

## Special Reports

### **Integrating the Totality of Food and Nutrition Evidence for Public Health Decision Making and Communication**

Navia JL, Byers T, Djordjevic D, Hentges E, King J, Klurfeld D, Llewellyn C, Milner J, Skrypec D, Weed D.

*Critical Reviews in Food Science and Nutrition*

Supported by the ILSI North America [Committee on Food and Chemical Safety](#), [Committee on Carbohydrates](#), and [Committee on Dietary Lipids](#)

For open-access: <http://www.informaworld.com/smpp/content~db=all~content=a930670477~frm=abslink>

**Significance:** This supplement includes a summary paper and expanded abstracts from an ILSI North America Workshop during which participants representing the nutrition and food safety communities in academia, industry, and government shared current practices in the interpretation of weak epidemiological associations, and explored avenues for appropriate interpretation and integration of animal study data, human intervention, and epidemiological data in the formulation of dietary advice for the public.

The interpretation and integration of epidemiological studies detecting weak associations ( $RR < 2$ ) with data from other study designs (e.g., animal models and human intervention trials) is both challenging and vital for making science-based dietary recommendations in the nutrition and food safety communities. The 2008 ILSI North America “Decision-Making for Recommendations and Communication Based on Totality of Food-Related Research” workshop provided an overview of epidemiological methods, and case-study examples of how weak associations have been incorporated into decision making for nutritional recommendations. Based on the workshop presentations and dialogue among the participants, three clear strategies were provided for the use of weak associations in informing nutritional recommendations for optimal health. First, enable more effective integration of data from all sources through the use of genetic and nutritional biomarkers; second, minimize the risk of bias and confounding through the adoption of rigorous quality-control standards, greater emphasis on the replication of study results, and better integration of results from independent studies, perhaps using adaptive study designs and Bayesian meta-analysis methods; and third, emphasize more effective and truthful communication to the public about the evolving understanding of the often complex relationship between nutrition, lifestyle, and optimal health.

### **Feeding the World Today and Tomorrow: The Importance of Food Science and Technology**

J.D. Floros, R. Newsome, W. Fisher, G.V. Barbosa-Cánovas, H. Chen, C.P. Dunne, et al.

*Comprehensive Reviews in Food Science and Food Safety*, Vol. 9, No. 5, pp. 572–599, September 2010

Link to full text: <http://www.ift.org/knowledge-center/read-ift-publications/science-reports/ift-scientific-review-feeding-the-world-today-and-tomorrow.aspx>

**Significance:** This report takes a historical look at the food system, the many challenges ahead, and the crucial role of food science and technology in meeting the needs of a growing world population.

The Institute of Food Technologists produced a scientific report to inform the public about the advances in food science and technology that are necessary to meet the needs of an evolving society, which today has much greater access to an abundant, diverse food supply that is largely safe, flavorful, nutritious, convenient, and less costly than ever before. This report summarizes the historical developments of agriculture and food technology, details various food manufacturing methods, and explains why food is processed. This report also describes and stresses why further advancements in food science and technology are needed—to more equitably meet growing world population food needs with enhanced food security in developing countries and solutions to complex diet-and-health challenges in industrialized countries. This report states that scientific and technological advancements must be accelerated and applied in developed and developing nations alike, if we are to feed a growing world population.

## Metabolic Syndrome

### Long-Term Effect of Betaine on Risk Factors Associated with the Metabolic Syndrome in Healthy Subjects

U. Schwab, G. Alfthan, A. Aro, M. Uusitupa

*European Journal of Clinical Nutrition*, Vol. 65, No. 1; pp. 70–76, 2011

Link to full text: <http://www.nature.com/ejcn/journal/v65/n1/full/ejcn2010230a.html>

**Significance:** Betaine had no effect on serum lipid profile in the long term in healthy subjects.

The effects of betaine on serum lipid profile, plasma homocysteine concentration and hemostatic factors were examined in a placebo-controlled, randomized, parallel double-blinded study. Sixty-three healthy subjects consumed mineral water 500mL/day with (betaine group,  $n=32$ ) or without (control group,  $n=31$ ) a 4-g betaine supplementation for 6 months. There was a significant interaction of time and group in serum total- and LDL-cholesterol concentrations and total-to-HDL-cholesterol ratio without a significant difference between or within the groups. Concentrations of HDL-cholesterol, triglycerides or oxidized LDL did not change during the study. Plasma homocysteine concentration did not change in either of the groups. Plasma plasminogen activator inhibitor 1 concentration increased in the betaine group ( $P=0.028$ ) and decreased in the control group ( $P=0.006$ ). There was a significant interaction of time and group in plasma fibrinogen and blood hemoglobin concentration without a significant difference between or within the groups.

## Cardiovascular Disease

### A Dose-Finding Trial of the Effect of Long-Term Folic Acid Intervention: Implications for Food Fortification Policy

P. Tighe, M. Ward, H. McNulty, O. Finnegan, A. Dunne, J.J. Strain, et al.

*American Journal of Clinical Nutrition*, Vol. 93, No. 1; pp. 11-18, 2011

Link to full text: <http://www.ajcn.org/content/93/1/11.full>

**Significance:** A folic acid dose as low as 0.2 mg/day can, if administered for 6 mos., effectively lower homocysteine concentrations.

The effectiveness of folic acid to lower homocysteine concentrations was examined in this randomized dose-finding trial. Of 203 participants screened, 101 patients with ischemic heart disease and 71 healthy volunteers completed the study. Participants were randomly assigned to receive placebo or folic acid at doses of 0.2, 0.4, or 0.8 mg/day for 26 wks; subsamples of patients with ischemic heart disease were also examined at 6 or 12 wks. Participants with higher baseline homocysteine concentrations had the greatest reductions in homocysteine in response to folic acid doses of 0.2 mg (−20.6%), 0.4 mg (−20.7%), and 0.8 mg (−27.8%); in those with lower baseline homocysteine concentrations, the responses were −8.2%, −8.9%, and −8.3%, respectively. In the patient group sampled at intervals during the intervention, the maximal homocysteine response appeared to be achieved by 6 wks in the 0.8-mg/day group and by 12 wks in the 0.4-mg/day group. However, the homocysteine response was suboptimal in the 0.2-mg/day group at both 6 and 12 wks compared with that at 26 wks.

### Fish Consumption and Myocardial Infarction: A Second Prospective Biomarker Study From Northern Sweden

M. Wennberg, I.A. Bergdahl, G. Hallmans, M. Norberg, T. Lundh, S. Skerfving, et al.

*American Journal of Clinical Nutrition*, Vol. 93, No. 1; pp. 27-36, 2011

Link to full text: <http://www.ajcn.org/content/93/1/27.full>

**Significance:** The biomarker results indicated a protective effect of fish consumption and no harmful effect of mercury in this low-exposed population.

This case-control study nested within the northern Sweden cohort, in which data and samples were collected prospectively, determined how fish consumption and erythrocyte concentrations of mercury (Ery-Hg) and selenium (Ery-Se) are related to the risk of myocardial infarction (MI) and whether omega 3 (n-3) fatty acids (eicosapentaenoic and docosahexaenoic acids) in plasma phospholipids (P-EPA+DHA) are protective. The study included 431 cases with an MI after data and sample collection, including 81 sudden cardiac deaths (SCDs) and 499 matched controls. Another 69 female cases with controls from a breast cancer screening registry were included in sex-specific analyses. Odds ratios for the third compared with the first tertile were 0.65 (95% CI: 0.46, 0.91) for Ery-Hg, 0.75 (95% CI: 0.53, 1.06) for Ery-Se, and 0.78 (95% CI: 0.54, 1.11) for P-EPA+DHA. Ery-Hg and P-

EPA+DHA were intercorrelated (Spearman's  $R=0.34$ ). Sex-specific analyses showed no differences in risk associations. High concentrations of Ery-Se were associated with an increased risk of SCD.

### **Milk and Dairy Consumption and Incidence of Cardiovascular Diseases and All-Cause Mortality: Dose-Response Meta-Analysis of Prospective Cohort Studies**

S.S. Soedamah-Muthu, E.L. Ding, W.K. Al-Delaimy, F.B. Hu, M.F. Engberink, W.C. Willett, et al.

*American Journal of Clinical Nutrition*, Vol. 93, No. 1; pp. 158-171, 2011

Link to full text: <http://www.ajcn.org/content/93/1/158.full>

**Significance:** Milk intake is not associated with total mortality but may be inversely associated with overall CVD risk.

This meta-analysis examined the associations of milk, total dairy products, and high- and low-fat dairy intakes with the risk of cardiovascular disease (CVD), including coronary heart disease (CHD) and stroke, and total mortality. Databases were searched for articles published through February 2010. Of >5000 titles evaluated, 17 met the inclusion criteria, all of which were original prospective cohort studies. In 17 studies, there were 2283 CVD, 4391 CHD, 15,554 stroke, and 23,949 mortality cases. A modest inverse association was found between milk intake and risk of overall CVD [4 studies; RR per 200 mL/d = 0.94; 95% CI=0.89, 0.99]. Milk intake was not associated with risk of CHD (6 studies; RR=1.00; 95% CI=0.96, 1.04), stroke (6 studies; RR=0.87; 95% CI=0.72, 1.05), or total mortality (8 studies; RR per 200 mL/d = 0.99; 95% CI=0.95, 1.03). Limited studies of the association of total dairy products and of total high-fat and total low-fat dairy products (per 200 g/d) with CHD showed no significant associations.

### **Total Antioxidant Capacity of the Diet is Associated with Lower Risk of Ischemic Stroke in a Large Italian Cohort**

D. Del Rio, C. Agnoli, N. Pellegrini, V. Krogh, F. Brighenti, T. Mazzeo, et al.

*Journal of Nutrition*, Vol. 141, No. 1; pp. 118-123, 2011

Link to full text: <http://jn.nutrition.org/content/141/1/118.full>

**Significance:** Antioxidants may play a role in reducing the risk of cerebral infarction but not hemorrhagic stroke.

The relation between dietary total antioxidant capacity (TAC) and risk of ischemic and hemorrhagic stroke in 41,620 men and women not previously diagnosed with stroke or myocardial infarction were investigated. The subjects represented the Italian segment of the European Prospective Investigation into Cancer and Nutrition. Controlling for potential confounders, a diet rich in TAC was associated with a reduction in hazard ratio (HR) for all types of stroke, but this association was only marginally significant (P-trend = 0.054). When only ischemic stroke cases were considered, data suggest a stronger inverse association with dietary TAC, with HR=0.41 (95% CI=0.23–0.74). Regarding single antioxidants, data from sub-analyses on stroke types suggest that vitamin C is significantly associated with a decreased risk of ischemic stroke [HR=0.58 (95% CI=0.34–0.99)], whereas vitamin E was

associated with increased HR of hemorrhagic stroke in the highest tertile of intake [HR=2.94 (95% CI=1.13–7.62)].

## Lipids

### **Pecans Acutely Increase Plasma Postprandial Antioxidant Capacity and Catechins and Decrease LDL Oxidation in Humans**

C. Hudthagosol, E.H. Haddad, K. McCarthy, P. Wang, K. Oda, J. Sabaté

*Journal of Nutrition*, Vol. 141, No. 1; pp. 56-62, 2011

Link to full text: <http://jn.nutrition.org/content/141/1/56.full>

**Significance:** Bioactive constituents of pecans are absorbable and contribute to postprandial antioxidant defenses.

This study examined postprandial changes in plasma oxygen radical absorbance capacity (ORAC) and in concentrations of tocopherols, catechins, oxidized LDL, and malondialdehyde (MDA) in response to pecan test meals. Sixteen healthy men and women were randomly assigned to 3 sequences of test meals composed of whole pecans, blended pecans, or an isocaloric meal of equivalent macronutrient composition but formulated of refined ingredients in a crossover design with a 1-wk washout period between treatments. Following the whole and blended pecan test meals, plasma concentrations of  $\gamma$ -tocopherols doubled at 8 h ( $P<0.001$ ) and hydrophilic- and lipophilic-ORAC increased 12 and 10% at 2 h, respectively. Post whole pecan consumption, oxidized LDL decreased 30, 33, and 26% at 2, 3, and 8 h, respectively ( $P<0.05$ ), and epigallocatechin-3-gallate concentrations at 1 h (mean $\pm$ SEM; 95.1 $\pm$ 30.6 nmol/L) and 2 h (116.3 $\pm$ 80.5 nmol/L) were higher than at baseline (0 h) and after the control test meal at 1 h ( $P<0.05$ ). The postprandial molar ratio of MDA:triglycerides decreased by 37, 36, and 40% at 3, 5, and 8 h, respectively ( $P<0.05$ ), only when whole and blended pecan data were pooled.

### **Effects of Different Forms of Hazelnuts on Blood Lipids and $\alpha$ -Tocopherol Concentrations in Mildly Hypercholesterolemic Individuals**

S.L. Tey, R.C. Brown, A.W. Chisholm, C.M. Delahunty, A.R. Gray, S.M. Williams

*European Journal of Clinical Nutrition*, Vol. 65, No. 1; pp. 117–124, 2011

Link to full text: <http://www.nature.com/ejcn/journal/v65/n1/full/ejcn2010200a.html>

**Significance:** The ingestion of three different forms of hazelnuts equally improved the lipoprotein profile and  $\alpha$ -tocopherol concentrations in mildly hypercholesterolemic individuals.

The effects on blood lipids of incorporating three different forms of hazelnuts (ground, sliced and whole) into the usual diet were investigated in a randomized crossover study. Forty-eight mildly hypercholesterolemic participants were asked to consume 30 g of ground, sliced or whole hazelnuts for 4 weeks. Body weight, plasma total cholesterol (TC), LDL-C, HDL-C, triacylglycerol (TAG), apolipoprotein (apo) A1, apo B100 and  $\alpha$ -tocopherol were measured at baseline and at the end of each dietary phase. There were no significant differences in any outcome

variable between the different forms of nuts. However, compared with baseline, mean values at the end of each hazelnut intervention were significantly higher for HDL-C ( $P=0.023$ ) and  $\alpha$ -tocopherol ( $P=0.005$ ), and significantly lower for TC ( $P<0.001$ ), LDL-C ( $P<0.001$ ), TC:HDL-C ratio ( $P<0.001$ ), apo B100 ( $P=0.002$ ) and apo B100:apo A1 ratio ( $P<0.001$ ), with no significant difference in body weight ( $P=0.813$ ).

## Phytochemicals

### Oolong Tea does not Improve Glucose Metabolism in Non-Diabetic Adults

D.J. Baer, J.A. Novotny, G.K. Harris, K. Stote, B. Clevidence, W.V. Rumpler

*European Journal of Clinical Nutrition*, Vol. 65, No. 1; pp. 87–93, 2011

Link to full text: <http://www.nature.com/ejcn/journal/v65/n1/full/ejcn2010192a.html>

**Significance:** Neither oolong tea nor oolong tea supplemented with catechins or other polyphenols produced improved glucose metabolism in healthy adult volunteers.

This double-blind crossover study examined the effects of oolong tea on glucose metabolism in 19 healthy males who consumed each of three tea products (oolong tea, oolong tea with added catechins and oolong tea with added oolong tea polyphenols) or a control beverage that included caffeinated water and unsupplemented water, as part of a controlled diet. Treatment beverages (1.4 L/day) were consumed for 5 days, followed by assessment of fasting plasma glucose, fasting serum insulin and an oral glucose tolerance test. On the fifth day of each treatment period, treatment beverages were consumed with a standardized meal, and glucose and insulin responses were assessed for 240 min. No significant differences were detected for fasting plasma glucose, fasting serum insulin, incremental plasma glucose area under the concentration time curve (AUC), total plasma glucose AUC or total serum insulin AUC.

### Prebiotic Evaluation of Cocoa-Derived Flavanols in Healthy Humans by Using a Randomized, Controlled, Double-Blind, Crossover Intervention Study

X. Tzounis, A. Rodriguez-Mateos, J. Vulevic, G.R. Gibson, C. Kwik-Urbe, J.P.E. Spencer

*American Journal of Clinical Nutrition*, Vol. 93, No. 1; pp. 62-72, 2011

Link to full text: <http://www.ajcn.org/content/93/1/62.full>

**Significance:** Consumption of cocoa flavanols can significantly affect the growth of select gut microflora in humans, which suggests the potential prebiotic benefits associated with the dietary inclusion of flavanol-rich foods.

The prebiotic potential of cocoa flavanols was assessed in a randomized, double-blind, crossover, controlled intervention study. Twenty-two healthy adults were randomly assigned to either a high-cocoa flavanol (HCF) group (494 mg cocoa flavanols/d) or a low-cocoa flavanol (LCF) group (23 mg cocoa flavanols/d) for 4 wk, followed by a 4-wk washout period before the subjects crossed to the alternant arm. Compared with the consumption of the LCF drink, the daily consumption of the HCF drink for 4 wk significantly increased the bifidobacterial ( $P<0.01$ ) and

lactobacilli ( $P < 0.001$ ) populations but significantly decreased clostridia counts ( $P < 0.001$ ). These microbial changes were paralleled by significant reductions in plasma triacylglycerol ( $P < 0.05$ ) and C-reactive protein (CRP) ( $P < 0.05$ ) concentrations. Furthermore, changes in CRP were linked to changes in lactobacilli counts ( $P < 0.05$ ,  $R^2 = -0.33$  for the model). These *in vivo* changes were closely paralleled by cocoa flavanol-induced bacterial changes in mixed-batch culture experiments.

## Glycemic Index

### Dietary Glycemic Load and Risk of Colorectal Cancer in Chinese Women

H-L. Li, G. Yang, X-O. Shu, Y-B. Xiang, W-H. Chow, B-T. Ji, et al.

*American Journal of Clinical Nutrition*, Vol. 93, No. 1; pp. 101-107, 2011

Link to full text: <http://www.ajcn.org/content/93/1/101.full>

**Significance:** This prospective study provides no evidence that a high-glycemic index diet or high glycemic load is associated with an increased risk of colorectal cancer.

The association of overall glycemic index and glycemic load with colorectal cancer risk was examined in a prospective cohort of Chinese women. A total of 73,061 women aged 40–70 y and free of cancer at enrollment were included in this analysis. Usual dietary intake was assessed at baseline (1997–2000) and reassessed during the first follow-up (2000–2002) through in-person interviews by using a validated food-frequency questionnaire. During an average follow-up of 9.1 y, 475 incident colorectal cancer cases were identified. Glycemic load was not associated with colorectal cancer risk ( $P$  for trend=0.84). The multivariable hazard ratio for the highest compared with the lowest quintile of glycemic load was 0.94 (95% CI=0.71, 1.24). Similar results were also observed for associations with dietary glycemic index and total carbohydrate intake, and results did not vary by excluding individuals with a history of diabetes from the analysis.

## Carbohydrates

### Effect of Carbohydrate Digestibility on Appetite and its Relationship to Postprandial Blood Glucose and Insulin Levels

H.P.F. Peters, P. Ravesteyn, H.T.W.M. van der Hijden, H.M. Boers, D.J. Mela

*European Journal of Clinical Nutrition*, Vol. 65, No. 1; pp. 47–54, 2011

Link to full text: <http://www.nature.com/ejcn/journal/v65/n1/full/ejcn2010189a.html>

**Significance:** Glycemic responses *per se* have minimal effects on appetite, when tested in products differing in only carbohydrate digestibility rate and extent.

Postprandial glucose, insulin and appetite responses to drinks differing only in rate and extent of digestibility of carbohydrates were examined by comparing different glucose polymers: maltodextrin (rapidly digestible) versus

medium-chain pullulan (slowly but completely digestible) versus long-chain pullulan (indigestible). In a randomized, double-blind, balanced crossover design, 35 subjects received drinks with 15 g test carbohydrate polymers. Key outcome measures were appetite scores, digestibility (*in vitro* test and breath hydrogen), and (in a subset) glucose and insulin levels. Digestibility, glucose and insulin data confirmed the rapid, slow and nondigestible nature of the test carbohydrates. Despite its low digestibility, only long-chain pullulan reduced appetite compared with the maltodextrin control, whereas the medium-chain pullulan did not.

## Type 2 Diabetes

### Dietary Omega-3 Fatty Acids and Fish Consumption and Risk of Type 2 Diabetes

L. Djoussé, J.M. Gaziano, J.E. Buring, I-M. Lee

*American Journal of Clinical Nutrition*, Vol. 93, No. 1; pp. 143-150, 2011

Link to full text: <http://www.ajcn.org/content/93/1/143.full>

**Significance:** An increased risk of type 2 diabetes was observed especially with higher intakes of long-chain omega-3 fatty acids, (i.e.,  $\geq 0.20$  g omega-3/d or  $\geq 2$  servings of fish/d).

This prospective study of 36,328 women who participated in the Women's Health Study evaluated whether dietary omega-3 fatty acids and fish consumption were associated with increased risk of type 2 diabetes (T2D). Subjects were followed from 1992 to 2008. During an average follow-up of 12.4 y, 2370 women developed T2D. Marine but not plant-based omega-3 fatty acids were positively associated with incident T2D. From the lowest to highest quintiles of marine omega-3 intake, the multivariable-adjusted hazard ratios (95% CIs) for T2D were 1.0 (referent), 1.17 (1.03, 1.33), 1.20 (1.05, 1.38), 1.46 (1.28, 1.66), and 1.44 (1.25, 1.65), respectively (P for trend < 0.0001). A similar association was observed with fish intake, but additional adjustment for docosahexaenoic acid led to the elimination of the association. The relation between marine omega-3 fatty acids and T2D was observed in hypertensive and nonhypertensive subjects and in women who reported infrequent fish consumption.

## Fiber

### The Role of Dietary Fiber in the Bioaccessibility and Bioavailability of Fruit and Vegetable

#### Antioxidants

H. Palafox-Carlos, J.F. Ayala-Zavala, G.A. González-Aguilar

*Journal of Food Science*, Vol. 76, No. 1; pp. R6–R15, 2011

Link to full text: <http://onlinelibrary.wiley.com/doi/10.1111/j.1750-3841.2010.01957.x/full>

**Significance:** This review compiles and analyzes evidence relating to the association between dietary fiber and antioxidants, and the physical and chemical interactions that modulate their release from the chyme in the gastrointestinal tract.

The bioaccessibility and bioavailability of antioxidants differs greatly, and the most abundant antioxidants in ingested fruit are not necessarily those leading to the highest concentrations of active metabolites in target tissues. Fruit antioxidants are commonly mixed with different macromolecules such as carbohydrates, lipids, and proteins to form a food matrix. In fruits and vegetables, carbohydrates are the major compounds found, mainly in free and conjugated forms. Dietary fiber, the indigestible cell wall component of plant material, is considered to play an important role in human diet and health. Most studies on antioxidant bioavailability are focused on foods and beverages from which antioxidants are easily released. There is evidence indicating that food microstructure affects the bioaccessibility and bioavailability of several nutrients, referring mostly to antioxidants.