

## **Lifestyle interventions in the treatment of selected diseases – Summary by disease**

### **Coronary heart disease/Cardiovascular disease**

**Epidemiological** studies – Hu, Optimal diets for Prev CHD (JAMA 2002 Nov 27;288(20):2569-78.); Sauvaget C, et al. Veg and fruit intake and stroke mortality in Hiroshima/Nagasaki Life Span Study. Stroke. 2003 Oct;34(10):2355-60.; AHS, NHS, etc.

**Intervention** studies – Ornish, Lifestyle Heart Trial (JAMA 1998 Dec 16;280(23):2001-7.); deLorgeril, Lyons Diet Heart Study (Lancet. 1994;343:1454-9; Circulation. 1999;99:779-785.); Obarzanek, Effects of DASH on lipids (AJCN. 2001 Jul;74(1):80-9.); Jenkins, Portfolio diet (JAMA 2003 Jul 23/30;290(4):502-10.); Koertge, Multicenter Lifestyle Demonstration Project (Am J Cardiol. 2003 Jun 1;91(11):1316-22.)

### **Hypertension**

**Epidemiological** studies – Appleby, HTN and BP among veg vs meat-eaters:EPIC-Oxford (Pub Hlth Nutr. 2002 Oct;5(5):645-54.); AHS, NHS, etc.

**Intervention** studies – Appel, Dietary effects on BP (NEJM 1997;336:1117-24); Moore, DASH effective Tx for ISH (Hypertension 2001 Aug;38:155-8.); Appel, Effects of Lifestyle mod on BP: PREMIER trial (JAMA 2003 Apr 23/30;289(16):2083-93.)

### **Type-2 diabetes**

**Epidemiological** studies – Jiang, Nuts and incidence of DM2 in women (JAMA. 2002 Nov 27;288(20):2554-60.); Steyn, Diet & prev of DM2 (Public Health Nutr. 2004 Feb;7(1A):147-65.); Hu FB, et al. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. N Engl J Med. 2001;345:790-797.; Jenkins, et al. Type 2 diabetes and the vegetarian diet. Am J Clin Nutr. 2003 Sep;78(3 Suppl):610S-616S.; Lee DH, et al. Association between serum gamma-glutamyltransferase and dietary factors: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. AJCN. 2004 Apr;79(4):600-5.

**Intervention** studies – Tuomilehto, LM prev DM2 in IGT: FDPS (NEJM 2001 May 3;344(18):1343-50); Knowler, DPP results (NEJM 2002 Feb 7;346(6):393-403.); Pan, effects of LM in prev DM2: Da Qing Study (Diabetes Care. 1997 Apr;20(4):537-44.)

### **Obesity**

**Epidemiological** studies – Spencer, Diet and BMI in EPIC-Oxford (Int J Obes Relat Metab Disord. 2003 Jun;27(6):728-34.); Trichopoulou A, et al. Lipid, protein and carbohydrate intake in relation to body mass index. (Eur J Clin Nutr. 2002 Jan;56(1):37-43.)

**Intervention** studies – Knowler, DPP results (NEJM 2002 Feb 7;346(6):393-403.)

### **Cancer**

**Epidemiological** studies – Thorogood, Risk of cancer in meat-eaters vs veg (BMJ. 1994 Jun 25;308(6945):1667-70.); Key, Mortality in vegs (Am J Clin Nutr. 1999 Sep;70(3 Suppl):516S-524S.); AHS, NHS, etc.

**Intervention** studies –

### **Longevity**

**Epidemiological** studies – Seccareccia F, et al. Veg and long-term survival Italy. Ann Epidemiol. 2003 Jul;13(6):424-30; Strandhagen E, et al. fruit may reduce mortality men. The Study of Men Born in 1913. Eur J Clin Nutr. 2000 Apr;54(4):337-41.

**Intervention** studies –

### **Rheumatoid arthritis**

**Epidemiological** studies –

**Intervention** studies – Hafstrom, vegan gluten-free diet improves RA with decr Ab (Rheumatology (Oxford). 2001 Oct;40(10):1175-9.); McDougall, Effect of low-fat vegan diet on RA (J Alt Compl Med. 2002 Feb;8(1):71-5.); Muller, meta-analysis of fasting followed by veg diet for RA (Scand J Rheumatol. 2001;30(1):1-10.); Kjeldsen-Kragh, RA treated with vegan diet (AJCN. 1999 Sep;70(3 Suppl):594S-600S.)

## Lifestyle interventions in the treatment of selected diseases – Published ABSTRACTS

### Coronary heart disease/Cardiovascular disease

Hu FB, et al. Optimal **Diets** for Prevention of Coronary **Heart Disease**. JAMA. 2002;288:2569-2578.

Context: Coronary heart disease (CHD) remains the leading cause of mortality in industrialized countries and is rapidly becoming a primary cause of death worldwide. Thus, identification of the dietary changes that most effectively prevent CHD is critical. Objective: To review metabolic, epidemiologic, and clinical trial evidence regarding diet and CHD prevention. Data Sources and Study Selection: We searched MEDLINE through May 2002 for epidemiologic and clinical investigations of major dietary factors (fat, cholesterol, omega-3 fatty acids, trans-fatty acids, carbohydrates, glycemic index, fiber, folate, specific foods, and dietary patterns) and CHD. We selected 147 original investigations and reviews of metabolic studies, epidemiologic studies, and dietary intervention trials of diet and CHD. Data Extraction: Data were examined for relevance and quality and extracted by 1 of the authors. Data Synthesis: Compelling evidence from metabolic studies, prospective cohort studies, and clinical trials in the past several decades indicates that at least 3 dietary strategies are effective in preventing CHD: substitute nonhydrogenated unsaturated fats for saturated and trans-fats; increase consumption of omega-3 fatty acids from fish, fish oil supplements, or plant sources; and consume a diet high in fruits, vegetables, nuts, and whole grains and low in refined grain products. However, simply lowering the percentage of energy from total fat in the diet is unlikely to improve lipid profile or reduce CHD incidence. Many issues remain unsettled, including the optimal amounts of monounsaturated and polyunsaturated fats, the optimal balance between omega-3 and omega-6 polyunsaturated fats, the amount and sources of protein, and the effects of individual phytochemicals, antioxidant vitamins, and minerals. Conclusions: Substantial evidence indicates that diets using nonhydrogenated unsaturated fats as the predominant form of dietary fat, whole grains as the main form of carbohydrates, an abundance of fruits and vegetables, and adequate omega-3 fatty acids can offer significant protection against CHD. Such diets, together with regular physical activity, avoidance of smoking, and maintenance of a healthy body weight, may prevent the majority of cardiovascular disease in Western populations.

**Sauvaget C, et al. Vegetable and fruit intake and stroke mortality in the Hiroshima/Nagasaki Life Span Study. Stroke. 2003 Oct;34(10):2355-60. Epub 2003 Sep 18.**

BACKGROUND AND PURPOSE: Fruits and vegetables are known for their beneficial effects on chronic diseases. The purpose of the present study was to investigate the protective effect of a diet rich in fruits and vegetables on total stroke mortality and its 2 main subtypes in men and women separately. METHODS: A prospective cohort study of 40 349 Japanese men and women was initiated in 1980-1981 and followed until 1998. Fruit and vegetable intake was assessed at baseline on the basis of the response to a food frequency questionnaire. During the 18-year follow-up period, deaths from stroke were registered. RESULTS: A total of 1926 stroke deaths were identified during the follow-up period. An increasing frequency of intake of green-yellow vegetables and fruit was associated with a reduced risk of death from intracerebral hemorrhage and cerebral infarction. Daily intake of green-yellow vegetables was associated with a significant 26% reduction in the risk of death from total stroke in men and women compared with an intake of once or less per week. The protective effect associated with daily fruit and vegetable intake was observed for both cerebral infarction and intracerebral hemorrhage mortality but was slightly stronger and clearer for infarction than for hemorrhage, with a 32% reduction in men and a 30% reduction in women. Daily fruit intake was associated with a significant 35% reduction in risk of total stroke in men and a 25% reduction in women and was equally strong for both intracerebral hemorrhage and cerebral infarction. CONCLUSIONS: Daily consumption of green-yellow vegetables and fruits is associated with a lower risk of total stroke, intracerebral hemorrhage, and cerebral infarction mortality. The protective effects are similar in both men and women.

**Ornish D, et al. Intensive lifestyle changes for reversal of coronary heart disease. JAMA 1998 Dec 16;280(23):2001-7.**

**CONTEXT:** The Lifestyle Heart Trial demonstrated that intensive lifestyle changes may lead to regression of coronary atherosclerosis after 1 year. **OBJECTIVES:** To determine the feasibility of patients to sustain intensive lifestyle changes for a total of 5 years and the effects of these lifestyle changes (without lipid-lowering drugs) on coronary heart disease. **DESIGN:** Randomized controlled trial conducted from 1986 to 1992 using a randomized invitational design. **PATIENTS:** Forty-eight patients with moderate to severe coronary heart disease were randomized to an intensive lifestyle change group or to a usual-care control group, and 35 completed the 5-year follow-up quantitative coronary arteriography. **SETTING:** Two tertiary care university medical centers. **INTERVENTION:** Intensive lifestyle changes (10% fat whole foods vegetarian diet, aerobic exercise, stress management training, smoking cessation, group psychosocial support) for 5 years. **MAIN OUTCOME MEASURES:** Adherence to intensive lifestyle changes, changes in coronary artery percent diameter stenosis, and cardiac events. **RESULTS:** Experimental group patients (20 [71%] of 28 patients completed 5-year follow-up) made and maintained comprehensive lifestyle changes for 5 years, whereas control group patients (15 [75%] of 20 patients completed 5-year follow-up) made more moderate changes. In the experimental group, the average percent diameter stenosis at baseline decreased 1.75 absolute percentage points after 1 year (a 4.5% relative improvement) and by 3.1 absolute percentage points after 5 years (a 7.9% relative improvement). In contrast, the average percent diameter stenosis in the control group increased by 2.3 percentage points after 1 year (a 5.4% relative worsening) and by 11.8 percentage points after 5 years (a 27.7% relative worsening) ( $P=.001$  between groups). Twenty-five cardiac events occurred in 28 experimental group patients vs 45 events in 20 control group patients during the 5-year follow-up (risk ratio for any event for the control group, 2.47 [95% confidence interval, 1.48-4.20]). **CONCLUSIONS:** More regression of coronary atherosclerosis occurred after 5 years than after 1 year in the experimental group. In contrast, in the control group, coronary atherosclerosis continued to progress and more than twice as many cardiac events occurred.

**de Lorgeril M, et al. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study.** *Circulation* 1999 Feb;99(6):779-85.

**BACKGROUND** The Lyon Diet Heart Study is a randomized secondary prevention trial aimed at testing whether a Mediterranean-type diet may reduce the rate of recurrence after a first myocardial infarction. An intermediate analysis showed a striking protective effect after 27 months of follow-up. This report presents results of an extended follow-up (with a mean of 46 months per patient) and deals with the relationships of dietary patterns and traditional risk factors with recurrence. **METHODS & RESULTS** Three composite outcomes (COs) combining either cardiac death and nonfatal myocardial infarction (CO 1), or the preceding plus major secondary end points (unstable angina, stroke, heart failure, pulmonary or peripheral embolism) (CO 2), or the preceding plus minor events requiring hospital admission (CO 3) were studied. In the Mediterranean diet group, CO 1 was reduced (14 events versus 44 in the prudent Western-type diet group,  $P=0.0001$ ), as were CO 2 (27 events versus 90,  $P=0.0001$ ) and CO 3 (95 events versus 180,  $P=0.0002$ ). Adjusted risk ratios ranged from 0.28 to 0.53. Among the traditional risk factors, total cholesterol (1 mmol/L being associated with an increased risk of 18% to 28%), systolic blood pressure (1 mm Hg being associated with an increased risk of 1% to 2%), leukocyte count (adjusted risk ratios ranging from 1.64 to 2.86 with count  $>9 \times 10^9/L$ ), female sex (adjusted risk ratios, 0.27 to 0.46), and aspirin use (adjusted risk ratios, 0.59 to 0.82) were each significantly and independently associated with recurrence. **CONCLUSIONS** The protective effect of the Mediterranean dietary pattern was maintained up to 4 years after the first infarction, confirming previous intermediate analyses. Major traditional risk factors, such as high blood cholesterol and blood pressure, were shown to be independent and joint predictors of recurrence, indicating that the Mediterranean dietary pattern did not alter, at least qualitatively, the usual relationships between major risk factors and recurrence. Thus, a comprehensive strategy to decrease cardiovascular morbidity and mortality should include primarily a cardioprotective diet. It should be associated with other (pharmacological?) means aimed at reducing modifiable risk factors. Further trials combining the 2 approaches are warranted.

**Obarzanek E, et. al. Effects on blood lipids of a blood pressure-lowering diet: the Dietary Approaches to Stop Hypertension (DASH) Trial.** *Am J Clin Nutr* 2001 Jul;74(1):80-9.

**BACKGROUND:** Effects of diet on blood lipids are best known in white men, and effects of type of carbohydrate on triacylglycerol concentrations are not well defined. **OBJECTIVE:** Our goal was to determine the effects of diet on plasma lipids, focusing on subgroups by sex, race, and baseline lipid concentrations. **DESIGN:** This was a randomized controlled outpatient feeding trial conducted in 4 field centers. The subjects were 436 participants of the Dietary Approaches to Stop Hypertension (DASH) Trial [mean age: 44.6 y; 60% African American; baseline total cholesterol: 6.7 mmol/L (260 mg/dL)]. The intervention consisted of 8 wk of a control diet, a diet increased in fruit and vegetables, or a diet increased in fruit, vegetables, and low-fat dairy products and reduced in saturated fat, total fat, and cholesterol (DASH diet), during which time subjects remained weight stable. The main outcome measures were fasting total cholesterol, LDL cholesterol, HDL cholesterol, and triacylglycerol. **RESULTS:** Relative to the control diet, the DASH diet resulted in lower total (-0.35 mmol/L, or -13.7 mg/dL), LDL- (-0.28 mmol/L, or -10.7 mg/dL), and HDL- (-0.09 mmol/L, or -3.7 mg/dL) cholesterol concentrations (all  $P < 0.0001$ ), without significant effects on triacylglycerol. The net reductions in total and LDL cholesterol in men were greater than those in women by 0.27 mmol/L, or 10.3 mg/dL ( $P = 0.052$ ), and by 0.29 mmol/L, or 11.2 mg/dL ( $P < 0.02$ ), respectively. Changes in lipids did not differ significantly by race or baseline lipid concentrations, except for HDL, which decreased more in participants with higher baseline HDL-cholesterol concentrations than in those with lower baseline HDL-cholesterol concentrations. The fruit and vegetable diet produced few significant lipid changes. **CONCLUSIONS:** The DASH diet is likely to reduce coronary heart disease risk. The possible opposing effect on coronary heart disease risk of HDL reduction needs further study.

**Jenkins DJ, et. al.** Effects of a **dietary portfolio** of cholesterol-lowering foods **vs Lovastatin** on serum lipids and C-reactive protein. *JAMA* 2003 Jul 23/30;290(4):502-10.

**CONTEXT:** To enhance the effectiveness of diet in lowering cholesterol, recommendations of the Adult Treatment Panel III of the National Cholesterol Education Program emphasize diets low in saturated fat together with plant sterols and viscous fibers, and the American Heart Association supports the use of soy protein and nuts. **OBJECTIVE:** To determine whether a diet containing all of these recommended food components leads to cholesterol reduction comparable with that of 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins). **DESIGN:** Randomized controlled trial conducted between October and December 2002. **SETTING AND PARTICIPANTS:** Forty-six healthy, hyperlipidemic adults (25 men and 21 postmenopausal women) with a mean (SE) age of 59 (1) years and body mass index of 27.6 (0.5), recruited from a Canadian hospital-affiliated nutrition research center and the community. **INTERVENTIONS:** Participants were randomly assigned to undergo 1 of 3 interventions on an outpatient basis for 1 month: a diet very low in saturated fat, based on milled whole-wheat cereals and low-fat dairy foods ( $n = 16$ ; control); the same diet plus lovastatin, 20 mg/d ( $n = 14$ ); or a diet high in plant sterols (1.0 g/1000 kcal), soy protein (21.4 g/1000 kcal), viscous fibers (9.8 g/1000 kcal), and almonds (14 g/1000 kcal) ( $n = 16$ ; dietary portfolio). **MAIN OUTCOME MEASURES:** Lipid and C-reactive protein levels, obtained from fasting blood samples; blood pressure; and body weight; measured at weeks 0, 2, and 4 and compared among the 3 treatment groups. **RESULTS:** The control, statin, and dietary portfolio groups had mean (SE) decreases in low-density lipoprotein cholesterol of 8.0% (2.1%) ( $P = .002$ ), 30.9% (3.6%) ( $P < .001$ ), and 28.6% (3.2%) ( $P < .001$ ), respectively. Respective reductions in C-reactive protein were 10.0% (8.6%) ( $P = .27$ ), 33.3% (8.3%) ( $P = .002$ ), and 28.2% (10.8%) ( $P = .02$ ). The significant reductions in the statin and dietary portfolio groups were all significantly different from changes in the control group. There were no significant differences in efficacy between the statin and dietary portfolio treatments. **CONCLUSION:** In this study, diversifying cholesterol-lowering components in the same dietary portfolio increased the effectiveness of diet as a treatment of hypercholesterolemia.

**Koertge J, et al.** Improvement in medical risk factors and quality of life in women and men with coronary artery disease in the **Multicenter Lifestyle Demonstration Project**. *Am J Cardiol*. 2003 Jun 1;91(11):1316-22.

This study examined medical and psychosocial characteristics of 440 patients (mean age 58 years, 21% women) with coronary artery disease at baseline and at 3-month and 12-month follow-ups. All patients were participants in the Multicenter Lifestyle Demonstration Project, aimed at improving diet (low fat, whole foods, plant-based), exercise, stress management, and social support. Spousal participation was

encouraged. Both genders evidenced significant improvements in their diet, exercise, and stress management practices, which they maintained over the course of the study. Both women and men also showed significant medical (e.g., plasma lipids, blood pressure, body weight, exercise capacity) and psychosocial (e.g., quality of life) improvement. Despite their worse medical, psychosocial, and sociodemographic status at baseline, women's improvement was similar to that of men's. These results demonstrate that a multi-component lifestyle change program focusing on diet, exercise, stress management, and social support can be successfully implemented at hospitals in diverse regions of the United States. Furthermore, this program may be particularly beneficial for women with coronary artery disease who generally have higher mortality and morbidity than men after a heart attack, angioplasty, or bypass surgery.

## Hypertension

**Appleby PN, Davey GK, Key TJ. Hypertension and blood pressure among meat eaters, fish eaters, vegetarians and vegans in EPIC-Oxford.** Public Health Nutr. 2002 Oct;5(5):645-54.

**OBJECTIVE:** To compare the prevalence of self-reported hypertension and mean systolic and diastolic blood pressures in four diet groups (meat eaters, fish eaters, vegetarians and vegans) and to investigate dietary and other lifestyle factors that might account for any differences observed between the groups. **DESIGN:** Analysis of cross-sectional data from participants in the Oxford cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC-Oxford). **SETTING:** United Kingdom. **SUBJECTS:** Eleven thousand and four British men and women aged 20-78 years at blood pressure measurement. **RESULTS:** The age-adjusted prevalence of self-reported hypertension was significantly different between the four diet groups, ranging from 15.0% in male meat eaters to 5.8% in male vegans, and from 12.1% in female meat eaters to 7.7% in female vegans, with fish eaters and vegetarians having similar and intermediate prevalences. Mean systolic and diastolic blood pressures were significantly different between the four diet groups, with meat eaters having the highest values and vegans the lowest values. The differences in age-adjusted mean blood pressure between meat eaters and vegans among participants with no self-reported hypertension were 4.2 and 2.6 mmHg systolic and 2.8 and 1.7 mmHg diastolic for men and women, respectively. Much of the variation was attributable to differences in body mass index between the diet groups. **CONCLUSIONS:** Non-meat eaters, especially vegans, have a lower prevalence of hypertension and lower systolic and diastolic blood pressures than meat eaters, largely because of differences in body mass index.

**Appel LJ, et. al. A Clinical Trial of the Effects of Dietary Patterns on Blood Pressure.** NEJM 1997;336:1117-24.

**BACKGROUND** It is known that obesity, sodium intake, and alcohol consumption influence blood pressure. In this clinical trial, Dietary Approaches to Stop Hypertension, we assessed the effects of dietary patterns on blood pressure. **METHODS** We enrolled 459 adults with systolic blood pressures of less than 160 mm Hg and diastolic blood pressures of 80 to 95 mm Hg. For three weeks, the subjects were fed a control diet that was low in fruits, vegetables, and dairy products, with a fat content typical of the average diet in the United States. They were then randomly assigned to receive for eight weeks the control diet, a diet rich in fruits and vegetables, or a "combination" diet rich in fruits, vegetables, and low-fat dairy products and with reduced saturated and total fat. Sodium intake and body weight were maintained at constant levels. **RESULTS** At base line, the mean ( $\pm$ SD) systolic and diastolic blood pressures were 131.3 $\pm$ 10.8 mm Hg and 84.7 $\pm$ 4.7 mm Hg, respectively. The combination diet reduced systolic and diastolic blood pressure by 5.5 and 3.0 mm Hg more, respectively, than the control diet ( $P < 0.001$  for each); the fruits-and-vegetables diet reduced systolic blood pressure by 2.8 mm Hg more ( $P < 0.001$ ) and diastolic blood pressure by 1.1 mm Hg more ( $P = 0.07$ ) than the control diet. Among the 133 subjects with hypertension (systolic pressure,  $>140$  mm Hg; diastolic pressure,  $>90$  mm Hg; or both), the combination diet reduced systolic and diastolic blood pressure by 11.4 and 5.5 mm Hg more, respectively, than the control diet ( $P < 0.001$  for each); among the 326 subjects without hypertension, the corresponding reductions were 3.5 mm Hg ( $P < 0.001$ ) and 2.1 mm Hg ( $P = 0.003$ ). **CONCLUSIONS** A diet rich in fruits, vegetables, and low-fat dairy foods and with reduced saturated and total fat can substantially

lower blood pressure. This diet offers an additional nutritional approach to preventing and treating hypertension.

**Moore TJ, et al. DASH (Dietary Approaches to Stop Hypertension) diet is effective treatment for stage 1 isolated systolic hypertension.** *Hypertension* 2001 Aug;38:155-8.

**BACKGROUND** Use of the DASH (Dietary Approaches to Stop Hypertension) diet, which is rich in fruits, vegetables, and low-fat dairy foods, significantly lowers blood pressure. **PARTICIPANTS** Among the 459 participants in the DASH Trial, 72 had stage 1 isolated systolic hypertension (ISH) (systolic blood pressure, 140 to 159 mm Hg; diastolic blood pressure, <90 mm Hg). **METHODS** We examined the blood pressure response in these 72 participants to determine whether the DASH diet is an effective treatment for stage 1 ISH. After a 3-week run-in period on a typical American (control) diet, participants were randomly assigned for 8 weeks to 1 of 3 diets: a continuation of the control diet (n=25), a diet rich in fruits and vegetables (n=24), or the DASH diet (n=23). Sodium content was the same in the 3 diets, and caloric intake was adjusted during the trial to prevent weight change. Blood pressure was measured at baseline and at the end of the 8-week intervention period with standard sphygmomanometry. **RESULTS** Use of the DASH diet significantly lowered systolic blood pressure compared with the control diet (-11.2 mm Hg; 95% confidence interval, -6.1 to -16.2 mm Hg;  $P<0.001$ ) and the fruits/vegetables diet (-8.0 mm Hg; 95% confidence interval, -2.5 to -13.4 mm Hg;  $P<0.01$ ). Overall, blood pressure in the DASH group fell from 146/85 to 134/82 mm Hg. Similar results were observed with 24-hour ambulatory blood pressure measurements. In the DASH diet group, 18 of 23 participants (78%) reduced their systolic blood pressure to <140 mm Hg, compared with 24% and 50% in the control and fruits/vegetables groups, respectively. **CONCLUSIONS** Our results indicate that the DASH diet, which is rich in fruits, vegetables, and low-fat dairy foods, is effective as first-line therapy in stage 1 ISH.

**Appel LJ, et. al. Effects of comprehensive lifestyle modification on blood pressure control: main results of the PREMIER clinical trial.** *JAMA* 2003 Apr 23/30;289(16):2083-93.

**CONTEXT:** Weight loss, sodium reduction, increased physical activity, and limited alcohol intake are established recommendations that reduce blood pressure (BP). The Dietary Approaches to Stop Hypertension (DASH) diet also lowers BP. To date, no trial has evaluated the effects of simultaneously implementing these lifestyle recommendations. **OBJECTIVE:** To determine the effect on BP of 2 multi-component, behavioral interventions. **DESIGN, SETTING, AND PARTICIPANTS:** Randomized trial with enrollment at 4 clinical centers (January 2000-June 2001) among 810 adults (mean [SD] age, 50 [8.9] years; 62% women; 34% African American) with above-optimal BP, including stage 1 hypertension (120-159 mm Hg systolic and 80-95 mm Hg diastolic), and who were not taking anti-hypertensive medications. **INTERVENTION:** Participants were randomized to one of 3 intervention groups: (1) "established," a behavioral intervention that implemented established recommendations (n = 268); (2) "established plus DASH," which also implemented the DASH diet (n = 269); and (3) an "advice only" comparison group (n = 273). **MAIN OUTCOME MEASURES:** Blood pressure measurement and hypertension status at 6 months. **RESULTS:** Both behavioral interventions significantly reduced weight, improved fitness, and lowered sodium intake. The established plus DASH intervention also increased fruit, vegetable, and dairy intake. Across the groups, gradients in BP and hypertensive status were evident. After subtracting change in advice only, the mean net reduction in systolic BP was 3.7 mm Hg ( $P<.001$ ) in the established group and 4.3 mm Hg ( $P<.001$ ) in the established plus DASH group; the systolic BP difference between the established and established plus DASH groups was 0.6 mm Hg ( $P = .43$ ). Compared with the baseline hypertension prevalence of 38%, the prevalence at 6 months was 26% in the advice only group, 17% in the established group ( $P = .01$  compared with the advice only group), and 12% in the established plus DASH group ( $P<.001$  compared with the advice only group;  $P = .12$  compared with the established group). The prevalence of optimal BP (<120 mm Hg systolic and <80 mm Hg diastolic) was 19% in the advice only group, 30% in the established group ( $P = .005$  compared with the advice only group), and 35% in the established plus DASH group ( $P<.001$  compared with the advice only group;  $P = .24$  compared with the established group). **CONCLUSION:** Individuals with above-optimal BP, including stage 1 hypertension, can make multiple lifestyle changes that lower BP and reduce their cardiovascular disease risk.

## Type-2 diabetes

**Jiang**, et al. **Nut** and peanut butter consumption and risk of type 2 **diabetes** in women. *JAMA*. 2002 Nov 27;288(20):2554-60.

CONTEXT: Nuts are high in unsaturated (polyunsaturated and monounsaturated) fat and other nutrients that may improve glucose and insulin homeostasis. OBJECTIVE: To examine prospectively the relationship between nut consumption and risk of type 2 diabetes. DESIGN, SETTING, AND PARTICIPANTS: Prospective cohort study of 83 818 women from 11 states in the Nurses' Health Study. The women were aged 34 to 59 years, had no history of diabetes, cardiovascular disease, or cancer, completed a validated dietary questionnaire at baseline in 1980, and were followed up for 16 years. MAIN OUTCOME MEASURE: Incident cases of type 2 diabetes. RESULTS: We documented 3206 new cases of type 2 diabetes. Nut consumption was inversely associated with risk of type 2 diabetes after adjustment for age, body mass index (BMI), family history of diabetes, physical activity, smoking, alcohol use, and total energy intake. The multivariate relative risks (RRs) across categories of nut consumption (never/almost never, <once/week, 1-4 times/week, and > or =5 times/week) for a 28-g (1 oz) serving size were 1.0, 0.92 (95% confidence interval [CI], 0.85-1.00), 0.84 (0.95% CI, 0.76-0.93), and 0.73 (95% CI, 0.60-0.89) (P for trend <.001). Further adjustment for intakes of dietary fats, cereal fiber, and other dietary factors did not appreciably change the results. The inverse association persisted within strata defined by levels of BMI, smoking, alcohol use, and other diabetes risk factors. Consumption of peanut butter was also inversely associated with type 2 diabetes. The multivariate RR was 0.79 (95% CI, 0.68-0.91; P for trend <.001) in women consuming peanut butter 5 times or more a week (equivalent to > or =140 g [5 oz] of peanuts/week) compared with those who never/almost never ate peanut butter. CONCLUSIONS: Our findings suggest potential benefits of higher nut and peanut butter consumption in lowering risk of type 2 diabetes in women. To avoid increasing caloric intake, regular nut consumption can be recommended as a replacement for consumption of refined grain products or red or processed meats.

**Steyn NP**, et al. Diet, **nutrition** and the prevention of type 2 **diabetes**. *Public Health Nutr*. 2004 Feb;7(1A):147-65.

OBJECTIVES: The overall objective of this study was to evaluate and provide evidence and recommendations on current published literature about diet and lifestyle in the prevention of type 2 diabetes. DESIGN: Epidemiological and experimental studies, focusing on nutritional intervention in the prevention of type 2 diabetes are used to make disease-specific recommendations. Long-term cohort studies are given the most weight as to strength of evidence available. SETTING AND SUBJECTS: Numerous clinical trials and cohort studies in low, middle and high income countries are evaluated regarding recommendations for dietary prevention of type 2 diabetes. These include, among others, the Finnish Diabetes Prevention Study, US Diabetes Prevention Program, Da Qing Study; Pima Indian Study; Iowa Women's Health Study; and the study of the US Male Physicians. RESULTS: There is convincing evidence for a decreased risk of diabetes in adults who are physically active and maintain a normal body mass index (BMI) throughout adulthood, and in overweight adults with impaired glucose tolerance who lose weight voluntarily. An increased risk for developing type 2 diabetes is associated with overweight and obesity; abdominal obesity; physical inactivity; and maternal diabetes. It is probable that a high intake of saturated fats and intrauterine growth retardation also contribute to an increased risk, while non-starch polysaccharides are likely to be associated with a decreased risk. From existing evidence it is also possible that omega-3 fatty acids, low glycaemic index foods and exclusive breastfeeding may play a protective role, and that total fat intake and trans fatty acids may contribute to the risk. However, insufficient evidence is currently available to provide convincing proof. CONCLUSIONS: Based on the strength of available evidence regarding diet and lifestyle in the prevention of type 2 diabetes, it is recommended that a normal weight status in the lower BMI range (BMI 21-23) and regular physical activity be maintained throughout adulthood; abdominal obesity be prevented; and saturated fat intake be less than 7% of the total energy intake.

**Hu FB**, et al. Diet, **lifestyle**, and the risk of type 2 **diabetes** mellitus in women. *NEJM*. 2001 Sep 13;345(11):790-7.

**BACKGROUND:** Previous studies have examined individual dietary and lifestyle factors in relation to type 2 diabetes, but the combined effects of these factors are largely unknown. **METHODS:** We followed 84,941 female nurses from 1980 to 1996; these women were free of diagnosed cardiovascular disease, diabetes, and cancer at base line. Information about their diet and lifestyle was updated periodically. A low-risk group was defined according to a combination of five variables: a bodymass index (the weight in kilograms divided by the square of the height in meters) of less than 25; a diet high in cereal fiber and polyunsaturated fat and low in trans fat and glycemic load (which reflects the effect of diet on the blood glucose level); engagement in moderate-to-vigorous physical activity for at least half an hour per day; no current smoking; and the consumption of an average of at least half a drink of an alcoholic beverage per day. **RESULTS:** During 16 years of follow-up, we documented 3300 new cases of type 2 diabetes. Overweight or obesity was the single most important predictor of diabetes. Lack of exercise, a poor diet, current smoking, and abstinence from alcohol use were all associated with a significantly increased risk of diabetes, even after adjustment for the body-mass index. As compared with the rest of the cohort, women in the low-risk group (3.4 percent of the women) had a relative risk of diabetes of 0.09 (95 percent confidence interval, 0.05 to 0.17). A total of 91 percent of the cases of diabetes in this cohort (95 percent confidence interval, 83 to 95) could be attributed to habits and forms of behavior that did not conform to the low-risk pattern. **CONCLUSIONS:** Our findings support the hypothesis that the vast majority of cases of type 2 diabetes could be prevented by the adoption of a healthier lifestyle.

**Jenkins**, et al. Type 2 diabetes and the **vegetarian** diet. *Am J Clin Nutr.* 2003 Sep;78(3 Suppl):610S-616S.

Based on what is known of the components of plant-based diets and their effects from cohort studies, there is reason to believe that vegetarian diets would have advantages in the treatment of type 2 diabetes. At present there are few data on vegetarian diets in diabetes that do not in addition have weight loss or exercise components. Nevertheless, the use of whole-grain or traditionally processed cereals and legumes has been associated with improved glycemic control in both diabetic and insulin-resistant individuals. Long-term cohort studies have indicated that whole-grain consumption reduces the risk of both type 2 diabetes and cardiovascular disease. In addition, nuts (eg, almonds), viscous fibers (eg, fibers from oats and barley), soy proteins, and plant sterols, which may be part of the vegetarian diet, reduce serum lipids. In combination, these plant food components may have a very significant impact on cardiovascular disease, one of the major complications of diabetes. Furthermore, substituting soy or other vegetable proteins for animal protein may also decrease renal hyperfiltration, proteinuria, and renal acid load and in the long term reduce the risk of developing renal disease in type 2 diabetes. The vegetarian diet, therefore, contains a portfolio of natural products and food forms of benefit for both the carbohydrate and lipid abnormalities in diabetes. It is anticipated that their combined use in vegetarian diets will produce very significant metabolic advantages for the prevention and treatment of diabetes and its complications.

**Lee** DH, et al. Association between serum gamma-glutamyltransferase and dietary factors: the Coronary Artery Risk Development in Young Adults (**CARDIA**) Study. *AJCN.* 2004 Apr;79(4):600-5.

**BACKGROUND:** Diet may be involved in the strong dose-response relation of gamma-glutamyltransferase (GGT) concentration with incident diabetes. **OBJECTIVE:** We examined dietary correlates of serum GGT activity. **DESIGN:** Study subjects were 3146 black and white men and women aged 17-35 y in 1985-1986. A diet history was taken at years 0 and 7. Food items were classified into alcohol; breaded, battered, or canned vegetables; fruit; fruit juice; refined grain; whole grain; dairy; legumes; meat; poultry; fish; fresh or frozen vegetables; nuts; and coffee. **RESULTS:** After adjustment for nondietary factors and other food groups, GGT was positively associated with alcohol consumption and meat intake. Geometric means of year 10 GGT across categories of alcohol consumption (0, 1-9, 10-19, 20-29, and  $\geq 30$  g/d) were 17.7, 18.8, 20.4, 21.8, and 24.8 U/L (P for trend  $< 0.01$ ); corresponding means across quintiles of meat intake were 19.2, 20.2, 20.5, 21.8, and 21.2 times/wk (P for trend  $< 0.01$ ). GGT was inversely associated with fruit intake. Among possible meat constituents, dietary heme iron, but not saturated fat, was associated with GGT. Dietary constituents typical of plant foods showed an inverse association. In contrast, vitamin supplements were positively associated with GGT. **CONCLUSIONS:** Serum GGT activity increased in a dose-response manner as alcohol and meat consumption increased

and fruit consumption decreased. Heme iron contained in meats and micronutrients contained in fruits may influence GGT metabolism. However, micronutrients taken as supplements had a positive association with GGT.

**Tuomilehto J, et al.** Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. **FDPS NEJM.** 2001 May 3;344(18):1343-50.

**BACKGROUND:** Type 2 diabetes mellitus is increasingly common, primarily because of increases in the prevalence of a sedentary lifestyle and obesity. Whether type 2 diabetes can be prevented by interventions that affect the lifestyles of subjects at high risk for the disease is not known. **METHODS:** We randomly assigned 522 middle-aged, overweight subjects (172 men and 350 women; mean age, 55 years; mean body-mass index [weight in kilograms divided by the square of the height in meters], 31) with impaired glucose tolerance to either the intervention group or the control group. Each subject in the intervention group received individualized counseling aimed at reducing weight, total intake of fat, and intake of saturated fat and increasing intake of fiber and physical activity. An oral glucose-tolerance test was performed annually; the diagnosis of diabetes was confirmed by a second test. The mean duration of follow-up was 3.2 years. **RESULTS:** The mean (+/-SD) amount of weight lost between base line and the end of year 1 was 4.2+/-5.1 kg in the intervention group and 0.8+/-3.7 kg in the control group; the net loss by the end of year 2 was 3.5+/-5.5 kg in the intervention group and 0.8+/-4.4 kg in the control group ( $P<0.001$  for both comparisons between the groups). The cumulative incidence of diabetes after four years was 11 percent (95 percent confidence interval, 6 to 15 percent) in the intervention group and 23 percent (95 percent confidence interval, 17 to 29 percent) in the control group. During the trial, the risk of diabetes was reduced by 58 percent ( $P<0.001$ ) in the intervention group. The reduction in the incidence of diabetes was directly associated with changes in lifestyle. **CONCLUSIONS:** Type 2 diabetes can be prevented by changes in the lifestyles of high-risk subjects.

**Knowler WC, et al.** Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. **DPP NEJM.** 2002 Feb 7;346(6):393-403.

**BACKGROUND:** Type 2 diabetes affects approximately 8 percent of adults in the United States. Some risk factors--elevated plasma glucose concentrations in the fasting state and after an oral glucose load, overweight, and a sedentary lifestyle--are potentially reversible. We hypothesized that modifying these factors with a lifestyle-intervention program or the administration of metformin would prevent or delay the development of diabetes. **METHODS:** We randomly assigned 3234 nondiabetic persons with elevated fasting and post-load plasma glucose concentrations to placebo, metformin (850 mg twice daily), or a lifestyle-modification program with the goals of at least a 7 percent weight loss and at least 150 minutes of physical activity per week. The mean age of the participants was 51 years, and the mean body-mass index (the weight in kilograms divided by the square of the height in meters) was 34.0; 68 percent were women, and 45 percent were members of minority groups. **RESULTS:** The average follow-up was 2.8 years. The incidence of diabetes was 11.0, 7.8, and 4.8 cases per 100 person-years in the placebo, metformin, and lifestyle groups, respectively. The lifestyle intervention reduced the incidence by 58 percent (95 percent confidence interval, 48 to 66 percent) and metformin by 31 percent (95 percent confidence interval, 17 to 43 percent), as compared with placebo; the lifestyle intervention was significantly more effective than metformin. To prevent one case of diabetes during a period of three years, 6.9 persons would have to participate in the lifestyle-intervention program, and 13.9 would have to receive metformin. **CONCLUSIONS:** Lifestyle changes and treatment with metformin both reduced the incidence of diabetes in persons at high risk. The lifestyle intervention was more effective than metformin.

**Pan XR, et al.** Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The **Da Qing** IGT and Diabetes Study. *Diabetes Care.* 1997 Apr;20(4):537-44.

**OBJECTIVE:** Individuals with impaired glucose tolerance (IGT) have a high risk of developing NIDDM. The purpose of this study was to determine whether diet and exercise interventions in those with IGT may delay the development of NIDDM, i.e., reduce the incidence of NIDDM, and thereby reduce the overall incidence of diabetic complications, such as cardiovascular, renal, and retinal disease, and the excess mortality attributable to these complications. **RESEARCH DESIGN AND METHODS:** In 1986, 110,660

men and women from 33 health care clinics in the city of Da Qing, China, were screened for IGT and NIDDM. Of these individuals, 577 were classified (using World Health Organization criteria) as having IGT. Subjects were randomized by clinic into a clinical trial, either to a control group or to one of three active treatment groups: diet only, exercise only, or diet plus exercise. Follow-up evaluation examinations were conducted at 2-year intervals over a 6-year period to identify subjects who developed NIDDM. Cox's proportional hazard analysis was used to determine if the incidence of NIDDM varied by treatment assignment. RESULTS: The cumulative incidence of diabetes at 6 years was 67.7% (95% CI, 59.8-75.2) in the control group compared with 43.8% (95% CI, 35.5-52.3) in the diet group, 41.1% (95% CI, 33.4-49.4) in the exercise group, and 46.0% (95% CI, 37.3-54.7) in the diet-plus-exercise group ( $P < 0.05$ ). When analyzed by clinic, each of the active intervention groups differed significantly from the control clinics ( $P < 0.05$ ). The relative decrease in rate of development of diabetes in the active treatment groups was similar when subjects were stratified as lean or overweight ( $BMI < \text{or} > \text{or} = 25 \text{ kg/m}^2$ ). In a proportional hazards analysis adjusted for differences in baseline BMI and fasting glucose, the diet, exercise, and diet-plus-exercise interventions were associated with 31% ( $P < 0.03$ ), 46% ( $P < 0.0005$ ), and 42% ( $P < 0.005$ ) reductions in risk of developing diabetes, respectively. CONCLUSIONS: Diet and/or exercise interventions led to a significant decrease in the incidence of diabetes over a 6-year period among those with IGT.

## Obesity

**Spencer EA, et al. Diet and body mass index in 38000 EPIC-Oxford meat-eaters, fish-eaters, vegetarians and vegans. Int J Obes Relat Metab Disord. 2003 Jun;27(6):728-34.**

OBJECTIVE: To compare body mass index (BMI) in four diet groups (meat-eaters, fish-eaters, vegetarians and vegans) in the Oxford cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC-Oxford) and to investigate lifestyle and dietary factors associated with any observed differences. DESIGN: Cross-sectional analysis of self-reported dietary, anthropometric and lifestyle data. PARTICIPANTS: A total of 37875 healthy men and women aged 20-97 y participating in EPIC-Oxford. RESULTS: Age-adjusted mean BMI was significantly different between the four diet groups, being highest in the meat-eaters (24.41 kg/m<sup>2</sup> in men, 23.52 kg/m<sup>2</sup> in women) and lowest in the vegans (22.49 kg/m<sup>2</sup> in men, 21.98 kg/m<sup>2</sup> in women). Fish-eaters and vegetarians had similar, intermediate mean BMI. Differences in lifestyle factors including smoking, physical activity and education level accounted for less than 5% of the difference in mean age-adjusted BMI between meat-eaters and vegans, whereas differences in macronutrient intake accounted for about half of the difference. High protein (as percent energy) and low fibre intakes were the dietary factors most strongly and consistently associated with increasing BMI both between and within the diet groups. CONCLUSIONS: Fish-eaters, vegetarians and especially vegans had lower BMI than meat-eaters. Differences in macronutrient intakes accounted for about half the difference in mean BMI between vegans and meat-eaters. High protein and low fibre intakes were the factors most strongly associated with increasing BMI.

**Trichopoulou A, et al. Lipid, protein and carbohydrate intake in relation to body mass index. Eur J Clin Nutr. 2002 Jan;56(1):37-43.**

OBJECTIVE: To examine whether the same amount of energy intake has different consequences on body mass index (BMI), depending on the source of energy from specific macronutrients. DESIGN: Cross-sectional study, in the context of the European Prospective Investigation into Cancer and nutrition (EPIC). SETTING: Communities all over Greece. SUBJECTS: A total of 27 862 apparently healthy volunteers, men and women, ages 25-82 y. INTERVENTIONS: None. METHODS: Dietary information was collected through an interviewer-administered semi-quantitative food frequency questionnaire. In the context of a cross-sectional analysis, we calculated changes of BMI per increments of energy intake from protein, carbohydrates, saturated, polyunsaturated and monounsaturated lipids and ethanol, controlling for mutual confounding and other confounders, among all participants, and after exclusion of under-reporters and/or those on a diet. RESULTS: Protein intake was positively associated with BMI. The association was evident when nutrients were not mutually adjusted for and increased after mutual adjustment among nutrients (beta=0.80 kg/m<sup>2</sup> per 418.4 kJ or 100 kcal increment, 95% confidence interval 0.55-1.06 for men, and beta=1.59, 95% CI 1.30-1.88 for women), as well as after exclusion of

under-reporters and/or those on a diet. The effects of other macronutrients were less substantial or consistent. **CONCLUSIONS:** There is evidence indicating that protein intake is conducive to obesity. Moreover, our data suggest that neither saturated or monounsaturated lipids nor carbohydrates are likely to play a major role in increasing BMI over and beyond that indicated by their energy content.

## Cancer

**Thorogood M, et al.** Risk of death from cancer and ischaemic heart disease in meat and **non-meat eaters**. *BMJ*. 1994 Jun 25;308(6945):1667-70.

**OBJECTIVE--**To investigate the health consequences of a vegetarian diet by examining the 12 year mortality of non-meat eaters and meat eating controls. **DESIGN--**Prospective observational study in which members of the non-meat eating cohort were asked to nominate friends or relatives as controls. **SETTING--**United Kingdom. **SUBJECTS--**6115 non-meat eaters identified through the Vegetarian Society of the United Kingdom and the news media (mean (SD) age 38.7 (16.8) years) and 5015 controls who were meat eaters (39.3 (15.4) years). **MAIN OUTCOME MEASURES--**Standardised mortality ratios for cancer, ischaemic heart disease, and total mortality in the two cohorts and death rate ratio in the non-meat eaters compared with meat eaters after adjustment for potentially confounding variables. **RESULTS--**Standardised mortality ratios (taking the value among the general population as 100) for ischaemic heart disease were 51 (95% confidence interval 38 to 66) for meat eaters and 28 (20 to 38) for non-meat eaters ( $P < 0.01$ ). Values for all cancers were 80 (64 to 98) and 50 (39 to 62) for meat eaters and non-meat eaters respectively. After adjustment for the effects of smoking, body mass index, and socioeconomic status death rate ratios in non-meat eaters compared with meat eaters were 0.72 (0.47 to 1.10) for ischaemic heart disease and 0.61 (0.44 to 0.84) for all cancers. **CONCLUSIONS--**The reduced mortality from cancer among those not eating meat is not explained by lifestyle related risk factors, which have a low prevalence among vegetarians. No firm conclusion can be made about deaths from ischaemic heart disease. These data do not justify advice to exclude meat from the diet since there are several attributes of a vegetarian diet apart from not eating meat which might reduce the risk.

**Key TJ, Fraser GE, et al.** Mortality in **vegetarians** and nonvegetarians: detailed findings from a **collaborative** analysis of 5 prospective studies. *AJCN*. 1999 Sep;70(3 Suppl):516S-524S.

We combined data from 5 prospective studies to compare the death rates from common diseases of vegetarians with those of nonvegetarians with similar lifestyles. A summary of these results was reported previously; we report here more details of the findings. Data for 76172 men and women were available. Vegetarians were those who did not eat any meat or fish ( $n = 27808$ ). Death rate ratios at ages 16-89 y were calculated by Poisson regression and all results were adjusted for age, sex, and smoking status. A random-effects model was used to calculate pooled estimates of effect for all studies combined. There were 8330 deaths after a mean of 10.6 y of follow-up. Mortality from ischemic heart disease was 24% lower in vegetarians than in nonvegetarians (death rate ratio: 0.76; 95% CI: 0.62, 0.94;  $P < 0.01$ ). The lower mortality from ischemic heart disease among vegetarians was greater at younger ages and was restricted to those who had followed their current diet for  $>5$  y. Further categorization of diets showed that, in comparison with regular meat eaters, mortality from ischemic heart disease was 20% lower in occasional meat eaters, 34% lower in people who ate fish but not meat, 34% lower in lactoovovegetarians, and 26% lower in vegans. There were no significant differences between vegetarians and nonvegetarians in mortality from cerebrovascular disease, stomach cancer, colorectal cancer, lung cancer, breast cancer, prostate cancer, or all other causes combined.

## Longevity

**Seccareccia F, et al.** **Vegetable** intake and long-term survival among middle-aged men in Italy. *Ann Epidemiol*. 2003 Jul;13(6):424-30.

**PURPOSE:** To examine prospectively the relationship between vegetable consumption and long-term survival. **METHODS:** In 1965, a total of 1536 Italian males from two Italian rural cohorts of the Seven Countries Study, aged 45-65 years, were examined. Information on lifestyle and food consumption

collected at this visit, and total and cause-specific mortality data collected in 30 years of follow-up were analyzed for the present study. **RESULTS:** During a period of 30 years, 1096 deaths occurred (308 from coronary heart disease, 325 from cancer, 158 from cerebrovascular disease and 305 from all other causes). The age-adjusted life expectancy for men consuming more than 60 g/day of vegetables was nearly 2 years longer than for men consuming less than 20 g/day. This increase in survival was more striking in smokers than nonsmokers (2.1 vs. a 1 year gain). The association also held for both geographic cohorts, although the pattern of vegetable consumption was very different in the two villages. **CONCLUSIONS:** The results suggest a positive association between vegetable intake and life expectancy. Vegetable intake may be especially protective for smokers although the biological explanation for such an effect is unclear.

**Strandhagen E, et al.** High **fruit** intake may reduce mortality among middle-aged and elderly men. The Study of Men Born in 1913. *Eur J Clin Nutr.* 2000 Apr;54(4):337-41.

**OBJECTIVE:** A number of long-term population-based studies have tried to study fruit and vegetable consumption in relation to cardiovascular disease, cancer and total mortality. Few of these studies are based on randomly selected population samples. The aim of the study was to investigate the long-term effect of fruit and vegetable consumption on mortality, cardiovascular disease, cardiovascular death, cancer morbidity and cancer death among middle-aged and elderly men. **DESIGN:** Prospective cohort study. **SETTING:** General community. The Study of Men Born in 1913. **SUBJECTS:** 792 men at age 54 who participated in a screening examination in 1967. **MAIN OUTCOME MEASURES:** A food frequency questionnaire was used to obtain information of the dietary habits in 730 of the men (92%). All men were followed up with repeated examinations until the age of 80. **RESULTS:** Cardiovascular as well as total mortality was significantly lower among men with high fruit consumption in univariate analysis. There was no correlation between fruit or vegetable consumption in relation to cancer incidence, cancer death and cardiovascular disease. In multivariate survival analysis where smoking, cholesterol and hypertension were taken into account, there was a significantly lower mortality among men with a high fruit consumption during 16 y follow up until the age of 70 ( $P=0.042$ ), but this finding was no longer statistically significant during 26 y follow-up at the age of 80 ( $P=0.051$ ). **CONCLUSIONS:** Daily fruit consumption seems to have positive effect on long-term survival independently of other traditional cardiovascular risk factors like smoking, hypertension and cholesterol. **SPONSORSHIP:** This study was supported by grants from the Swedish Medical Research Council (K98-274-06276-17) King Gustav V and Queen Victoria's Foundation, and the Goteborg University.

## **Rheumatoid arthritis**

**Hafstrom I, et al.** A **vegan** diet free of gluten improves the signs and symptoms of rheumatoid arthritis: the effects on arthritis correlate with a reduction in antibodies to food antigens. *Rheumatology (Oxford).* 2001 Oct;40(10):1175-9.

**OBJECTIVE:** Whether food intake can modify the course of rheumatoid arthritis (RA) is an issue of continued scientific and public interest. However, data from controlled clinical trials are sparse. We thus decided to study the clinical effects of a vegan diet free of gluten in RA and to quantify the levels of antibodies to key food antigens not present in the vegan diet. **METHODS:** Sixty-six patients with active RA were randomized to either a vegan diet free of gluten (38 patients) or a well-balanced non-vegan diet (28 patients) for 1 yr. All patients were instructed and followed-up in the same manner. They were analysed at baseline and after 3, 6 and 12 months, according to the response criteria of the American College of Rheumatology (ACR). Furthermore, levels of antibodies against gliadin and beta-lactoglobulin were assessed and radiographs of the hands and feet were performed. **RESULTS:** Twenty-two patients in the vegan group and 25 patients in the non-vegan diet group completed 9 months or more on the diet regimens. Of these diet completers, 40.5% (nine patients) in the vegan group fulfilled the ACR20 improvement criteria compared with 4% (one patient) in the non-vegan group. Corresponding figures for the intention to treat populations were 34.3 and 3.8%, respectively. The immunoglobulin G (IgG) antibody levels against gliadin and beta-lactoglobulin decreased in the responder subgroup in the vegan diet-treated patients, but not in the other analysed groups. No retardation of radiological destruction was apparent in any of the groups. **CONCLUSION:** The data provide evidence that dietary modification may

be of clinical benefit for certain RA patients, and that this benefit may be related to a reduction in immunoreactivity to food antigens eliminated by the change in diet.

**McDougall J**, et al. Effects of a very low-fat, **vegan** diet in subjects with rheumatoid arthritis. *J Altern Complement Med.* 2002 Feb;8(1):71-5.

**OBJECTIVE:** To demonstrate the effects of a very low-fat, vegan diet on patients with rheumatoid arthritis (RA). **DESIGN:** Single-blind dietary intervention study. **SUBJECTS AND STUDY INTERVENTIONS:** This study evaluated the influence of a 4-week, very low-fat (approximately 10%), vegan diet on 24 free-living subjects with RA, average age, 56 +/- 11 years old. Outcome measurements: Prestudy and poststudy assessment of RA symptomatology was performed by a rheumatologist blind to the study design. Biochemical measures and 4-day diet data were also collected. Subjects met weekly for diet instruction, compliance monitoring, and progress assessments. **RESULTS:** There were significant ( $p < 0.001$ ) decreases in fat (69%), protein (24%), and energy (22%), and a significant increase in carbohydrate (55%) intake. All measures of RA symptomatology decreased significantly ( $p < 0.05$ ), except for duration of morning stiffness ( $p > 0.05$ ). Weight also decreased significantly ( $p < 0.001$ ). At 4 weeks, C-reactive protein decreased 16% (ns,  $p > 0.05$ ), RA factor decreased 10% (ns,  $p > 0.05$ ), while erythrocyte sedimentation rate was unchanged ( $p > 0.05$ ). **CONCLUSION:** This study showed that patients with moderate-to-severe RA, who switch to a very low-fat, vegan diet can experience significant reductions in RA symptoms.

**Muller H**, de Toledo FW, Resch KL. **Fasting** followed by **vegetarian** diet in patients with rheumatoid arthritis: a systematic review. *Scand J Rheumatol.* 2001;30(1):1-10.

Clinical experience suggests that fasting followed by vegetarian diet may help patients with rheumatoid arthritis (RA). We reviewed the available scientific evidence, because patients frequently ask for dietary advice, and exclusive pharmacological treatment of RA is often not satisfying. Fasting studies in RA were searched in MEDLINE and by checking references in relevant reports. The results of the controlled studies which reported follow-up data for at least three months after fasting were quantitatively pooled. Thirty-one reports of fasting studies in patients with RA were found. Only four controlled studies investigated the effects of fasting and subsequent diets for at least three months. The pooling of these studies showed a statistically and clinically significant beneficial long-term effect. Thus, available evidence suggests that fasting followed by vegetarian diets might be useful in the treatment of RA. More randomised long-term studies are needed to confirm this view by methodologically convincing data.

**Kjeldsen-Kragh J**. Rheumatoid arthritis treated with **vegetarian** diets. *AJCN.* 1999 Sep;70(3 Suppl):594S-600S.

The notion that dietary factors may influence rheumatoid arthritis (RA) has been a part of the folklore of the disease, but scientific support for this has been sparse. In a controlled, single-blind trial we tested the effect of fasting for 7-10 d, then consuming an individually adjusted, gluten-free, vegan diet for 3.5 mo, and then consuming an individually adjusted lactovegetarian diet for 9 mo on patients with RA. For all clinical variables and most laboratory variables measured, the 27 patients in the fasting and vegetarian diet groups improved significantly compared with the 26 patients in the control group who followed their usual omnivorous diet throughout the study period. One year after the patients completed the trial, they were reexamined. Compared with baseline, the improvements measured were significantly greater in the vegetarians who previously benefited from the diet (diet responders) than in diet nonresponders and omnivores. The beneficial effect could not be explained by patients' psychologic characteristics, antibody activity against food antigens, or changes in concentrations of prostaglandin and leukotriene precursors. However, the fecal flora differed significantly between samples collected at time points at which there was substantial clinical improvement and time points at which there were no or only minor improvements. In summary, the results show that some patients with RA can benefit from a fasting period followed by a vegetarian diet. Thus, dietary treatment may be a valuable adjunct to the ordinary therapeutic armamentarium for RA.