake during the past year.

Results

- Whole grain intake was inversely associated with risk of type 2 diabetes after multivariate adjustment.
- The relative risk of developing type 2 diabetes for the highest vs. lowest quintile of whole grain intake was 0.63 (95% CI 0.57-0.69) for NHS I and 0.68 (95% CI 0.57-0.81) for NHS II.
- After additional adjustment for BMI, the relative risk of developing type 2 diabetes was 0.70 (95% CI 0.62-0.79) for NHS I and 0.83 (95% CI 0.70-0.98) for NHS II.
- Each 40 g increment in whole grain intake was associated with a relative risk of type 2 diabetes of 0.54 (95% CI 0.48-0.61) for NHS I and 0.64 (95% CI 0.54-0.76) for NHS II.

Discussion:

- There was a substantial inverse association between whole grain intake and risk of type 2 diabetes.
- This finding is consistent with cohort studies that have reported a direct association between whole grain consumption and insulin sensitivity.
- Adjusting for BMI weakened the observed association between whole grain intake and risk of type 2 diabetes, suggesting that the relationship between whole grain intake and diabetes risk may be partly mediated by effects on body weight.

Introduction:

- While advanced age, hypertension, diabetes, obesity, and myocardial infarction are recognized as predictors of heart failure, limited data are available on the effects of modifiable lifestyle factors on the risk of heart failure.
- Studies have suggested that higher consumption of whole grain products may confer a lower risk of hypertension, coronary heart disease, hypercholesterolemia, and mortality.
- It is not known whether a higher consumption of breakfast cereals is associated with a lower risk of heart failure.

Methods:

- The relationship between breakfast cereal intake and heart failure was prospectively examined in a cohort of male physicians (n = 21,376) in the Physicians' Health Study.
- Incident heart failure over 19.6 years of follow-up was ascertained through annual follow-up questionnaires and validated using Framingham criteria.
- Cereal consumption was estimated using a semiquantitative food frequency questionnaire.

Results:

- For average weekly cereal consumption of 0 servings, 1 or fewer, 2 to 6, and 7 or more servings, hazard ratios (95% CI) for heart failure were 1.0, 0.92 (0.78-1.09), 0.79 (0.67-0.93), and 0.71 (0.60-0.85), respectively, after multivariate adjustment.
- The association was limited to the intake of whole grain cereals (P < 0.001) but not refined grain cereals (P = 0.70).

Discussion:

- A higher consumption of breakfast cereals was associated with a lower risk of heart failure among US male physicians.
- This association was mainly present in individuals consuming whole grain but not refined grain breakfast cereals.
- The reduced risk of heart failure is likely mediated through beneficial effects of whole grains on risk factors of heart failure such as hypertension, myocardial infarction, diabetes mellitus, and obesity.

Erkkilä et al., *Am Heart J.*, 150: 94-101, 2005.

Cereal fiber and whole-grain intake are associated with reduced progression of coronary-artery atherosclerosis in postmenopausal women with coronary artery disease.

Introduction:

- Numerous studies indicate that increased dietary fiber and whole grain intake is associated with lower rates of coronary artery disease morbidity and mortality.
- The effect may be due to favorable effects of dietary fibers on lipids, glucose and insulin metabolism, blood pressure, hemostatic factors, and inflammation.
- However, no study to date has examined the association between dietary fiber and whole grain intake and progression of coronary atherosclerosis in women.

Methods:

- Angiographic assessments were made at baseline and after 3 years in a cohort of postmenopausal women with coronary artery disease (CAD) in the Estrogen Replacement and Atherosclerosis Trial (n = 229).
- The relationship between baseline total, cereal, fruit, and vegetable fiber intake and changes in coronary artery diameter and appearance of new lesions was assessed.
- Usual dietary intake was assessed at baseline with a validated semiquantitative food frequency questionnaire.

Results:

- Changes in minimum coronary artery diameter (MCAD) were significantly smaller in women who consumed >6 servings of whole grains/week compared with women who consumed <6 servings/week after multivariate adjustment (P=0.04).
- Changes in mean percent stenosis tended to be smaller in women who consumed >6 servings of whole grains/week compared with women who consumed <6 servings/week after multivariate adjustment (P = 0.07)
- A higher than median intake of cereal fiber but not fiber from fruit and vegetable sources was associated with a smaller change in MCAD compared with a lower intake (P = 0.05)

Discussion:

- There was a modest reduction in atherosclerosis progression in postmenopausal women with CAD who consumed >6 servings of whole grains per week compared with those with lower intakes.
- These findings are in agreement with other studies that have shown reduced CAD risk with a high intake of cereal fiber but not with fruit and vegetable fiber.
- The results support dietary recommendations for increased consumption of fiber-rich foods, especially whole-grain products, among postmenopausal women.

Good et al., *J Am Coll Nutr.*, 27: 80-87, 2007.

Whole grain consumption and body mass index in adult women: an analysis of NHANES 1999-2000 and the USDA pyramid servings database.

Introduction:

- The worldwide obesity epidemic has led to increased interest in identifying lifestyle factors that promote a healthy weight.
- Previous epidemiological studies have reported an inverse relationship between consumption of whole grain foods and body mass index (BMI).
- However the majority of intake data available do not contain quantified whole grain intake measures.

Methods:

- Dietary intake data (24-hour recalls) from the National Health and Nutrition Examination Survey (NHANES) 1999-2000 were analyzed using the USDA Pyramid Servings Database.
- Women ≥ 19 years ($n = 2,092$) were classified into one of three groups based on their average whole grain intake (0 servings, between 0 and 1 servings, or ≥ 1 servings).
- Within these classifications, mean BMI, waist circumference, and percent overweight/obese were determined.

Results:

- Women who consumed at least one serving of whole grains/day had a significantly lower BMI and waist circumference than women with no whole grain consumption after multivariate adjustment ($P < 0.05$).
- The odds ratio for having a BMI ≥ 25 after multivariate adjustment was 1.47 (95% CI 1.12-1.94, $P = 0.13$) for women consuming no whole grains compared to those consuming at least one serving.

Discussion:

- This nationally representative, cross-sectional sample of women indicates inverse associations between whole grain intake and measures of overweight.
- The influence of whole grains on body weight regulation may be partially mediated by the effects of dietary fiber.
- These findings are consistent with prior studies, suggesting whole grains may contribute to maintenance of a healthy weight.

Hsu et al, *J Nutr Sci Vitaminol.*, 54: 163-168, 2008.

Effects of pre-germinated brown rice on blood glucose and lipid levels in free-living patients with impaired fasting glucose or type 2 diabetes.

Introduction:

- Large-scale prospective cohort studies have shown that maintaining blood glucose levels is important to prevent diabetes and its related complications.
- Previous studies showed that pre-germinated brown rice was better than white rice at preventing the rapid increase in postprandial blood glucose concentrations.
- Pre-germinated brown rice is richer in vitamins, minerals, and dietary fiber than white rice. It is made by soaking brown rice kernels in water to germinate.
- The present study aimed to determine the clinical usefulness of a diet including pre-germinated brown rice in patients with type 2 diabetes.

Methods:

- Eleven free-living subjects (6M, 5W) were randomly allocated to two 6-week experimental periods of either white rice or pre-germinated brown rice in a crossover design.
- Cooked rice packages were given to each subject and they were instructed to eat 180 g of the cooked rice three times daily. Subjects were instructed to maintain similar activities of daily living.
- Outcomes measured included weight, blood pressure, dietary intake, plasma glucose, serum fructosamine, insulin, and total, LDL, and HDL cholesterol.

Results:

- No significant differences in dietary consumption were identified except the dietary fiber content of Group 2 was significantly higher after the pre-germinated brown rice diet ($P < 0.05$).
- With the pre-germinated brown rice diet, fasting blood glucose decreased significantly from 153 ± 9 mg/dL to 135 ± 7 mg/dL, but no marked changes were observed with the white rice diet ($P < 0.01$ between groups).
- Levels of fructosamine, total cholesterol, and triglycerides significantly decreased after the pre-germinated brown rice diet ($P < 0.05$).

Discussion:

- These results show that unlike white rice, consuming pre-germinated brown rice as a staple food significantly decreases fasting blood glucose and fructosamine in patients with type 2 diabetes.
- The reason for the improved markers of glycemic control with the pre-germinated brown rice is suggested to be that the physical shape of the grains delays digestion and absorption of carbohydrates.
- While the present study was only a small-scale study lasting 6 weeks, the results suggest that consumption of pre-germinated brown rice as a staple food in patients with type 2 diabetes is useful in improving blood glucose and lipid levels.

Jacobs et al., *Am J Clin Nutr.*, 85: 1606-1614.

Whole-grain consumption is associated with a reduced risk of noncardiovascular, noncancer death attributed to inflammatory diseases in the Iowa Women's Health Study.

Introduction:

- It was previously reported that whole-grain intake in post-menopausal women was associated with a 15% reduction in total mortality.
- The reduction in mortality was attributed largely to cardiovascular disease, but there was little investigation into what other diseases contributed.
- Because whole grain intake is inversely related to inflammatory markers in observational studies, it was hypothesized that intake of whole grains reduces the risk of diseases in which inflammation or oxidative stress is a main contributing factor.

Methods:

- Postmenopausal women (n = 27,312) age 55-69 without cardiovascular disease, cancer, diabetes, colitis, or liver cirrhosis at baseline were followed for 17 years.
- Noncardiovascular, noncancer inflammatory diseases were considered to be those that had an inflammatory, oxidative stress, or infectious component as the predominant pathophysiology.
- Dietary intake was assessed using a 127-item food frequency questionnaire.

Results:

- Of 27,312 participants, 5,552 had died after 17 years of follow-up; the deaths of 1,071 of these participants were attributed to inflammatory causes.
- Noncardiovascular, noncancer inflammatory death was inversely related to whole grain intake after multivariate adjustment.
- Compared with women who rarely or never ate whole grains, there was a 21-36% reduced risk for those who consumed ≥ 4 servings per week ($P = 0.008$).
- The strongest and statistically significant associations were for respiratory system disorders, especially noninfectious ones.
- There was a 15% greater increase in risk for participants in the highest quintile of refined grain intake compared with the lowest quintile ($P = 0.04$).

Discussion:

- The reduction in inflammatory mortality associated with habitual whole-grain intake was larger than that previously reported for coronary heart disease and diabetes.
- Inflammatory disease as an underlying cause included most infectious and various chronic degenerative diseases including rheumatoid arthritis, gout, asthma, type 1 and 2 diabetes, emphysema, and obstructive pulmonary disease.
- Many components in whole grains may act as antioxidants and thereby reduce or prevent the damaging effects of chronic inflammation.

Jensen et al., *Am J Clin Nutr.*, 83: 275-283, 2006.

Whole grains, bran, and germ in relation to homocysteine and markers of glycemic control, lipids, and inflammation.

Introduction:

- Consumption of whole grains was inversely associated with mortality from and incidence of diabetes and ischemic heart disease in several prospective studies.
- The observed lower risk of diabetes and ischemic heart disease may be mediated through effects on glycemic control, plasma lipids, or inflammation.

Methods

- The associations between daily intake of whole grains and plasma concentrations of homocysteine, markers of glycemic control, lipids, and inflammation were examined in healthy subsamples of the Health Professionals Follow-up Study (HPFS) and the Nurses' Health Study (NHS) II (n = 938).
- Dietary information was collected with a validated semiquantitative food frequency questionnaire
- A food composition database of the grams of whole grains per food was used to estimate each participant's whole grain intake in grams per day.

Results

- Mean concentrations of insulin, C-peptide and leptin were inversely related to intake of whole grains. Participants in the highest vs. lowest quintile of whole grain intake had 11-14% lower concentrations of insulin (P=0.13), C-peptide (P=0.03) and leptin (P=0.03) after multivariate adjustment.
- A strong inverse association was observed between homocysteine and whole grain intake after multivariate adjustment. The mean concentration of homocysteine was 17% lower in participants in the highest quintile of whole grain intake compared with participants in the lowest quintile.
- Modestly inverse, but not statistically significant associations were observed between whole-grain intake and concentrations of C-reactive protein and IL-6.
- Inverse associations were observed between whole grain intake and total cholesterol (P= 0.02), HDL-cholesterol (P=0.05), and LDL cholesterol (P=0.10).

Discussion

- Intake of whole grains was inversely related to makers of diabetes and ischemic heart disease.
- The results of this analysis are consistent with those of other cross-sectional studies of whole grain foods and markers of insulin sensitivity and lipid status.

Karmally et al., *J Am Diet Assoc.*, 105: 967-970, 2005.

Cholesterol-lowering benefits of oat-containing cereal in Hispanic Americans.

Introduction:

- Hispanic Americans have higher risk scores for coronary heart disease than non-Hispanic whites.
- Foods containing soluble fiber have been shown to effectively lower total and LDL cholesterol, and may be beneficial in this population.
- However, studies of the efficacy of these foods in managing hypercholesterolemia in Hispanics are limited.

Methods:

- One-hundred fifty-two Hispanic Americans, age 30-70, with baseline LDL-C levels between 120 and 190 mg/dL and triglycerides < 400 mg/dL were included.
- After eating a National Cholesterol Education Program Step 1 diet for 5 weeks, participants were randomly assigned to consume 90 g of corn (no brand specified) or oat (Cheerios) cereal per day for the next 6 weeks.
- Compliance was assessed by 3-day food records, unannounced telephone calls for 24-hour recalls, daily cereal intake records, participant interviews, and the number of unopened and empty cereal packets at each visit.

Results:

- Compliance was 100% in the corn cereal group and 99% in the oat cereal group. Body weight was stable during the study.
- Adding the oat cereal resulted in significant reductions in total cholesterol (-10.9 mg/dL; -4.5%) and LDL-C (-9.4 mg/dL; -5.3%).
- There were no significant changes in total cholesterol (1.2 mg/dL) and LDL-C (1.2 mg/dL) in the corn cereal group.
- There were no significant effects of either cereal on plasma levels of HDL-C, triglycerides, or apoA-1.

Discussion:

- The ready-to-eat oat cereal was efficacious in lowering cholesterol levels in men and women with mild to moderate hypercholesterolemia.
- These data add support to results of previous randomized, controlled trials reporting a cholesterol-lowering effect of oats and soluble fiber.
- An oat cereal can be used as a therapeutic option together with a cholesterol-lowering diet for treatment of mild to moderate hypercholesterolemia.

Katcher et al., *Am J Clin Nutr.*, 87: 79-90, 2008.

The effects of a whole grain-enriched hypocaloric diet on cardiovascular risk factors in men and women with metabolic syndrome.

Introduction:

- Whole grain foods are associated with a lower body mass index and lower cardiovascular disease (CVD) risk in observational studies.
- However, few clinical trials have tested whether incorporating whole grains into a hypocaloric diet increases weight loss and improves CVD risk factors.

Methods:

- Fifty obese adults (25M, 25F) with metabolic syndrome were randomly assigned to receive dietary advice to either avoid whole grain foods or have all of their grain servings from whole grains for 12 weeks
- All participants were given the same dietary advice in all other respects for weight loss.
- A fasting blood draw, 2-hour oral glucose tolerance test (OGTT), dual energy x-ray absorptiometry (DXA) scan, and biometric measurements were done at baseline and at the end of the 12-week study period.

Results:

- Body weight, waist circumference, and percentage body fat decreased significantly in both groups over the study period ($P < 0.001$)
- C-reactive protein decreased 38% in the whole grain group, but was unchanged in the refined grain group ($P = 0.01$ between groups).
- There was a significantly greater decrease in percentage body fat in the abdominal region in participants in the whole grain group than the refined grain group ($-2.2 \pm 2.2\%$ vs. $-0.9 \pm 1.8\%$, $P = 0.03$).
- There was a 10% decrease in the area under the curve for insulin after the OGTT in the whole grain group, compared with a 2% decrease in the refined grain group.

Discussion:

- Despite similar weight loss in the whole grain and refined grain groups, there was a significantly greater reduction in CRP and percent body fat in the abdomen in the whole grain group compared with the refined grain group.
- The magnitude of reduction in CRP concentrations in the whole grain group was similar to that seen with statins.
- Since this study was conducted in a free-living population, the results easily translate to persons at risk of CVD who want to include whole grains in their diet with the goal of losing weight.

Lammert et al., *Exp Clin Endocrinol Diabetes*, 116: 132-134, 2008.

Clinical benefit of a short-term dietary oatmeal intervention in patients with type 2 diabetes: a pilot study.

Introduction:

- Insulin resistance is a central feature of type 2 diabetes.
- As established intervention to improve insulin resistance and glucose control in patients with type 2 diabetes (T2DM) is the use of a diet rich in complex carbohydrates and dietary fiber.
- While still applied in clinical practice today, there is no published scientific study on the effectiveness of this approach in patients with uncontrolled T2DM.

Methods:

- Patients (n = 14) with uncontrolled type 2 diabetes and insulin resistance were consecutively enrolled in an inpatient clinical setting.
- Patients had a 2-day run-in phase with a ~1500 kcal diet (50-55% carbohydrate, 15-20% protein, 30% fat). The dietary intervention was then performed for 2 days with 15 carbohydrate units of oatmeal. This diet had 1100 kcal and was 63% carbohydrate, 12% protein, 6% fat, and 16.2g fiber.
- Patients were evaluated before and after the 2-day intervention, and after 4 weeks of follow-up in an outpatient setting.

Results:

- Consecutive treatment with oatmeal for two days significantly reduced the insulin dosage needed by 42.5% (P < 0.001).
- The oatmeal treatment was also associated with a significant improvement in mean blood glucose (decreased from 158 ± 47 mg/dL to 118 ± 37 mg/dL, P < 0.05) and paralleled by a significant reduction (-26.4%) in serum leptin levels.
- Despite returning to a regular diet within 4 weeks, patients showed a persistent improvement in glycemic control (glucose 141 ± 20.7 mg/dL) and significantly reduced insulin doses (-39.3%, P < 0.01). HbA1c showed a trend for reduction (from 8.6 to 8.2%, P = 0.09) and adiponectin increased by 53.8% (P < 0.05).

Discussion:

- In this pilot study, the two-day oatmeal intervention achieved a 40% reduction in insulin dose accompanied with almost normalization of mean blood glucose.
- Although the intervention lasted only for two days there was a lasting significant reduction in insulin dosage and ameliorated mean blood glucose in the following 4 weeks after hospital discharge.
- Further studies are necessary to validate and explore the concept of a high-carbohydrate, high-fiber diet for treatment of insulin resistance in patients with T2DM.

Lutsey et al., *Brit J Nutr.*, 98: 397-405, 2007.

Whole grain intake and its cross-sectional association with obesity, insulin resistance, inflammation, diabetes, and subclinical CVD: The MESA study.

Introduction:

- Whole grain intake has been related to reductions in total mortality, coronary artery disease mortality and morbidity, and diabetes incidence, independent of other health behaviors.
- Despite the strong body of evidence relating high consumption of whole grain intake to cardiovascular disease (CVD) risk, there have been no studies of whole grain intake and subclinical atherosclerosis.
- Additionally, little research has assessed whether racial/ethnic heterogeneity exists in the relationship between whole grain intake and CVD risk factors.

Methods:

- The relationship between whole grain intake and obesity, insulin resistance, diabetes, and subclinical CVD was examined using baseline data from the Multi-Ethnic Study of Atherosclerosis (MESA)
- Whole grain intake was measured by a food frequency questionnaire in 5,496 men and women free of coronary heart disease and previously known diabetes.
- Subclinical CVD was assessed by (1) measurement of carotid artery intima-media thickness using high-resolution B-mode ultrasonography and (2) measurement of coronary artery calcification using computed tomography.

Results:

- Inverse associations were found between whole grain intake and BMI, insulin, homeostasis model assessment, and homocysteine after multivariate adjustment ($P < 0.01$ for all).
- Whole grain intake was inversely associated with the probability of having any coronary artery atherosclerosis in the base model, but this association was attenuated after further adjustment. Whole grain intake was not associated with carotid artery intima media thickness.

Discussion:

- These findings are consistent with several other studies that have observed more favorable values of obesity, insulin, and homocysteine among whole grain eaters.
- Since whole grain intake showed little cross-sectional relationship with subclinical markers of vascular disease, it is possible that whole grain intake reduces risk of CHD ways other than through direct reduction of atherosclerosis.

Mellen et al., *Am J Clin Nutr.*, 85: 1495-1502, 2007.

Whole grain intake and carotid artery atherosclerosis in a multiethnic cohort: the Insulin Resistance Atherosclerosis Study.

Introduction:

- Numerous studies have found that higher whole-grain intakes are associated with a lower incidence of type 2 diabetes and cardiovascular disease.
- However, the relationship between whole-grain intake and atherosclerosis is less well established.
- Erkkilä et al. observed less angiographic progression in postmenopausal women with pre-existing heart disease with a whole grain intake above the median. However, it is unclear whether these findings are generalizable to the larger population.

Methods:

- The relationship between whole grain intake and carotid intimal medial thickness (IMT) and IMT progression was evaluated in a multiethnic cohort (62% were not white) participating in the Insulin Resistance Atherosclerosis study (n = 1178).
- Whole grain intake was estimated using a validated semiquantitative food-frequency questionnaire
- Bilateral carotid IMT was evaluated by ultrasound at baseline and after 5 years.

Results:

- There was a strong inverse association between whole grain intake and common carotid artery IMT after multivariate adjustment (P = 0.005).
- There was a trend towards an inverse association between whole grain intake and common carotid artery IMT progression over 5 years after multivariate adjustment (P = 0.09).
- The observed association between whole grain intake and IMT persisted after adjusting for nutrients that might account for the association (i.e. magnesium, thiamin, vitamin B-6, fiber, vitamin E, glycemic index)

Discussion:

- In this multiethnic cohort, whole-grain intake was inversely and independently associated with common carotid artery IMT and IMT progression.
- This confirms and extends findings of the prior study by Erkkilä et al., which found that a high whole grain intake was associated with less atherosclerosis progression in postmenopausal women with established heart disease.
- These findings provide further support for the potential benefit of whole grains in reducing atherosclerotic cardiovascular disease.

Merchant et al., *Am J Clin Nutr.*, 83: 1395-1400, 2006.

Whole-grain and fiber intakes and periodontitis risk in men.

Introduction:

- The risk, severity, and extent of periodontitis have been attributed to the hyperglycemic state.
- Greater whole-grain and fiber intakes are associated with improved insulin sensitivity, and consequently, with improved glycemic control.
- Consequently, the associations between dietary whole grain and fiber intake with periodontitis risk was examined in a large cohort of men.

Methods:

- Male US health professionals (n = 34,160) participating in the Health Professionals Follow-up study were prospectively followed for 12 years.
- Periodontitis was determined by professionally diagnosed disease that was validated by a diagnosis of periodontitis by a periodontist from a blinded review of radiographs.
- Diet was evaluated every four years using a validated semiquantitative food frequency questionnaire.

Results:

- Men who consumed more whole grains (median intake 3.4 servings/day) were 23% less likely to get periodontitis than were those who consumed less (median intake 0.3 servings/day) (multivariate RR 0.77; 95% CI 0.66 to 0.89, P < 0.001).
- Periodontitis was not associated with refined grain intake (multivariate RR for extreme quintiles of intake 1.94; 95% CI 0.89 to 1.23, P = 0.37).
- Periodontitis risk declined 6% for every 1.0 g/day increase in whole grain intake (multivariate RR 0.94; 95% CI 0.90 to 0.97).
- Cereal fiber was inversely related to periodontitis risk; however when whole grain and cereal fiber were entered in the same model, whole grain remained inversely associated with periodontitis risk (RR =0.73) but cereal fiber did not (RR =1.04).

Discussion:

- This is the first study to evaluate whole grain intake in relation to periodontitis risk.
- Periodontitis risk decreased with higher whole grain intake after multivariate adjustment. There was no relation between refined grain intake and periodontitis risk.
- It is plausible that a high intake of whole grains reduces periodontitis risk by improving insulin sensitivity.
- These findings suggest that eating ≥ 3.5 servings of whole grains/day without increasing total calories may reduce periodontitis risk.

Nettleton et al., *J Am Diet Assoc.*, 108: 1881-1887, 2008.

Incident heart failure is associated with lower whole-grain intake and greater high-fat dairy and egg intake in the Atherosclerosis Risk in Communities (AIRC) study.

Introduction:

- Heart failure affects approximately 5 million people in the United States, resulting in heavy demands on health care resources.
- Little diet-related research has been specific to heart failure, despite the increasing health care burden of this disease.
- The Atherosclerosis Risk in Communities (AIRC) study provides an opportunity to investigate the relationship between dietary intake and heart failure in men and women in a biracial sample (whites and African Americans).

Methods:

- The AIRC study is a population-based observational cohort study (n = 14,153) including African-American and white men and women age 45-64 years.
- Participants completed an interviewer-administered, semiquantitative food frequency questionnaire at baseline (1987-1989) and at follow-up (1993-1995).
- Incident heart failure cases were identified through review of county death certificates and local hospital discharge lists.

Results:

- Greater intake of whole grains was associated with a lower risk of heart failure [RR per 1 serving/day = 0.93 (95% CI 0.87 to 0.99)] after multivariate adjustment.
- Additional adjustment for BMI and incident CVD, diabetes, and hypertension had a minimal effect on the risk estimate [RR = 0.90 (95% CI 0.82 to 0.98)].

Discussion:

- After 13.3 years of follow-up, greater intake of whole-grain foods was associated with a lower risk of incident heart failure. This association was independent of demographic characteristics, lifestyle factors, CVD, diabetes, hypertension, and other food groups.
- This study is in agreement with a 2007 report from the Physician's Health Study, which showed that greater cereal intake, particularly whole-grain cereal, was associated with a significantly lower risk of heart failure.
- Although risk estimates were modest, the totality of literature in this area suggests it would be prudent to recommend whole grains to those at risk of heart failure, along with other healthful dietary practices.

Newby et al., *Am J Clin Nutr.*, 86: 1745-1753, 2007.

Intake of whole grains, refined grains, and cereal fiber measured with 7-d diet records and associations with risk factors for chronic disease.

Introduction:

- Significant inverse associations have been observed between whole grain intake and risk of cardiovascular disease, stroke, cancer, diabetes, obesity, and metabolic syndrome.
- Whole grains contain many bioactive components that might be responsible for their protective effect, including fiber, resistant starch, oligosaccharides, vitamins, minerals, phytate, phytoestrogens, and phytosterols.
- The objective of this study was to examine the association between intake of whole grains, refined grains, and cereal fiber measured in grams with selected risk factors for chronic disease.

Methods:

- Associations between dietary intake and risk factors for chronic disease were analyzed in participants in the Baltimore Longitudinal Study of Aging (n = 1,516).
- Dietary intake was assessed by 7-day diet records.

Results:

- Subjects in the highest quintile of whole grain intake had a lower BMI (P < 0.001), weight (P = 0.004), and waist circumference (P = 0.002) compared with those in the lowest quintile after multivariate adjustment. Subjects in the highest quintile of whole-grain intake had the lowest prevalence of overweight compared with the lowest quintile (39% vs. 54%).
- Whole grain intake was inversely associated with total and LDL cholesterol (P = 0.02 and P = 0.04, respectively, as well as 2-hour glucose (P = 0.0006) after multivariate adjustment.
- A positive association was observed between refined grain intake and fasting insulin in women (P = 0.002) after multivariate adjustment.
- Cereal fiber was also inversely related to BMI, weight, waist circumference, total cholesterol, and 2-hour glucose level after multivariate adjustment.

Discussion

- The inverse association observed between whole grain intake and risk factors for chronic disease is in agreement with findings from other observational studies.
- The protective effects of whole grains may be due to their content of fiber, phytosterols, phytoestrogens, antioxidants, and/or minerals.
- Similar associations between whole grains and cereal fiber with weight, BMI, waist circumference, plasma cholesterol, and 2-hour glucose suggest that cereal fiber and its constituents may in part mediate the inverse relationship between whole grain intake and CVD risk.

Panlasigui et al., *Int J Food Sci Nutr.*, 57: 151-158, 2006.

Blood glucose lowering effects of brown rice in normal and diabetic subjects.

Introduction:

- A low blood glucose response to carbohydrate containing foods has been suggested to be beneficial to individuals with type 2 diabetes and hyperlipidemia.
- Limited studies on the effects of brown rice compared with milled rice on glucose and insulin levels are contradictory and not well controlled.
- This study determined the rate of starch digestion and blood glucose response to brown and milled rice from the same batch and variety of rice.

Methods:

- The starch digestion rate of freshly cooked brown and white rice was determined *in vitro* by incubating it with a mixture of human saliva and distilled water in a dialysis bag maintained at 37°C. Aliquots of the dialysates were removed every hour for three hours and analyzed by HPLC for individual sugars released.
- After a 10-12 hour fast, ten healthy and nine type 2 diabetic volunteers consumed in random order a breakfast test meal containing 50 g available carbohydrate of the freshly cooked rice samples. Each participant also tested white bread as a control.
- Blood samples were obtained for 1 hour in healthy subjects and for 3 hours in diabetic subjects.

Results:

- *In vitro*, the total sugars released were 23.7% lower in brown rice than milled rice.
- In healthy volunteers, the incremental blood glucose area and glycemic index were 19.8% and 12.1% lower, respectively, in brown rice than milled rice.
- In diabetic subjects, the respective values were 35.2% and 35.6% lower in brown rice than milled rice.
- Brown rice had higher concentrations of dietary fiber, fat, phytic acid, and total polyphenol contents than white rice.

Discussion:

- This study demonstrated that brown rice is digested slower and results in a lower blood glucose response in both healthy and diabetic subjects compared to milled rice prepared from the same rice variety and batch.
- This may be related in part to differences in chemical composition and physiochemical properties.
- Brown rice appears to be more beneficial for health than milled rice, especially for individuals with diabetes and hyperglycemia.

Qi et al., *Diabetes Care*, 29: 207-211, 2006.

Whole grain, bran, and cereal fiber intake and markers of systemic inflammation in diabetic women.

Introduction:

- Consumption of whole grains and dietary fiber is associated with a reduced risk of cardiovascular disease (CVD) risk in epidemiological studies.
- The biologic mechanisms underlying this effect are not well understood.
- Since the inflammatory process plays a pivotal role in the pathogenesis of CVD, the relationship between long-term whole grain intake and markers of inflammation were examined.

Methods:

- Whole grain intake and inflammatory markers were measured in 902 diabetic women in the Nurses' Health Study.
- Whole grain intake was assessed using a semi-quantitative food frequency questionnaire.

Results:

- There was a significant decrease in C-reactive protein (CRP) with increasing quintiles of whole grain ($P = 0.03$) and bran ($P = 0.007$) intake after multivariate adjustment.
- There was also a significant decrease in TNF-R2 with increasing quintiles of whole grain intake ($P = 0.017$) after multivariate adjustment.
- Increasing cereal fiber intake was also significantly associated with decreased CRP ($P = 0.03$) and TNF-R2 ($P = 0.01$).

Discussion:

- Among women with type 2 diabetes, intakes of whole grains and cereal fiber were associated with lower levels of CRP and TNF-R2 after adjusting for age, BMI, lifestyle, and dietary covariates.
- These data indicate that whole grains may reduce systemic inflammation among women with type 2 diabetes.

Rave et al., *Br J Nutr.*, 98:929-936, 2007.

Improvement of insulin resistance after diet with a whole-grain based dietary product: results of a randomized, controlled crossover study in obese subjects with elevated fasting blood glucose.

Introduction:

- Type 2 diabetes and its long-term complications are major causes of morbidity and mortality worldwide and the prevalence continues to rise.
- A diet therapy that achieves weight loss and improves insulin sensitivity can potentially reduce the incidence of type 2 diabetes in obese individuals.
- The aim of this study was to determine if a hypo-energetic diet with a whole-grain based dietary product derived from double-fermented wheat affects insulin resistance in obese subjects at risk of developing type 2 diabetes.

Methods:

- Study participants were 31 men and women with a BMI > 29 and elevated fasting blood glucose (> 6.1 and ≤ 7.1 mmol/L).
- Participants replaced at least two daily meals with a whole-grain based dietary product with low starch content derived from double-fermented wheat or a meal replacement (Slim Fast) in a randomized crossover study with 4-week treatment periods.
- General advice was given to limit saturated fat intake, favor food rich in fiber, avoid sugary beverages and food, increase intake of fresh fruit and vegetables, and drink at least 2 liters of water per day.

Results:

- In both groups there was a decrease in body weight, fasting blood glucose, total cholesterol, and HOMA insulin resistance score, with no significant differences between the treatments.
- After statistical adjustment for the amount of body weight lost, there was a greater decrease in fasting insulin (P = 0.031) and HOMA insulin resistance score (0.049) in the whole grain group than the meal replacement group.

Discussion:

- In the present study, a hypo-energetic diet with a whole grain dietary product and a meal replacement resulted in weight loss and a decrease in blood glucose, insulin, and insulin resistance in obese subjects with elevated fasting glucose.
- Adjusting for the amount of weight lost revealed a better improvement insulin resistance after the diet with whole grains than meal replacements.
- The beneficial effect of the whole grain product likely resulted from synergistic effects from properties of the whole grain product including a high content of insoluble fiber, low amount of digestible carbohydrates, and low glycemic index.

Rose et al., *J Nutr Educ Behav.*, 39: 90-94, 2007.

Whole grain intake is associated with body mass index in college students.

Introduction:

- Longitudinal data in adults suggests that increasing intake of whole grains and dietary fiber protects against major weight gain.
- However there are no studies examining whole grain intake or its relationship with body mass index (BMI) in college students.
- Almost half of all college students report that they have attempted some form of weight loss, indicating that this population is responsive to diet and lifestyle messages.

Methods:

- College students enrolled in an introductory nutrition course (n = 159) participated in this cross-sectional study.
- Participants were trained in completing food records, and recorded their food and beverage intake for seven consecutive days.
- Participants completed the seven-day food records on two occasions to determine whether there were any changes in consumption over the semester.
- Whole grain food items were defined as those that contained a whole grain as the first ingredient on the food label.

Results:

- On average, students reported consuming 5.4 grain servings per day, with 13% of that amount (0.7 servings/day) from whole grain foods.
- Ready to eat cereals and whole grain bread composed >70% of whole grain intake.
- Whole grain intake was significantly higher ($P < 0.05$) in normal-weight students (0.8 ± 0.8 servings/day) than those who were either overweight (0.6 ± 0.7 servings/day) or obese (0.3 ± 0.4 servings/day).

Discussion:

- The low intake of whole grains in this population of college students indicates a need for interventions aimed at increasing whole grain intake.
- The inverse association between whole grain intake and risk of being overweight may be useful to motivate more young adults to increase their consumption of whole grain foods.

Sahyoun et al., *Am J Clin Nutr.*, 83: 124-131, 2006.

Whole-grain intake is inversely associated with metabolic syndrome and mortality in older adults.

Introduction:

- Diets that are rich in whole-grain foods have been linked to a lower prevalence of the metabolic syndrome.
- Whole grain foods may confer protection by decreasing weight gain, or by its constituents directly affecting insulin sensitivity and/or other components of metabolic syndrome.
- Most studies have estimated dietary intake using a food-frequency questionnaire. This is the first study on metabolic syndrome to estimate grain intake using food records.
- This is also the first study to examine the relationship between whole grain intake and CVD risk in an exclusively older population.

Methods:

- The relationship between whole grain intake and cardiovascular disease (CVD) risk factors, prevalence of metabolic syndrome, and CVD mortality was examined in an older population (≥ 60 years, $n = 535$) who were followed for 12-15 years.
- Dietary intake was assessed using a 3-day food record.
- The metabolic syndrome was defined using criteria set by the National Cholesterol Education Program

Results:

- Fasting glucose and BMI decreased across increasing quartiles of whole-grain intake, even after adjustment for demographic and lifestyle factors.
- Individuals in the highest quartile of whole grain intake (median 2.9 servings/day) had a 54% lower risk of having metabolic syndrome compared with those in the lowest quartile (< 1 serving/day).
- There was more than a two-fold increase in risk of metabolic syndrome in individuals in the highest quartile of refined grain intake compared with those in the lowest quartile (OR 2.16, 95% CI 1.20-3.87, $P < 0.01$).
- There was a 52% lower risk of death from CVD over 11-14 years in individuals in the highest quartile of whole grain intake compared with those in the lowest.

Discussion:

- A higher intake of whole-grain foods was associated with reduced CVD risk factors, lower prevalence of metabolic syndrome, and a lower incidence of CVD mortality.
- In contrast, intake of refined grain products was not related to CVD mortality, but was associated with a higher prevalence of metabolic syndrome.
- Whole grain intake is a modifiable dietary risk factor that may lead to substantial health benefits, even in an older population.

Schatzkin et al., *Gastroenterology*, 135: 1163-1167, 2008.

Prospective study of dietary fiber, whole grain foods, and small intestinal cancer.

Introduction:

- A number of epidemiologic studies have found dietary fiber and whole grain intake to be inversely associated with colorectal cancer.
- However, studies of dietary and other risk factors for small intestinal cancer are sparse and all have been a case-control design.
- None of these previous studies have focused on the relationship between fiber and whole grain intake with risk of small intestinal cancer.
- Prospective cohort studies of the role of dietary factors in small intestinal cancer are desirable but need to be large given the relative rarity of the disease (~2/100,000).

Methods:

- Dietary data from 293,703 men and 198,618 women participating in the National Institutes of Health-AARP Diet and Health Study were analyzed. Participants were followed for an average of seven years.
- Cancer cases were identified using 11 state cancer registry databases.
- Dietary intake was assessed by a validated 124-item food frequency questionnaire.

Results:

- Over seven years of follow-up, 165 cases of small intestinal cancer were identified.
- Fiber from grains was significantly inversely associated with small intestinal cancer risk (multivariate RR: 0.51; 95% CI 0.29-0.89, P = 0.01).
- Neither fruit nor vegetable fiber was associated with small intestinal cancer incidence.
- Intake of whole grains was marginally inversely related to small intestinal cancer risk (multivariate RR 0.59; 95% CI 0.33-1.05, P = 0.06).

Discussion:

Intake of whole grain foods and fiber from grains were inversely associated with small intestinal cancer risk in this cohort.

No other prospective study has examined these dietary factors in relation to small intestinal cancer.

Possible mechanisms include (a) stool bulking, (b) decreased transit time, (c) bile acid and carcinogen binding, (d) short chain fatty acid production via fermentation, and (e) actions of vitamins, minerals, phenols, and phytoestrogens.

The similar protective associations for grain fiber and whole grain foods in small and large intestinal cancer support a causal role for these dietary factors.

Schatzkin et al., *Am J Clin Nutr.*, 85: 1353-1360, 2007.

Dietary fiber and whole grain consumption in relation to colorectal cancer in the NIH-AARP Diet and Health Study.

Introduction:

- Whether the intake of dietary fiber can protect against colorectal cancer is a long-standing question of considerable health importance.
- Several plausible pathophysiologic processes have been proposed as possible mechanisms, including stool bulking with subsequent dilution of colonic carcinogens and production of anticarcinogenic short chain fatty acids.
- However, epidemiologic evidence has been inconsistent.

Methods:

- The relationship between dietary fiber and whole grain intake with colorectal cancer risk was examined in a large prospective cohort (291,988 men and 197,623 women) in the NIH-AARP Diet and Health Study.
- Participants were followed over 5 years, during which 2974 incident colorectal cancer cases were identified.
- Dietary fiber and whole grain intake were assessed using a food frequency questionnaire.

Results:

- The age and sex adjusted analyses showed a statistically significant inverse relation between dietary fiber and colorectal cancer, with a 25% reduction in risk for those in the highest compared with the lowest quintile.
- After adjustment for other diet and lifestyle factors, the association became null.
- Only fiber from grains had a significant, inverse relationship to colorectal cancer risk after multivariate adjustment (RR 0.86, 95% CI 0.76-0.98).
- Whole grain intake was inversely related to colorectal cancer in multivariate analyses, with a significant 20% reduction in risk for those in the highest compared with the lowest quintile.

Discussion:

- In this large prospective cohort study, total dietary fiber intake was not associated with colorectal cancer risk, where as whole grain consumption was associated with a modest reduced risk.
- These findings suggest that whole-grain components other than fiber – e.g. vitamins, minerals, phenols, and phytoestrogens affect colorectal carcinogenesis.
- The hypothesis that whole grains are protective against colorectal cancer warrants further investigation.

van Dam et al., *Diabetes Care*, 29: 2238-2243, 2006.

Dietary calcium and magnesium, major food sources, and risk of type 2 diabetes in U.S. black women.

Introduction:

- In previous studies in predominantly white populations, a higher intake of magnesium and whole grains was associated with a lower risk of type 2 diabetes.
- It is unclear whether these findings can be extrapolated to blacks.
- The aim of this study was to determine the relationship between magnesium and major food sources with type 2 diabetes in the prospective Black Women's Study.

Methods:

- Women participating in the Black Women's Health Study (n = 41,186) without a history of diabetes were prospectively followed for eight years.
- Diabetes was assessed by questionnaire every two years by asking whether the women had been diagnosed with diabetes.
- Dietary intake was assessed at baseline using the 68-item Block food frequency questionnaire.

Results:

- For magnesium intake, the multivariate adjusted hazard ratio for type 2 diabetes was 0.69 (95% CI 0.59-0.81, P < 0.0001) for the highest compared with the lowest quintile.
- Higher consumption of whole grains was also associated with a lower risk of type 2 diabetes.
- The association remained after adjusting for magnesium intake (hazard ratio 0.73 [95% CI 0.63-0.85] for ≥ 1 serving/day vs. <1 serving/week; P < 0.0001).

Discussion:

- In this 8-year prospective study of U.S. black women, a higher dietary magnesium and whole grain intake was associated with a lower risk of type 2 diabetes.
- Magnesium status may influence glucose homeostasis by affecting oxidative stress, glucose metabolism, and/or insulin sensitivity and secretion.
- These results are consistent with observational data from diverse populations and results of metabolic studies.

van de Vijver et al., *Eur J Clin Nutr.*, Epub Sept 2007.

Whole-grain consumption, dietary fiber intake and body mass index in the Netherlands cohort study.

Introduction:

- Whole grains may help in preventing overweight and obesity by increasing satiety and by slowing down starch digestion and absorption, which can favor fat oxidation and lipolysis rather than fat storage.
- Thus far, only a few studies have reported the association between whole grain intake with body mass index (BMI) and weight gain.

Methods:

- The association between consumption of whole grain foods and dietary fiber with BMI, overweight, and obesity was assessed in participants in the Netherlands Cohort Study in a cross-sectional (n = 4,237) and in a prospective (n = 1,257) setting.
- Dietary intake was assessed using a validated semi-quantitative food frequency questionnaire.

Results:

- Whole grain intake was inversely associated with BMI in men and women after multivariate adjustment.
- The risk of being obese as compared to normal weight was 10% (95% CI 2-16%) and 4% (95% CI 1-7%) lower for each additional gram of dry whole grain consumption in men and women, respectively.
- It is estimated that a 33 g/day increase in dry whole grain intake is associated with a decrease of 1 unit BMI.
- There was a slight inverse association between baseline fiber intake and weight gain over 20 years.

Discussion:

- The results of this study in a healthy middle-aged population indicate that men and women with a high intake of whole grains have a lower BMI and lower risk of overweight and obesity than men and women with a low intake of whole grains.
- Intervention studies are needed to determine if there is a causal relationship between whole grain consumption and body weight.

Wang et al., *Am J Clin Nutr.*, 86: 472-479, 2007.

Whole- and refined-grain intakes and the risk of hypertension in women.

Introduction:

- The effects of whole and refined grain intakes on the development of cardiovascular disease are attributable, in part, to changes in blood pressure.
- Epidemiologic evidence regarding the relationship between whole and refined grain intakes with the risk of developing hypertension remains limited

Methods:

- The association between baseline whole and refined grain intake and the development of hypertension during 10 years of follow-up was examined in 28,926 middle-aged and older women (mean 53.8 ± 6.6 years) in the Women's Health Study.
- Dietary intake was measured by a validated semiquantitative food frequency questionnaire.

Results:

- Whole grain intake was associated with a modest but significant dose-related reduction in the risk of hypertension.
- Compared with women in the lowest quintile of whole grain intake (median 0.21 servings/day), the multivariate adjusted relative risk of incident hypertension was 0.89 (95% CI 0.82 - 0.97) in the highest quintile (median 3.07 servings/day).
- Compared with women who consumed < 0.5 servings of whole grains/day, those who consumed ≥ 4 servings/day had a relative risk of 0.77 (95% CI 0.66 - 0.89).
- Refined grain intake was not associated with the risk of hypertension.

Discussion:

- In this large, prospective cohort study, whole grain intake was inversely associated with subsequent risk of hypertension.
- The association was modest but dose related and independent of known factors of hypertension.
- Possible mechanisms involve reductions in abdominal obesity, increases in peripheral insulin sensitivity, and improvements in vascular endothelial function.