Health Benefits of Nutritional Supplements

Selected Readings from the Last 26 Years (1990-2016)

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Foreword

The importance of nutrition for human health has long been recognized. Prior to 1960, interest in this field focused primarily on the etiology and prevention of acute nutrient deficiency diseases, such as scurvy, rickets, and pellagra. Some 50 essential nutrients (vitamins, minerals, antioxidants, cofactors, essential amino acids, and essential fatty acids) were identified, and recommended daily intakes for those essential nutrients were developed. These recommendations, in turn, proved valuable in eradicating acute nutrient deficiency diseases.

During the past 26 years, attention has shifted to the role of diet and nutrition in the pathogenesis of chronic degenerative diseases. Heart disease, some cancers, osteoporosis, type II diabetes, and macular degeneration are well-known examples of diseases with dietary risk factors, and research is currently underway on many more nutrient-disease interactions. Unfortunately, these associations are difficult to study, in part because of the timeframes involved. Chronic degenerative diseases develop over decades (or lifetimes), and it is extremely difficult to conduct research programs spanning more than several years in length. Nevertheless, advances in epidemiological and clinical research have uncovered a great deal of information about the impact of diet and nutrient intakes on long-term health.

Over the past decade, science and healthcare researchers have paid increasing attention to the role of nutritional supplements as possible dietary components with roles in preventing and treating chronic disease. Hundreds of scientific studies have been conducted and published, each spanning a broad range of potential health issues. These studies have employed a wide variety of methodologies and they have produced both positive and negative results. In some areas – such as the role of calcium and vitamin D supplements in slowing the progression of osteoporosis, or

"We recommend that all adults take one multivitamin daily. This practice is justified mainly by the known and suspected benefits of supplemental folate and vitamins B12, B6, and D in preventing cardiovascular disease, cancer, and osteoporosis…

We recommend multivitamins, rather than individual vitamins, because multivitamins are simpler to take and cheaper than the individual vitamins taken separately and because a large proportion of the population needs supplements of more than one vitamin."

-Fletcher RH, Fairfield KM. Vitamins for chronic disease prevention in adults: clinical applications. 2002. JAMA 287:3127-9.

the role of folic acid supplements in preventing certain birth defects – results have been largely consistent, and these nutrients have become an accepted part of modern healthcare practices. In other areas (e.g. the role of antioxidant supplementation in preventing heart disease), results have been less consistent, and firm conclusions remain controversial.

The following is an enumerative bibliography of peer-reviewed research examining possible health benefits of nutritional supplements and functional foods. This list is not exhaustive. Papers have been selected on the basis of scientific merit and relevance to the field, regardless of whether positive or negative results were obtained. Our objective in compiling this list is to provide readers with a good cross-section of recent scientific literature, with hopes of contributing to a better understanding of the current state of nutritional research.

For convenience, references have been sorted by health issue:

- Cardiovascular Health
- Cancer
- Bone and Joint Health
- Healthy Pregnancies and Healthy Babies
- Immune Function
- Healthy Vision
- Other

Cardiovascular Health

1. Abbey M, Nestel PJ, Baghurst PA. Antioxidant vitamins and low-density-lipoprotein oxidation. 1993. Am J Clin Nutr 58(4):525-32.
2. Adank C, Green TJ, Skeaff CM, Briars B. Weekly high-dose folic acid supplementation is effective in lowering serum homocysteine concentrations in women. 2003. Ann Nutr Metab 47(2):55-9.
3. Allender PS, Cutler JA, Follmann D, Cappuccio FP, Pryer J, Elliott P. Dietary calcium and blood pressure: a meta-analysis of randomized clinical trials. 1996. Ann Intern Med 124(9):825-31.
4. Agarwal S, Rao AV. Tomato lycopene and low density lipoprotein oxidation: a human dietary intervention study. 1998. Lipids 33(10):981-4.
5. Aminbakhsh A, Mancini J. Chronic antioxidant use and changes in endothelial dysfunction: a review of clinical investigations. 1999. Can J Cardiol 15(8):895-903.

"As indicated in Table 1, the 900 mg/day target for EPA/DHA could require 3–21 servings of fish/week depending upon the source/type chosen. Consequently, a high quality fish oil supplement/concentrate and functional foods enriched in EPA/DHA will become important vehicles for enhancing current low intakes of EPA/DHA..."

-DJ Holub, et al.

6. Anderson JW, Allgood LD, Lawrence A, Altringer LA, Jerdack GR, Hengehold DA, Morel JG. Cholesterol-lowering effects of psyllium intake adjunctive to diet therapy in men and women with hypercholesterolemia: meta-analysis of 8 controlled trials. 2000. Am J Clin Nutr 71(2):472-9.
7. Anderson JW, Davidson MH, Blonde L, Brown WV, Howard WJ, Ginsberg H, Allgood LD, Weingand KW. Long-term cholesterol-lowering effects of psyllium as an adjunct to diet therapy in the treatment of hypercholesterolemia. 2000. Am J Clin Nutr 71(6):1433-8.
8. Ascherio A, Rimm EB, Hernan MA, Giovannucci E, Kawachi I, Stampfer MJ, Willett WC. Relation of consumption of vitamin E, vitamin C, and carotenoids to risk for stroke among men in the United States. 1999. Ann Intern Med 130(12):963-70.
9. Bao B, Prasad AS, Beck FW, Fitzgerald JT, Snell D, Bao GW, Singh T, Cardozo LJ. Zinc decreases C-reactive protein, lipid peroxidation, and inflammatory cytokines in elderly subjects: a potential implication of zinc as an atheroprotective agent. 2010. AJCN 91:1634-41.
10. Baur JA, Sinclair DA. Therapeutic potential of resveratrol: the in vivo evidence. 2006. Nat Rev Drug Discov 5(6):493-506.
11. Bellamy MF, McDowell IF, Ramsey MW, Brownlee M, Newcombe RG, Lewis MJ. Oral folate enhances endothelial function in hyperhomocysteinaemic subjects. 1999. Eur J Clin Invest 29:659-62.

"Mg^{2+} [magnesium] deficiency or a reduction in dietary intake of Mg^{2+} plays an important role in the etiology of diabetes and numerous cardiovascular diseases including thrombosis, atherosclerosis, ischemic heart disease, myocardial infarction, hypertension, arrhythmias and congestive heart failure in humans. Mg2+ supplementation can bring about a significant decrease in blood pressure and a stabilization of cardiac arrhythmias and acute myocardial infarction."

-S Chakraborti, et al.

12. Berman M, ERman A, Ben-Gal T, Dvir D, Georghiou GP, Stamler A, Vered Y, Vidne BA, Aravot D. Coenzyme Q10 in patients with end-stage heart failure awaiting cardiac transplantation: a randomized, placebo-controlled study. 2004. Clin Cardiol 27(5):295-9.
13. Boaz M, Smetana S, Weinstein T, Matas Z, Gafter U, Iaina A, Knecht A, Weissgarten Y, Brunner D, Fainaru M, Green MS. Secondary prevention with antioxidants of cardiovascular disease in end-stage renal disease (SPACE): randomized placebo-controlled trial. 2000. Lancet 356(9237):1213-8.
14. Bor-Jen Lee et al. A significant correlation between the plasma levels of coenzyme Q10 and vitamin B-6 and a reduced risk of coronary artery disease. Nutrition Research 32(10):751-756, October 2012.
15. Bronstrup A, Hages M, Prinz-Langenohl R, Pietrzik K. Effects of folic acid and combinations of folic acid and vitamin B-12 on plasma homocysteine concentrations in healthy, young women. 1998. AJCN 68(5):1104-10.

16. Brouwer IA, van Dusseldorp M, Thomas CM, Duran M, Hautvast JG, Eskes TK, Steegers-Theunissen RP. Low-dose folic acid supplementation decreases plasma homocysteine concentration: a randomized trial. 1999. Am J Clin Nutr 69(1):99-104.

17. Brouwer IA, van Rooij IA, van Dusseldorp M, Thomas CM, Blom HJ, Hautvast JG, Eskes TK, Steegers-Theunissen RP. Homocysteine-lowering effect of 500 microg folic acid every other day versus 250 microg/day. 2000. Ann Nutr Metab 44(5-6):194-7.

18. Brown AA, Hu FB. Dietary modulation of endothelial function: implications for cardiovascular disease. 2001. Am J Clin Nutr 73:673-86.

19. Brown BG, Zhao XQ, Chait A, Fisher LD, Cheung MC, Morse JS, Dowdy AA, Marino EK, Bolson EL, Alaupovic P, Frohlich J, Albers JJ. Simvastatin and niacin, antioxidant vitamins or the combination for the prevention of coronary disease. 2001. N Engl J Med 345(22):1583-92.

20. Brown L, Rosner B, Willett WW, Sacks FM. Cholesterol-lowering effects of dietary fiber: a meta-analysis. 1999. Am J Clin Nutr 69(1):30-42.

21. Bucher HC, Cook RJ, Guyatt GH, Lang JD, Cook DJ, Hatala R, Hunt DL. Effects of dietary calcium supplementation on blood pressure. A meta-analysis of randomized controlled trials. 1996. JAMA 275(13):1016-22.

22. Bucher HC, Hengstler P, Schindler C, Meier G. N-3 polyunsaturated fatty acids in coronary heart disease: a meta-analysis of randomized controlled trials. 2002. Am J Med 112(4):298-304.

"In this large prospective study of women, we observed a modest inverse association between intake of vitamin C and incidence of CHD [coronary heart disease]. Women in the highest quintile of vitamin C intake (≥360 mg/day) from diet and supplements had a 27% lower risk of nonfatal MI and fatal CHD than women in the lowest quintile of intake (≤93 mg/day). The reduction in risk appeared to be limited to women who took vitamin C supplements. Among users of vitamin C supplements, we observed a significant 28% lower risk of nonfatal MI and fatal CHD than among non-users. Although risk did not vary significantly according duration of use of supplements or dose of supplements, the reduction in risk was somewhat stronger for women taking at least 400 mg/day."

-SK Osganian, et al.

23. Chakraborti S, Chakraborti T, Mandal M, Mandal A, Das S, Ghosh S. Protective role of magnesium in cardiovascular diseases: A review. 2002. Molecular and Cellular Biochemistry 238:163-79.

24. Chambers JC, McGregor A, Jean-Marie J, Obeid OA, Kooner JS. Demonstration of rapid onset vascular endothelial dysfunction after hyperhomocysteinemia: an effect reversible with vitamin C therapy. 1999. Circulation 99:1156-60.

25. Cheng S, Massaro JM, Fox CS, Larson MG, Keyes MJ, McCabe EL, Robins SJ, O'Donnell CJ, Hoffmann U, Jacques PF, Booth SL, Vasan RS, Wolf M, Wang TJ. Adiposity, cardiometabolic risk, and vitamin D status: the Framingham Heart Study. 2010. Diabetes 59(1):242-8.

26. Cheung MC, Zhao XQ, Chait A, Albers JJ, Brown BG. Antioxidant supplements block the response of HDL to simvastatin-niacin therapy in patients with coronary artery disease and low HDL. 2001. Arterioscler Thromb Vasc Biol 21:1320-6.

27. Collaborative Group of the Primary Prevention Project (PPP). Low-dose aspirin and vitamin E in people at cardiovascular risk: a randomised trial in general practice. 2001. Lancet 357(9250):89-95.

28. Connor WE. Importance of n-3 fatty acids in health and disease. 2000. Am J Clin Nutr 71(suppl):171S-5S.

29. Constans J, Blann AD, Resplandy F, Parrot F, Renard M, Seigneur M, Guerin V, BoisseauM, Conri C. Three months supplementation of hyperhomocysteinaemic patients with folic acid and vitamin B6 improves biological markers of endothelial dysfunction. 1999. Br J Haematol 107:776-8.

"Vitamin C, carotenoids, and vitamin E, the three main dietary sources of antioxidants, each affect lipid peroxidation and may reduce atherogenesis and lower the risk of coronary heart disease (CHD)."

-EB Rimm, et al.)

30. Cos P, De Bruyne T, Hermans N, Apers S, Berghe DV, Vlietinck AJ. Proanthocyanidins in health care: current and new trends. 2004. Curr Med Chem 11(10):1345-59.

31. Cui R, Iso H, Date C, Kikuchi S, Tamakoshi A, the Japan Collaborative Cohort Study Group. Dietary Folate and Vitamin B6 and B12 Intake in Relation to Mortality from Cardiovascular Diseases - Japan Collaborative Cohort Study. 2010. Stroke 41:1285-9.

32. Davi G, Romano M, Mezzetti A, et al. Increased levels of soluble P-selectin in hypercholesterolemic patients. 1998. Circulation 97-953-7.

33. Davidson MH, Maki KC, Kong JC, Dugan LD, Torri SA, Hall HA, Drennan KB, Anderson SM, Fulgoni VL, Saldanha LG, Olson BH. Long-term effects of consuming foods containing psyllium seed husk on serum lipids in subjects with hypercholesterolemia. 1998. Am J Clin Nutr 67(3):367-76.

"Overall, DHA supplementation reduced the concentrations of atherogenic lipids and lipoproteins and increased concentrations of cardioprotective lipoproteins."

-DS Kelley, et al.

34. Devaraj S, Jialal I. Alpha tocopherol supplementation decreases serum C-reactive protein and monocyte interleukin-6 levels in normal volunteers and type 2 diabetic patients. 2000. Free Radic Biol Med 29(8):790-2.

35. Devaraj S, Li D, Jialai I. The effects of alpha tocopherol supplementation on monocyte function. Decreased lipid oxidation, interleukin 1beta, and monocyte adhesion to endothelium. 1996. J Clin Invest 98:756-63.

36. Dieber-Rotheneder M, Puhl H, Waeg G, Striegl G, Esterbauer H. Effect of oral supplementation with d-alphatocopherol on the vitamin E content of human density lipoproteins and resistance to oxidation. 1991. J Lipid Res 32(8):1325-32.

37. Din JN et al. Effect of ω-3 fatty acid supplementation on endothelial function, endogenous fibrinolysis and platelet activation in male cigarette smokers. Heart. 2013 Feb;99(3):168-74.

38. Djousse L, Arnett DK, Carr JJ, Eckfeldt JH, Hopkins PN, Province MA, Ellison RC. Dietary linolenic acid is inversely associated with calcified atherosclerotic plaque in the coronary arteries: the National Heart, Lung, and Blood Institute Family Heart Study. 2005. Circulation 7;111(22):2921-6.

39. Duffy SJ, Gokce N, Holbrook M, Huang A, Frei B, Keaney JF Jr, Vita JA. Treatment of hypertension with ascorbic acid. 1999. Lancet 354(9195):2048-9.

40. Duffy SJ, Gokce N, Holbrook M, Hunter LM, Biegelsen ES, Huang A, Keaney JF Jr, Vita JA. Effect of ascorbic acid treatment on conduit vessel endothelial dysfunction in patients with hypertension. 2001. Am J Physiol Heart Circ Physiol 280(2):H528-34.

41. Dutta A, Dutta SK. Vitamin E and its Role in the Prevention of Atherosclerosis and Carcinogenesis - A Review. 2003. JACN 22(4):258-68.

42. Dwyer JH, Dwyer KM, Scribner RA, Sun P, Li L, Nicholson LM, Davis IJ, Hohn AR. Dietary calcium, calcium supplementation, and blood pressure in African American adolescents. 1998. Am J Clin Nutr 68(3):648-55.

43. Elliott TG, Barth JD, Mancini GB. Effects of vitamin E on endothelial function in men after myocardial infarction. 1995. Am J Cardiol 76(16):1188-90.

"The NHEFS findings are consistent with the hypothesis that high levels of antioxidant vitamins (such as vitamins C, E, and A) increase the body's defense system against free radicals and reduce the risk of arteriosclerosis. Furthermore, the NHEFS findings are plausible in the sense that they are consistent with the secular trends during the last 20 years of large increases in the consumption of supplements containing vitamin C and large declines in age-adjusted death rates (total, cardiovascular disease, and stomach cancer) in the general population that are only partially explained by established risk factors."

-JE Enstrom, et al.

44. Emmert DH, Kirchner JT. The role of vitamin E in the prevention of heart disease. 1999. Arch Fam Med 8(6):537-42.

45. Engelen W, Keenoy BM, Vertommen J, De Leeuw I. Effects of long-term supplementation with moderate pharmacologic doses of vitamin E are saturable and reversible in patients with type 1 diabetes. 2000. Am J Clin Nutr 72(5):1142-9.

46. Enstrom JE, Kanim LE, Klein MA. Vitamin C Intake and Mortality among a Sample of the United States Population. 1992. Epidemiology 3:194-202.

47. Eritsland J, Arnesen H, Seljeflot I, Hostmark AT. Long-term metabolic effects of n-3 polyunsaturated fatty acids in patients with coronary artery disease. 1995. Am J Clin Nutr 61:831-6.

48. Fang JC, Kinlay S, Beltrame J, Hikiti H, Wainstein M, Behrendt D, Suh J, Frei B, Mudge GH, Selwyn AP, Ganz P. Effect of vitamins C and E on progression of transplant-associated arteriosclerosis: a randomized trial. 2002. Lancet 359(9312):1108-13.

49. Farina EK, Kiel DP, Roubenoff R, Schaefer EJ, Cupples LA, Tucker KL. Protective effects of fish intake and interactive effects of long-chain polyunsaturated fatty acid intakes on hip bone mineral density in older adults: the Framingham Osteoporosis Study. Am J Clin Nutr. 2011;93(5):1142-51.

50. Fleischhauer FJ, Yan WD, Fischell TA. Fish oil improves endothelium-dependent coronary vasodilation in heart transplant recipients. 1993. J Am Coll Cardiol 21:982-9.

51. Fotino AD, Thompson-Paul AM, Bazzano LA. Effect of coenzyme Q10 supplementation on heart failure: a meta-analysis. Am J Clin Nutr 2013 Feb;97(2):268-75.

52. Fotherby MD, Williams JC, Forster LA, Craner P, Ferns GA. Effect of vitamin C on ambulatory blood pressure and plasma lipids in older persons. 2000. J Hypertens 18(4):411-5.

"In mammals, there is growing evidence that resveratrol can prevent or delay the onset of cancer, heart disease, ischaemic and chemically induced injuries, diabetes, pathological inflammation and viral infection."

-JA Baur, et al.

53. Freedman JE, Parker C, Li L, Perlman JA, Frei B, Ivanov V, Deak LR, Iafrati MD, Folts JD. Select flavonoids and whole juice from purple grapes inhibit platelet function and enhance nitric oxide release. 2001. Circulation 103:2792-8.

54. Galley HF, Thornton J, Howdle PD, Walker BE, Webster NR. Combination oral antioxidant supplementation reduces blood pressure. 1997. Clin Sci (Colch) 92(4):361-5.

55. Gilligan DM, Sack MN, Guetta V, Casino PR, Quyyumi AA, Rader DJ, Panza JA, Cannon RO. Effect of antioxidant vitamins on low density lipoprotein oxidation and impaired endothelium-dependent vasodilation in patients with hypercholesterolemia. 1994. J Am Coll Cardiol 24(7):1611-7.

56. GISSI-Prevenzione Investigators. Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results from the GISSI-Prevenzione trial. 1999. Lancet 354:447-55.

57. Gillman MW, Hood MY, Moore LL, Nguyen US, Singer MR, Andon MB. Effect of calcium supplementation on blood pressure in children. 1995. J Pediatr 127(2):186-92.

58. Glore SR, Van Treeck D, Knehans AW, Guild M. Soluble fiber and serum lipids: a literature review. 1994. J Am Diet 94(4):425-36.

59. Gocke N, Keaney JF Jr, Frei B, Holbrook M, Olesiak M, Zachariah BJ, Leeuwenburgh C, Heinecke JW, Vita JA. Long-term ascorbic acid administration reverses endothelial vasomotor dysfunction in patients with coronary artery disease. 1999. Circulation 99(25):3234-40.

60. Goodfellow J, Bellamy MF, Ramsey MW, Jones CJH, Lewis MJ. Dietary supplementation with marine omega-3 fatty acids improve systemic large artery endothelial function in subjects with hypercholesterolemia. 2000. J Am Coll Cardiol 35(2):265-70.

61. Green D, O'Driscoll G, Rankin JM, Maiorana AJ, Taylor RR. Beneficial effect of vitamin E administration on nitric oxide function in subjects with hypercholesterolaemia. 1998. Clin Sci (Colch) 95(3):361-7.

62. Griffith LE, Guyatt GH, Cook RJ, Bucher HC, Cook DJ. The influence of dietary and nondietary calcium supplementation on blood pressure: an updated metaanalysis of randomized controlled trials. 1999. Am J Hypertens 12(1 Pt 1):84-92.

63. Guyton JR, Blazing MA, Hagar J, Kashyap ML, Knopp RH, McKenney JM, Nash DT, Nash SD, Niaspan-Gemfibrozil Study Group. Extended-release niacin vs gemfibrozil for the treatment of low levels of high-density lipoprotein cholesterol. 2000. Arch Intern Med 160(8):1177-84.

64. Harris WS. n-3 fatty acids and serum lipoproteins: human studies. 1997. Am J Clin Nutr 65(5 Suppl):1645S-54S.

65. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of antioxidant vitamin supplementation in 20,536 high-risk individuals: a randomized placebo-controlled trial. 2002. Lancet 360(9326):23-33.

66. Hodis HN, Mack WJ, Dustin L, Mahrer PR, Azen SP, Detrano R, Selhub J, Alaupovic P, Liu CR, Liu CH, Hwang J, Wilcox AG, Selzer RH, BVAIT Research Group. High-dose B vitamin supplementation and progression of subclinical atherosclerosis: a randomized controlled trial. 2009. Stroke 40(3):730-6.

67. Hodis HN, Mack WJ, LaBree L, Cashin-Hemphill L, Sevanian A, Johnson R, Azen SP. Serial coronary angiographic evidence that antioxidant vitamin intake reduces progression of coronary artery atherosclerosis. 1995. JAMA 273(23):1849-54.

68. Holmquist C, Larsson S, Wolk A, de Faire U. Multivitamin

"It appears that coenzyme Q10 may be of benefit in a variety of clinical situations. It may have a role in the prevention of cardiovascular disease because of its role in preventing LDL oxidation, though this role requires further research. It appears that this substance is deficient in many patients with a variety of cardiovascular disorders, and that some of them—particularly those with coronary artery disease, heart failure, and cardiomyopathy—may benefit from its ability to enhance the efficiency of myocardial energy production."

-B Sarter

supplements are inversely associated with risk of myocardial infarction in men and women – Stockholm Heart Epidemiology Program (SHEEP). 2003. J Nutr 133(8):2650-4.

69. Holub DJ, Holub BJ. Omega-3 fatty acids from fish oils and cardiovascular disease. 2004. Mol Cell Biochem 263(1-2):217-25.

70. Hornig B, Arakawa N, Kohler C, Drexler H. Vitamin C improves endothelial function of conduit arteries in patients with chronic heart failure. 1998. Circulation 97:363-8.

71. Horsch S, Walther C. Ginkgo biloba special extract EGb 761 in the treatment of peripheral arterial occlusive disease (PAOD) - a review based on randomized, controlled studies. 2004. Int J Clin Pharmacol Ther 42(2):63-72.

"Supplemental CoQ10 alters the natural history of cardiovascular illnesses and has the potential for prevention of cardiovascular disease through the inhibition of LDL cholesterol oxidation and by the maintenance of optimal cellular and mitochondrial function throughout the ravages of time and internal and external stresses."

-PH Langsjoen, et al.

72. Iuliano L, Mauriello A, Sbarigia E, Spagnoli LG, Violi F. Radiolabeled native low-density lipoprotein injected into patients with carotid stenosis accumulates in macrophages of atherosclerotic plaque: effect of vitamin E supplementation. 2000. Cir 101(11):1249-54.

73. Jacques PF, Lyass A, Massaro JM, Vasan RS, D'Agostino Sr RB. Relationship of lycopene intake and consumption of tomato products to incident CVD. Br J Nutr. 2013 Jan 15:1-7.

74. Jain SK, McVie R, Jaramillo JJ, Palmer M, Smith T, Meachum ZD, Little RL. The effect of modest vitamin E supplementation on lipid peroxidation products and other cardiovascular risk factors in diabetic patients. 1996. Lipids Suppl:S87-90.

75. Jialal I, Grundy SM. Effect of combined supplementation with alpha-tocopherol, ascorbate, and beta-carotene on low-density lipoprotein oxidation. 1993. Circulation 88(6):2780-6.

76. Johansen O, Seljflot I, Hostmark AT, Arnesen H. The effect of supplementation with omega-3 fatty acids on soluble markers of endothelial function in patients with coronary heart disease. 1999. Arterioscler Thromb Vasc Biol 19:1681-6.

77. John P. Forman et al. Effect of Vitamin D Supplementation on Blood Pressure in Blacks. Hypertension. 2013; 61: 779-785.

78. Juonala M et al. Childhood 25-OH Vitamin D Levels and Carotid Intima-Media Thickness in Adulthood: The Cardiovascular Risk in Young Finns Study. J Clin Endocrinol Metab. 2015 Feb 10:jc20143944.

79. Katz DL, Nawaz H, Boukhalil J, Giannamore V, Chan W, Ahmadi R, Sarrel PM. Acute effects of oats and vitamin E on endothelial responses to ingested fat. 2001. Am J Prev Med 20(2):124-9.

80. Kawano Y, Matsuoka H, Takishita S, Omae T. Effects of magnesium supplementation in hypertensive patients: assessment by office, home, and ambulatory blood pressures. 1998. Hypertension 32(2):260-5.

81. Keith ME, Walsh NA, Darling PB, Hanninen SA, Thirugnanam S, Leong-Poi H, Barr A, Sole MJ. B-vitamin deficiency in hospitalized patients with heart failure. 2009. J Am Diet Assoc 109(8):1406-10.

82. Kelley DS, Siegel D, Vemuri M, Mackey BE. Docosahexaenoic acid supplementation improves fasting and postprandial lipid profiles in hypertriglyceridemic men. 2007. Am J Clin Nutr 86:324-33.

83. Kendrick J, Targher G, Smits G, Chonchol M. 25-Hydroxyvitamin D deficiency is independently associated with cardiovascular disease in the Third National Health and Nutrition Examination Survey. 2009. Atherosclerosis 205(1):255-60.

"In this study we demonstrated that higher intake of dietary linolenic acid was associated with a lower prevalence of CAC as measured by cardiac CT in both men and women, after adjustment for confounding factors, in a dose-response fashion. This association was independent of age, education, income, energy intake, ratio of n-6 to n-3 fatty acids, and fish consumption."

-L Djousse, et al.

84. Klipstein-Grobusch K, Geleijnse JM, den Breeijen JH, Boeing H, Hofman A, Grobbee DE, Witteman JC. Dietary antioxidants and risk of myocardial infarction in the elderly: the Rotterdam Study. 1999. Am J Clin Nutr 69(2):261-6.

85. Kris-Etherton PM, Harris WS, Appel LJ, American Heart Association – Nutrition Committee. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. 2002. Circulation 106(21):2747-57.

86. Kritchevsky SB, Tell GS, Shimakawa T, Dennis B, Li R, Kohlmeier L, Steere E, Heiss G. Provitamin A carotenoid intake and carotid artery plaques: the Atherosclerosis Risk in Communities Study. 1998. Am J Clin Nutr 68(3):726-33.

87. Kugiyama K, Motoyama T, Doi H, Kawano H, Hirai N, Soejima

H, Miyao Y, Takazoe K, Moriyama Y, Mizuno Y, Tsunoda R, Ogawa H, Sakamoto T, Sugiyama S, Yasue H. Improvement of endothelial vasomotor dysfunction by treatment with alpha-tocopherol in patients with high remnant lipoproteins levels. 1999. J Am Coll Cardiol 33:1512-8.

88. Kushi LH, Folsom AR, Prineas RJ, Mink PJ, Wu Y, Bostick RM. Dietary antioxidant vitamins and death from coronary heart disease in postmenopausal women. 1996. N Engl J Med 334(18):1156-62.

89. Langsjoen PH, Langsjoen AM. Overview of the use of CoQ10 in cardiovascular disease. 1999. BioFactors 9:273-84.

90. Leaf A, Kang JX, Xiao YF, Billman GE. n-3 fatty acids in the prevention of cardiac arrhythmias. 1999. Lipids 34 Suppl:S187-9.

"In this large cohort of men followed for 12 [years], we found an inverse association between folate intake and risk of PAD [peripheral artery disease] that was independent of other PAD risk factors."

-AT Merchant, et al.

91. Lee BJ, Huang MC, Chung LJ, Cheng CH, Lin KL, Su KH, Huang YC. Folic acid and vitamin B12 are more effective than vitamin B6 in lowering fasting plasma homocysteine concentration in patients with coronary artery disease. 2004. Eur J Clin Nutr 58(3):481-7.

92. Lee JH, O'Keefe JH, Bell D, Hensrud DD, Holick MF. Vitamin D deficiency an important, common, and easily treatable cardiovascular risk factor?. 2008. J Am Coll Cardiol 52(24):1949-56.

93. Leppala JM, Virtamo J, Fogelholm R, Albanes D, Heinonen OP. Different risk factors for different stroke subtypes: association of blood pressure, cholesterol, and antioxidants. 1999. Stroke 30(12):2535-40.

94. Leppala JM, Virtamo J, Fogelholm R, Albanes D, Taylor PR, Heinonen OP. Vitamin E and beta carotene supplementation in high risk for stroke: a subgroup analysis of the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. 2000. Arch Neurol 57(10):1503-9.

95. Levine GN, Frei B, Koulouris SN, Gerhard MD, Keaney JF, Vita JA. Ascorbic acid reverses endothelial vasomotor dysfunction in patients with coronary artery disease. 1996. Circulation 93(6):1107-13.

96. Levy AP, Friedenberg P, Lotan R, Ouyang P, Tripputi M, Higginson L, Cobb FR, Tardif JC, Bittner V, Howard BV. The effect of vitamin therapy on the progression of coronary artery atherosclerosis varies by haptoglobin type in postmenopausal women. 2004. Diabetes Care 27(4):925-30.

97. Lindeman RD, Romero LJ, Koehler KM, Liang HC, LaRue A, Baumgartner RN, Garry PJ. Serum vitamin B12, C and folate concentrations in the New Mexico Elder Health Survey: Correlations with cognitive and affective functions. 2000. J Am Coll Nutr 19(1):68-76.

98. Losonczy KG, Harris TB, Havlik RJ. Vitamin E and vitamin C supplement use and risk of all-cause and coronary heart dis-ease mortality in older persons: the established populations for epidemiologic studies of the elderly. 1996. Am J Clin Nutr 64(2):190-6.

99. Major GC, Alarie F, Doré J, Phouttama S, Tremblay A. Supplementation with calcium + vitamin D enhances the beneficial effect of weight loss on plasma lipid and lipoprotein concentrations. 2007. AJCN 85(1): 54-9.

100. Malinow MR, Nieto FJ, Kruger WD, Duell PB, Hess DL, Gluckman RA, Block PC, Holzgang CR, Anderson PH, Seltzer D, Upson B, Lin QR. The effects of folic acid supplementation on plasma total homocysteine are modulated by multivitamin use and methylenetetrahydrofolate reductase genotypes. 1997. Arterioscler Thromb Vasc Biol 17(6):1157-62.

101. Maresta A, Balduccelli M, Varani E, Marzilli M, Falli C, Heiman F, DStat, Lavezzari M, Stragliotto E, De Caterina R. Prevention of postcoronary angioplasty restenosis by omega-3 fatty acids: Main results of the Esapent for Prevention of Restenosis Italian Study (ESPRIT). 2002. Am Heart J 143:e5.

"We conclude that CoQ10 administration can improve recovery of the mitochondrion and the cardic myocyte from stress. When given for one week prior to surgery, CoQ10 can accelerate cardiac recovery and lead to earlier discharge of the patient from the hospital."

-FL Rosenfeldt, et al.

102. McKay DL, Perrone G, Rasmussen H, Dallal G, Blumberg JB. Multivitamin/mineral supplementation improves plasma B-vitamin status and homocysteine concentration in healthy older adults consuming a folate-fortified diet. 2000. J Nutr 130(12):3090-6.

103. Marta Guasch-Ferré et al. Dietary Magnesium Intake Is Inversely Associated with Mortality in Adults at High Cardiovascular Risk. J Nutr. 2014 Jan;144(1):55-60.

104. McKinley MC, McNulty H, McPartlin J, Strain JJ, Pentieva K, Ward M, Weir DG, Scott JM. Low-dose vitamin B-6 effectively lowers fasting plasma homocysteine in healthy elderly persons who are folate and riboflavin replete. 2001. Am J Clin Nutr 73(4):759-64.

105. Merchant AT, Hu FB, Spiegelman D, Willett WC, Rimm EB, Ascherio A. The use of B vitamin supplements and peripheral arterial disease risk in men are inversely related. 2003. J Nutr 133(9):2863-7.

106. Meyer F, Bairati I, Dagenais GR. Lower ischemic heart disease incidence and mortality among vitamin supplement users. 1996. Can J Cardiol 12(10):930-4.

107. Michos ED, Melamed ML. Vitamin D and cardiovascular disease risk. 2008. Curr Opin Clin Nutr Metab Care 11(1):7-12.

108. Mietus-Snyder M, Malloy MJ. Endothelial dysfunction occurs in children with two genetic hyperlipidemias: improvement with antioxidant vitamin therapy. 1998. J Pediatr 133(1):35-40.

109. Morris, CD, Carson, S. Routine vitamin supplementation to prevent cardiovascular disease: a summary of the evidence for the U.S. Preventive Services Task Force. 2003. Ann Intern Med 139:56-70.

110. Morris MC, Sacks F, Rosner B. Does fish oil lower blood pressure? A meta-analysis of controlled trials. 1993. Circulation 88(2):523-33.

"In conclusion, our results showed that consumption of a calcium+D supplement enhanced the beneficial effect of body weight loss on the lipid and lipoprotein profile in overweight or obese women with usual low calcium intake… [In] the clinical context of obesity treatment, calcium supplementation could be recommended in women with inadequate calcium intake to improve the cardiovascular disease risk profile."

-GC Major, et al.

111. Mosca L, Rubenfire M, Mandel C, Rock C, Tarshis T, Tsai A, Pearson T. Antioxidant nutrient supplementation reduces the susceptibility of low density lipoprotein to oxidation in patients with coronary artery disease. 1997. J Am Coll Cardiol 30(2):392-9.

112. Motoyama T, Kawano H, Kugiyama K, Hirashima O, Ohgushi M, Tsunoda R, Moriyama Y, Miyao Y, Yoshimura M, Ogawa H, Yasue H. Vitamin E administration improves impairment of endothelium-dependent vasodilation in patients with coronary spastic angina. 1998. J Am Coll Cardiol 32:1672-9.

113. Mottram P, Shige H, Nestel P. Vitamin E improves arterial compliance in middle-aged men and women. 1999. Atherosclerosis 145(2):399-404.

114. Nallamothu BK, Fendrick AM, Rubenfire M, Saint S, Bandekar RR, Omenn GS. Potential clinical and economic effects of homocyst(e)ine lowering. 2000. Arch Intern Med 160(22):3406-12.

115. Ness A, Sterne J. Hypertension and ascorbic acid. 2000. Lancet 355(9211):1271; discussion 1273-4.

116. Neunteufl T, Kostner K, Katzenschlager R, Zehetgruber M, Maurer G, Weidinger F. Additional benefit of vitamin E supplementation to simvastatin therapy on vasoreactivity of the brachial artery of hypercholesterolemic men. 1998. J Am Coll Cardiol 32(3):711-6.

117. Neunteufl T, Priglinger U, Heher S, Zehetgruber M, Soregi G, Lehr S, Huber K, Maurer G, Weidinger F, Kostner K. Effects of vitamin E on chronic and acute endothelial dysfunction in smokers. 2000. J Am Coll Cardiol 35:277-83.

118. Nitta K. Impact of Vitamin D Metabolism on Cardiovascular Disease. International Journal of Clinical Medicine. 2011;02(05):531–537.

119. Osganian SK, Stampfer MJ, Rimm E, Spiegelman D, Hu FB, Manson JE, Willett WC. Vitamin C and risk of coronary heart disease in women. 2003. J Am Coll Cardiol 42(2):246-52.

120. Pfeifer M, Begerow B, Minne HW, Nachtigall D, Hansen C. Effects of a short-term vitamin D(3) and calcium supplementation on blood pressure and parathyroid hormone levels in elderly women. 2001. J Clin Endocrinol Metab 86(4):1633-7.

"Polyunsaturated fatty acids (PUFAs) of the n-6 and n-3 series are essential nutrients that exert an important influence on plasma lipids and serve cardiac and endothelial functions to impact the prevention and treatment of coronary heart diseases (CHD). Both n-6 and n-3 PUFAs have distinct biological effects contributing to their cardioprotective action."

-V Wijendran, et al.

121. Pilz S, Dobnig H, Fischer JE, Wellnitz B, Seelhorst U, Boehm BO, März W. Low vitamin d levels predict stroke in patients referred to coronary angiography. 2008. Stroke 39(9):2611-3.

122. Pilz S, März W, Wellnitz B, Seelhorst U, Fahrleitner-Pammer A, Dimai HP, Boehm BO, Dobnig H. Association of vitamin D deficiency with heart failure and sudden cardiac death in a large cross-sectional study of patients referred for coronary angiography. 2008. J Clin Endocrinol Metab 93(10):3927-35.

123. Plotnick GD, Corretti MC, Vogel RA. Effect of antioxidant vitamins on the transient impairment of endothelium-dependent brachial artery vasoactivity following a single high-fat meal. 1997. JAMA 278(20):1682-6.

124. Porkkala-Sarataho EK, Nyyssonen MK, Kaikkonen JE, Poulsen

HE, Hayn EM, Salonen RM, Salonen JT. A randomized, single-blind, placebo-controlled trial of the effects of 200 mg alpha-tocopherol on the oxidation resistance of atherogenic lipoproteins. 1998. Am J Clin Nutr 68(5):1034-41.

125. Pryor WA. Vitamin E and heart disease: basic science to clinical intervention trials. 2000. Free Radic Biol Med 28(1):141-64.

126. Quinlivan EP, McPartlin J, McNulty H, Ward M, Strain JJ, Weir DG, Scott JM. Importance of both folic acid and vitamin B12 in reduction of risk of vascular disease. 2002. Lancet 359(9302):227-8.

"The administration of CoQ10 to heart transplant candidates led to a significant improvement in functional status, clinical symptoms, and quality of life."

-M Berman, et al.

127. Rapola JM, Virtamo J, Haukka JK, Heinonen OP, Albanes D, Taylor PR, Huttunen JK. Effect of vitamin E and beta carotene on the incidence of angina pectoris. A randomized, double-blind, controlled trial. 1996. JAMA 275(9):693-8.

128. Raitakari OT, Adams MR, McCredie RJ, Griffiths KA, Stocker R, Celermajer DS. Oral vitamin C and endothelial function in smokers: short-term improvement, but no sustained beneficial effect. 2000. J Am Coll Cardiol 35:1616-21.

129. Reid IR, Mason B, Horne A, Ames R, Clearwater J, Bava U, Orr-Walker B, Wu F, Evans MC, Gamble GD. Effects of calcium supplementation on serum lipid concentrations in normal older women: a randomized controlled trial. 2002. Am J Med 112(5):343-7.

130. Rimm EB, Stampfer MJ. The role of antioxidants in preventive cardiology. 1997. Curr Opin Cardiol 12(2):188-94.

131. Rimm EB, Stampfer MJ, Ascherio A, Giovannucci E, Colditz GA, Willett WC. Vitamin E consumption and the risk of coronary heart disease in men. 1993. N Engl J Med 328(20):1450-6.

132. Rimm EB, Willett WC, Hu FB, Sampson L, Colditz GA, Manson JE, Hennekens C, Stampfer MJ. Folate and vitamin B6 from diet and supplements in relation to risk of coronary heart disease among women. 1998. JAMA 279(5):359-64.

133. Rosenfeldt FL, Pepe S, Linnane A, Nagley P, Rowland M, Ou R, Marasco S, Lyon W, Esmore D. Coenzyme Q10 protects the aging heart against stress: studies in rats, human tissues, and patients. 2002. Ann N Y Acad Sci 959:355-9, 463-5.

134. Rossig L, Hoffmann J, Hugel B, Mallat Z, Haase A, Freyssinet JM, Tedgui A, Aicher A, Zeiher AM, Dimmeler S. Vitamin C inhibits endothelial cell apoptosis in congestive heart failure. 2001. Circulation 104:2182-7.

135. Rydlewicz A, Simpson JA, Taylor RJ, Bond CM, Golden MN. The effect of folic acid supplementation on plasma homocysteine in an elderly population. 2002. QJM 95(1):27-35.

136. Sacks FM, Stone PH, Gibson CM, Silverman DI, Rosner B, Pasternak RC. Controlled trial of fish oil for regression of human coronary atherosclerosis. 1995. J Am Coll Cardiol 25:1492-8.

137. Sarter B. Coenzyme Q10 and cardiovascular disease: a review. 2002. J Cardiovasc Nurs 16(4):9-20.

138. Schnyder G, Roffi M, Flammer Y, Pin R, Hess OM. Effect of homocysteine-lowering therapy with folic acid, vitamin B12, and vitamin B6 on clinical outcome after percutaneous coronary intervention: the Swiss Heart study: a randomized controlled trial. 2002. JAMA 288(8):973-9.

139. Schnyder G, Roffi M, Pin R, Flammer Y, Lange H, Eberli FR, Meier B, Turi ZG, Hess OM. Decreased rate of coronary restenosis after lowering of plasma homocysteine levels. 2001. N Engl J Med 345(22):1593-1600.

140. Seljeflot I, Arnesen H, Brude IR, Nenseter MS, Drevon CA, Hjermann I. Effects of omega-3 fatty acids and/or antioxidants on endothelial cell markers. 1998. Eur J Clin Invest 28:629-35.

141. Simons LA, von Konigsmark M, Simons J, Stocker R, Celermajer DS. Vitamin E ingestion does not improve arterial endothelial dysfunction in older adults. 1999. Atherosclerosis 143:193-9.

"Several epidemiological studies have revealed an inverse relationship between vitamin E intake and the progression of chronic diseases. It is believed that vitamin E's various actions, including its role as an antioxidant, have both antiatherogenic effects and chemoprotective action."

-A Dutta, et al.

142. Singh RB, Niaz MA, Sharma JP, Kumar R, Rastogi V, Moshiri M. Randomized, double-blind, placebo-controlled trial of fish oil and mustard oil in patients with suspected acute myocardial infarction: the Indian experiment of infarct survival – 4. 1997. Cardiovasc Drugs Ther 11:485-91.

143. Skyrme-Jones RA, O'Brien RC, Berry KL, Meredith IT. Vitamin E supplementation improves endothelial function in type I diabetes mellitus: a randomized, placebo-controlled study. 2000. J Am Coll Cardiol 36(1):94-102.

144. Spence JD, Bang H, Chambless LE, Stampfer MJ. Vitamin intervention for stroke prevention trial: an efficacy analysis. 2005. Stroke 36(11):2404-9.

145. Stampfer MJ, Hennekens CH, Manson JE, Colditz GA, Rosner B, Willett WC. Vitamin E consumption and the risk of coronary disease in women. 1993. N Engl J Med 328(20):1444-9.

146. Stampfer MJ, Rimm EB. Epidemiologic evidence for vitamin E in prevention of cardiovascular disease. 1995. Am J Clin Nutr 62(6 Suppl):1365S-9S.

147. Steinberg FM, Chait A. Antioxidant vitamin supplementation and lipid peroxidation in smokers. 1998. Am J Clin Nutr 68(2):319-27.

148. Steiner M, Glantz M, Lekos A. Vitamin E plus aspirin compared with aspirin alone in patients with transient ischemic attacks. 1995. Am J Clin Nutr 62(suppl):1381S-4S.

"This review confirms the efficacy of Ginkgo biloba extract EGb 761. It demonstrates not only the statistical significance of the difference with respect to placebo but also the clinical relevance for the treatment of patients with PAOD [peripheral arterial occlusive disease]."

-S Horsch, et al.

149. Stephens NG, Parsons A, Schofield PM, Kelly F, Cheeseman K, Mitchinson MJ. Randomised controlled trial of vitamin E in patients with coronary disease: Cambridge Heart Antioxidant Study. 1996. Lancet 347(9004):781-6.

150. Studer M, Briel M, Leimenstoll B, Glass TR, Bucher HC. Effect of different antilipidemic agents and diets on mortality: a systematic review. 2005. Arch Intern Med 165(7):725-30.

151. Thambyrajah J, Landray MJ, McGlynn FJ, Jones HJ, Wheeler DC, Townend JN. Does folic acid decrease plasma homocysteine and improve endothelial function in patients with predialysis renal failure?. 2000. Circulation 102:871-5.

152. Thies F, Garry JM, Yaqoob P, Rerkasem K, Williams J, Shearman CP, Gallagher PJ, Calder PC, Grimble RF. Association of n-3 polyunsaturated fatty acids with stability of atherosclerotic plaques: a randomized controlled trial. 2003. Lancet 361(9356):477-85.

153. Thomas VL, Gropper SS. Effect of chromium nicotinic acid supplementation on selected cardiovascular disease risk factors. 1996. Biol Trace Elem Res 55(3):297-305.

154. Title LM, Cummings PM, Giddens K, Genest JJ Jr, Nassar BA. Effect of folic acid and antioxidant vitamins on endothelial dysfunction in patients with coronary artery disease. 2000. J Am Coll Cardiol 36(3):758-65.

155. Toole JF, Malinow MR, Chambless LE, Spence JD, Pettigrew LC, Howard VJ, Sides EG, Wang CH, Stampfer M. Lowering homocysteine in patients with ischemic stroke to prevent recurrent stroke, myocardial infarction, and death: the Vitamin Intervention for Stroke Prevention (VISP) randomized controlled trial. 2004. JAMA 291(5):565-75.

156. Ubbink JB, Vermaak WJ, van der Merwe A, Becker PJ. Vitamin B-12, vitamin B-6, and folate nutritional status in men with hyperhomocysteinemia. 1993. Am J Clin Nutr 57(1):47-53.

157. Usui M, Matsuoka H, Miyazaki H, Ueda S, Okuda S, Imaizumi T. Endothelial dysfunction by acute hyperhomocyst(e)inaemia: restoration by folic acid. 1999. Clin Sci (Colch) 96:235-9.

158. Van den Berg M, Boers GH, Franken DG, Blom HJ, Van Kamp GJ, Jakobs C, Rauwerda JA, Kluft C, Stehouwert CD. Hyperhomocysteinaemia and endothelial dysfunction in young patients with peripheral arterial occlusive disease. 1995. Eur J Clin Invest 25:176-81.

159. Van den Berg M, Franken DG, Boers GH, Blom HJ, Jakobs C, Stehouwer CD, Rauwerda JA. Combined vitamin B6 plus folic acid therapy in young patients with arteriosclerosis and hyperhomocysteinemia. 1994. J Vasc Surg 20(6):933-40.

160. Van Guelpen B, Hultdin J, Johansson I, Stegmayr B, Hallmans G, Nilsson TK, Weinehall L, Witthoft C, Palmqvist R, Winkvist A. Folate, vitamin B12, and risk of ischemic and hemorrhagic stroke: a prospective, nested case-referent study of plasma concentrations and dietary intake. 2005. Stroke 36(7):1426-31.

"The combined cardiovascular effects of resveratrol and other plant phenolic compounds and bioflavonoids with vitamin E should also be encouraged. Finally, resveratrol should be evaluated as an interesting candidate for non-drug approaches to combat blood vessel-related diseases in humans."

-JM Wu, et al.

161. Venn BJ, Green TJ, Moser R, Mann JI. Comparison of the effect of low-dose supplementation with L-5methyltetrahydrofolate or folic acid on plasma homocysteine: a randomized placebo-controlled study. 2003. Am J Clin Nutr 77(3):658-62.

162. Venn BJ, Mann JI, Williams SM, Riddell LJ, Chisholm A, Harper MJ, Aitken W, Rossaak JI. Assessment of three levels of folic acid on serum folate and plasma homocysteine: a randomized placebo-controlled double-blind dietary intervention trial. 2002. Eur J Clin Nutr 56(8):748-54.

163. Verhaar MC, Wever RM, Kastelein JJ, van Loon D, Milstien

S, Koomans HA, Rabelink TJ. Effects of oral folic acid supplementation on endothelial function in familial hypercholesterolemia. A randomized placebo-controlled trial. 1999. Circulation 100:335-8.

164. Vermeulen EG, Stehouwer CD, Twisk JW, van den Berg M, de Jong SC, Mackaay AJ, van Campen CM, Visser FC, Jakobs CA, Bulterjis EJ, Rauwerda JA. Effect of homocysteine-lowering treatment with folic acid plus vitamin B6 on progression of subclinical atherosclerosis: a randomized, placebo-controlled trial. 2000. Lancet 355(9203):517-22.

165. Vermeulen EG, Stehouwer CD, Valk J, van der Knaap M, van den Berg M, Twisk JW, Prevoo W, Rauwerda JA. Effect of homocysteine-lowering treatment with folic acid plus vitamin B on cerebrovascular atherosclerosis and white matter abnormalities as determined by MRA and MRI: a placebo-controlled, randomized trial. 2004. Eur J Clin Invest 34(4):256-61.

166. Vivekananthan DP, Penn MS, Sapp SK, Hsu A, Topol EJ. Use of antioxidant vitamins for the prevention of cardiovascular disease: meta-analysis of randomized trials. 2003. Lancet 361:2017-23.

"In summary, the results of the present study suggest that moderate to severe vitamin D deficiency is a risk factor for developing cardiovascular disease. These findings may have potentially broad public health implications, given the high prevalence of vitamin D deficiency in developed countries, the contribution of lifestyle and geography to vitamin D status, and the ease, safety, and low cost of treating vitamin D deficiency."

-TJ Wang, et al.

167. Von Schacky C, Angerer P, Kothny W, Theisen K, Mudra H. The effect of dietary w-3 fatty acids on coronary atherosclerosis. 1999. Ann Intern Med 130:554-62.

168. Wald DS, Bishop L, Wald NJ, Law M, Hennessy E, Weir D, McPartlin J, Scott J. Randomized trial of folic acid supplementation and serum homocysteine levels. 2001. Arch Intern Med 161:695-700.

169. Wang L, Manson JE, Buring JE, Lee IM, Sesso HD. Dietary intake of dairy products, calcium, and vitamin D and the risk of hypertension in middle-aged and older women. 2008. Hypertension 51(4):1073-9.

170. Wang L, Manson JE, Song Y, Sesso HD. Systematic review: Vitamin D and calcium supplementation in prevention of cardiovascular events. 2010. Ann Intern Med 152(5):315-23.

171. Wang TJ, Pencina MJ, Booth SL, Jacques PF, Ingelsson E, Lanier K, Benjamin EJ, D'Agostino RB, Wolf M, Vasan RS. Vitamin D deficiency and risk of cardiovascular disease. 2008. Circulation 117(4):503-11.

"In conclusion, our data indicate that oral treatment with folic acid restores endothelial dysfunction and abolishes the increase in radical-damage end products induced by triglyceride-rich lipoproteins. In combination, these data imply that folic acid enhances NO [nitric oxide] bioavailability through inhibition of lipid-induced oxygen radical stress. These data underscore a potential beneficial effect of folic acid supplementation for cardiovascular prevention strategies, especially in patients with an impaired cholesterol remnant clearance, such as in diabetes and familial combined hyperlipidemia. It is also of interest that higher dietary folate intake apparently may also protect healthy humans from daily fat-associated endothelial insults."

-HW Wilmink, et al.

172. Waters DD, Alderman EL, Hsia J, Howard BV, Cobb FR, Rogers WJ, Ouyang P, Thompson P, Tardif JC, Higginson L, Bittner V, Steffes M, Gordon DJ, Proschan M, Younes N, Verter JI. Effects of hormone replacement therapy and antioxidant vitamin supplements on coronary atherosclerosis in postmenopausal women: a randomized controlled trial. 2002. JAMA 288(19):2432-40.

173. Watts GF, Playford DA, Croft KD, Ward NC, Mori TA, Berke V. Coenzyme Q(10) improves endothelial dysfunction of the brachial artery in Type II diabetes mellitus. 2002. Diabetologia 45(3):420-6.

174. Weber C, Erl W, Weber K, Weber PC. Increased adhesiveness of isolated monocytes to endothelium is prevented by vitamin C intake in smokers. 1996. Circulation 93:1488-92.

175. Weber KT, Simpson RU, Carbone LD. Vitamin D and calcium dyshomoeostasis-associated heart failure. 2008. Heart 94(5):540-1.

176. Wijendran V, Hayes KC. Dietary n-6 and n-3 fatty acid balance and cardiovascular health. 2004. Annu Rev Nutr 24:597-615.

177. Wilmink HW, Stroes ESG, Erkelens WD, Gerritsen WB, Wever R, Banga JD, Rabelink TJ. Influence of folic acid on postprandial endothelial dysfunction. 2000. Arterioscler Thromb Vasc Biol 20(1):185-8.

178. Wink J, Giacoppe G, King J. Effect of very-low-dose niacin on high-density lipoprotein in patients undergoing long-term statin therapy. 2002. Am Heart J 143(3):514-8.

179. Witham MD, Crighton LJ, Gillespie ND, Struthers AD, McMurdo ME. The effects of vitamin D supplementation on physical function and quality of life in older patients with heart failure: a randomized controlled trial. 2010. Circ Heart Fail 3(2):195-201.

180. Witte KKA, Nikitin NP, Parker AC, von Haehling S, Volk HD, Anker SD, Clark AL, Cleland JGF. The effect of micronutrient supplementation on quality-of-life and left ventricular function in elderly patients with chronic heart failure. 2005. European Heart J 26:2238-44.

181. Woo KS, Chook P, Lolin YI, Sanderson JE, Metreweli C, Celermajer DS. Folic acid improves arterial endothelial function in adults with hyperhomocystinemia. 1999. J Am Coll Cardiol 34:2002-6.

182. Woodside JV, Yarnell JW, McMaster D, Young IS, Harmon DL, McCrum EE, Patterson CC, Gey KF, Whitehead AS, Evans A. Effect of B-group vitamins and antioxidant vitamins on hyperhomocysteinemia: a double-blind, randomized, factorial-design, controlled trial. 1998. Am J Clin Nutr 67(5):858-66.

183. Wu JM, Wang ZR, Hsieh TC, Bruder JL, Zou JG, Huang YZ. Mechanism of cardioprotection by resveratrol, a phenolic antioxidant present in red wine (Review). 2001. Int J Mold Med 8(1):3-17.

184. Ye Z, Song H. Antioxidant vitamins intake and the risk of coronary heart disease: meta-analysis of cohort studies. 2008. Eur J Cardiovasc Prev Rehabil 15(1):26-34.

185. Yochum LA, Folsom AR, Kushi LH. Intake of antioxidant vitamins and risk of death from stroke in postmenopausal women. 2000. Am J Clin Nutr 72(2):476-83.

186. Yusuf S, Dagenais G, Pogue J, Bosch J, Sleight P. Vitamin E supplementation and cardiovascular events in high-risk patients. The heart outcomes prevention evaluation study investigators. 2000. N Engl J Med 342(3):154-60.

187. Zureik M, Galan P, Bertrais S, Mennen L, Czernichow S, Blacher J, Ducimetiere P, Hercberg S. Effects of long-term daily low-dose supplementation with antioxidant vitamins and minerals on structure and function of large arteries. 2004. Arterioscler Thromb Vasc Biol 24(8):1485-91.

"Evidence from prospective secondary prevention studies suggests that EPA/DHA supplementation ranging from 0.5 to 1.8 g/d (either as fatty fish or supplements) significantly reduces subsequent cardiac and all-cause mortality."

-PM Kris-Etherton, et al.

Cancer

188. Ahn J, Peters U, Albanes D, Purdue MP, Abnet CC, Chatterjee N, Horst RL, Hollis BW, Huang WY, Shikany JM, Hayes RB; Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial Project Team. Serum vitamin D concentration and prostate cancer risk: a nested case-control study. 2008. J Natl Cancer Inst 100(11):796-804.

189. Albanes D, Heinonen OP, Huttunen JK, Taylor PR, Virtamo J, Edwards BK, Haapakoski J, Rautalahti M, Hartman AM, Palmgren J, et al. Effects of alpha-tocopherol and beta-carotene supplements on cancer incidence in the Alpha-Tocopherol Beta-Carotene Cancer Prevention Study. 1995. Am J Clin Nutri 62(6 Suppl):1427S-30S.

190. Albanes D, Malila N, Taylor PR, Huttunen JK, Virtamo J, Edwards BK, Rautalahti M, Hartman AM, Barrett MJ, Pietinen P, Hartman TJ, Sipponen P, Lewin K, Teerenhovi L, Hietanen P, Tangrea JA, Virtanen M, Heinonen OP. Effects of supplemental alpha-tocopherol and beta-carotene on colorectal cancer: results from a controlled trial (Finland). 2000. Cancer Causes Control 11(3):197-205.

"The results of this randomized controlled trial do not support the hypothesis that selenium supplementation reduces the risk of BCC or SCC of the skin, showing no statistically significant treatment effect on their incidence. However, selenium supplementation was found to be associated with significant reductions in secondary end points of total cancer incidence (all-sites combined), long, colorectal and prostate cancer incidences, and lung cancer mortality."

- LC Clark, et al.

191. Ames BN. DNA damage from micronutrient deficiencies is likely to be a major cause of cancer. 2001. Mutat Res 475(1-2):7-20.

192. Bairati I, Meyer F, Gelinas M, Fortin A, Nabid A, Brochet F, Mercier JP, Tetu B, Harel F, Masse B, Vigneault E, Vass S, del Vecchio P, Roy J. A randomized trial of antioxidant vitamins to prevent second primary cancers in head and neck cancer patients. 2005. J Natl Cancer Inst 97(7):481-8.

193. Baron JA, Beach M, Mandel JS, van Stolk RU, Haile RW, Sandler RS, Rothstein R, Summers RW, Snover DC, Beck GJ, Bond JH, Greenberg ER. Calcium supplements for the prevention of colorectal adenomas. Calcium Polyp Prevention Study Group. 1999. N Engl J Med 340(2):101-7.

194. Benner SE, Winn RJ, Lippman SM, Poland J, Hansen KS, Luna MA, Hong WK. Regression of oral leukoplakia with alpha-tocopherol: a community clinical oncology program chemoprevention study. 1993. J Natl Cancer Inst 85(1):44-7.

195. Bjelakovic G, Nikolova D, Simonetti RG, Gluud C. Antioxidant supplements for prevention of gastrointestinal cancers: a systematic review and meta-analysis. 2004. Lancet 364:1219-28.

196. Block G. Vitamin C and cancer prevention: the epidemiologic evidence. 1991. AJCN 53(1 Suppl):270S-82S.

197. Blot WJ. Vitamin/mineral supplementation and cancer risk: international chemoprevention trials. 1997. Proc Soc Exp Biol Med 216(2):291-6.

"In vitro, animal and clinical studies strongly indicate that vitamin D may have anticancer benefits, including against progression (such as metastasis) in colorectal cancer and possibly other cancers. Thus improving vitamin D status could be potentially beneficial against either incidence or mortality, or both."

-E Giovannucci

198. Blot WJ, Li JY, Taylor PR, Guo W, Dawsey S, Wang GQ, Yang CS, Zheng SF, Gail M, Li GY, et al. Nutrition intervention trials in Linxian, China: supplementation with specific vitamin/mineral combinations, cancer incidence, and disease-specific mortality in the general population. 1993. J Natl Cancer Inst 85(18):1483-92.

199. Bonithon-Kopp C, Kronborg O, Giacosa A, Rath U, Faivre J, European Cancer Prevention Organisation Study Group. Calcium and fibre supplementation in prevention of colorectal adenoma recurrence: a randomized intervention trial. 2000. Lancet 356(9238):1300-6.

200. Bostick RM, Potter JD, McKenzie DR, Sellers TA, Kushi LH, Steinmetz KA, Folsom AR. Reduced risk of colon cancer with high intake of vitamin E: the Iowa Women's Health Study. 1993. Cancer Res 53(18):4230-7.

201. Brasky TM, Lampe JW, Potter JD, Patterson RE, White E. Specialty Supplements and Breast Cancer Risk in the VITamins And Lifestyle (VITAL) Cohort. 2010. Cancer Epidemiol Biomarkers Prev 19(7):1696-708.

202. B S van der Meij et al. Oral nutritional supplements containing n-3 polyunsaturated fatty acids affect quality of life and functional status in lung cancer patients during multimodality treatment: an RCT. European Journal of Clinical Nutrition (2012) 66, 399–404.

203. Chan JM, Stampfer MJ, Ma J, Rimm EB, Willett WC, Giovannucci EL. Supplemental vitamin E intake and prostate cancer risk in a large cohort of men in the United States. 1999. Cancer Epidemiol Biomarkers Prev 8(10):893-9.

204. Chlebowski RT, Johnson KC, Kooperberg C, Pettinger M, Wactawski-Wende J, Rohan T, Rossouw J, Lane D, O'Sullivan MJ, Yasmeen S, Hiatt RA, Shikany JM, Vitolins M, Khandekar J, Hubbell FA. Calcium Plus Vitamin D Supplementation and the Risk of Breast Cancer. 2008. J Natl Cancer Inst 100(22):1581-91.

"In this case-control study of North Carolina women, we found only very limited support for the hypothesis that vitamin supplement use is associated with a decreased risk of breast cancer. Among white women, any use of multivitamins, vitamin C or vitamin E in the past five years was each associated with an approximately 20% decrease in breast cancer risk; however, the confidence intervals around these estimates all included one. There was no evidence of a dose-response relationship between duration of use and breast cancer risk. In contrast to the modest inverse associations with certain vitamin supplements suggested for white women, there was essentially no evidence of a protective effect among black women for any of the vitamins examined."

- PG Moorman, et al.

205. Cho E, Smith-Warner SA, Spiegelman D, Beeson WL, vanden Brandt PA, Colditz GA, Folsom AR, Fraser GE, Freudenheim JL, Giovannucci E, Goldbohm RA, Graham S, Miller AB, Pietinen P, Potter JD, Rohan TE, Terry P, Toniolo P, Virtanen MJ, Willett WC, Wolk A, Wu K, Yaun SS, Zeleniuch-Jacquotte A, Hunter DJ. Dairy foods, calcium, and colorectal cancer: a pooled analysis of 10 cohort studies. 2004. J Natl Cancer Inst 96(13):1015-22.

206. Choi SW, Mason JB. Folate and carcinogenesis: an integrated scheme. 2000. J Nutr 130(2):129-32.

207. Clark LC, Combs GF Jr, Turnbull BW, Slate EH, Chalker DK, Chow J, Davis LS, Glover RA, Graham GF, Gross EG, Krongrad A, Lesher JL Jr, Park HK, Sanders BB Jr, Smith CL, Taylor JR. Effects of selenium supplementation for cancer prevention in patients with carcinoma of the skin. A randomized controlled trial. Nutritional Prevention of Cancer Study Group. 1996. JAMA 276(24):1957-63.

208. Clark LC, Dalkin B, Krongrad A, Combs GF Jr, Turnbull BW, Slate EH, Witherington R, Herlong JH, Janosko E, Carpenter D, Borosso C, Falk S, Rounder J. Decreased incidence of prostate cancer with selenium supplementation: results of a double-blind cancer prevention trial. 1998. Br J Urol 81(5):730-4.

209. Clarke R, Halsey J, Lewington S, Lonn E, Armitage J, Manson JAE. Bønaa KH, Spence JD, Nygård O, Jamison R, Gaziano JM, Guarino P, Bennett D, Mir F, Peto R, Collins R, B-Vitamin Treatment Trialists' Collaboration. Effects of Lowering Homocysteine Levels with B Vitamins on Cardiovascular Disease, Cancer, and Cause-Specific Mortality. 2010. Arch Intern Med 170(18):1622-31.

"In this cohort, we observed a statistically significant inverse association between vitamin E intake and bladder cancer risk, which was strongest among those who had been taking vitamin E supplements for many years. A suggestive inverse association was noted for intake of vitamin C supplement dose and bladder cancer risk. No associations were observed between intake of total energy, macronutrients, or other micronutrients and bladder cancer risk."

-DS Michaud

210. Combs GF Jr, Clark LC, Turnbull BW. Reduction of cancer risk with an oral supplement of selenium. 1997. Biomed Environ Sci 10(2-3):227-34.

211. Cook NR, Le IM, Manson JE, Buring JE, Hennekens CH. Effects of beta-carotene supplementation on cancer incidence by baseline characteristics in the Physicians' Health Study (United States). 2000. Cancer Causes Control 11(7):617-26.

212. Correa P, Fontham ET, Bravo JC, Bravo LE, Ruiz B, Zarama G, Realpe JL, Malcom GT, Li D, Johnson WD, Mera R. Chemoprevention of gastric dysplasia: randomized trial of antioxidant supplements and anti-helicobacter pylori therapy. 2000. J Natl Cancer Inst 92(23):1881-8.

213. Davis CD. Vitamin D and cancer: current dilemmas and future research needs. 2008. Am J Clin Nutr 88(2): 565S-9S.

214. Duffield-Lillico AJ, Slate EH, Reid ME, Turnbull BW, Wilkins PA, Combs GF Jr, Park HK, Gross EG, Graham GF, Stratton MS, Marshall JR, Clark LC: Nutritional Prevention of Cancer Study Group. Selenium supplementation and secondary prevention of nonmelanoma skin cancer in a randomized trial. 2003. J Natl Cancer Inst 95(19):1477-81.

215. Ebbing M, Bønaa KH, Nygård O, Arnesen E, Ueland PM, Nordrehaug JE, Rasmussen K, Njølstad I, Refsum H, Nilsen DW, Tverdal A, Meyer K, Vollset SE. Cancer incidence and mortality after treatment with folic acid and vitamin B12. 2009. JAMA 302(19):2119-26.

"The SU.VI.MAX trial followed a pragmatic approach in testing the effect of a combination of 5 antioxidant vitamins or mineral at low doses. It is thus not possible to identify which individual micronutrient or combination is responsible for the preventative effect observed. Nevertheless, our study results support the hypothesis that chemoprevention of prostate cancer can be achieved with antioxidant vitamins and minerals."

- F Meyer, et al.

216. Egan KM, Signorello LB, Munro HM, Hargreaves MK, Hollis BW, Blot WJ. Vitamin D insufficiency among African-Americans in the southeastern United States: implications for cancer disparities (United States). 2008. Cancer Causes Control 19(5):527-35.

217. Fedirko V, Bostick RM, Goodman M, Flanders WD, Gross MD. Blood 25-hydroxyvitamin D3 concentrations and incident sporadic colorectal adenoma risk: a pooled case-control study. 2010. Am J Epidemiol 172(5):489-500.

218. Fleischauer AT, Olson SH, Mignone L, Simonsen N, Caputo TA, Harlap S. Dietary antioxidants, supplements, and risk of epithelial ovarian cancer. 2001. Nutr Cancer 40(2):92-8.

219. Fleischauer AT, Simonsen N, Arab L. Antioxidant supplements and risk of breast cancer recurrence and breast cancer-related mortality among postmenopausal women. 2003. Nutr Cancer 46(1):15-22.

220. Flood A, Peters U, Chatterjee N, Lacey JV Jr, Schairer C, Schatzkin A. Calcium from diet and supplements is associated with reduced risk of colorectal cancer in a prospective cohort of women. 2005. Cancer Epidemiol Biomarkers Prev 14(1):126-32.

221. Freedman DM, Chang SC, Falk RT, Purdue MP, Huang WY, McCarty CA, Hollis BW, Graubard BI, Berg CD, Ziegler RG. Serum levels of vitamin D metabolites and breast cancer risk in the prostate, lung, colorectal, and ovarian cancer screening trial. 2008. Cancer Epidemiol Biomarkers Prev 17(4):889-94.

222. Gandini S, Raimondi S, Gnagnarella P, Doré JF, Maisonneuve P, Testori A. Vitamin D and skin cancer: a meta-analysis. 2009. Eur J Cancer 45(4):634-41.

223. Garland CF, Gorham ED, Mohr SB, Garland FC. Vitamin D for cancer prevention: global perspective. 2009. Ann Epidemiol 19(7):468-83.

"In the 11 non-hormone-dependent cancer sites described above, 46 studies have specifically reported on a vitamin C index or plasma ascorbate values; 33 of these found statistically significant protective effects, and several more were in the protective direction but did not achieve significance. None has found elevated risk with increasing intake. In addition to those, 29 studies reported on the effect of fruit consumption, 21 of which found significant protection associated with frequent consumption or high risk associated with low consumption. For oral, esophageal, gastric, and pancreatic cancer, the evidence is extremely strong, with virtually all studies showing a significant protective effect."

- G Block

224. Gaziano JM, Glynn RJ, Christen WG, Kurth T, Belanger C, MacFadyen J, Bubes V, Manson JE, Sesso HD, Buring JE. Vitamins E and C in the prevention of prostate and total cancer in men: the Physicians' Health Study II randomized controlled trial. 2009. JAMA 301(1):52-62.

225. Gaziano J, Sesso HD, Christen WG, et al. Multivitamins in the Prevention of Cancer in Men: The Physicians' Health Study II Randomized Controlled Trial. JAMA. 2012;308(18):1871-1880.

226. Giovannucci E. The epidemiology of vitamin D and colorectal cancer: recent findings. 2006. Curr Opin Gastroenterol 22(1):24-9.

227. Giovannucci E. Vitamin D and cancer incidence in the Harvard cohorts. 2009. Ann Epidemiol 19(2):84-8.

228. Giovannucci E, Stampfer MJ, Colditz GA, Hunter DJ, Fuchs C, Rosner BA, Speizer FE, Willett WC. Multivitamin use, folate, and colon cancer in women in the Nurses' Health Study. 1998. Ann Intern Med 129(7):517-24.

229. Goodwin PJ, Ennis M, Pritchard KI, Koo J, Hood N. Frequency of vitamin D (Vit D) deficiency at breast cancer (BC) diagnosis and association with risk of distant recurrence and death in a prospective cohort study of T1–3, N0–1, M0 B. 2008. J Clin Oncology 26(15S; May 20 Supplement):511.

230. Gorham ED, Garland CF, Garland FC, Grant WB, Mohr SB, Lipkin M, Newmark HL, Giovannucci E, Wei M, Holick MF. Optimal vitamin D status for colorectal cancer prevention: a quantitative meta analysis. 2007. Am J Prev Med 32(3):210-6.

231. Grau MV, Baron JA, Sandler RS, Haile RW, Beach ML, Church TR, Heber D. Vitamin D, calcium supplementation, and colorectal adenomas: results of a randomized trial. 2003. J Natl Cancer Inst 95(23):1736-7.

232. Gridley G, McLaughlin JK, Block G, Blot WJ, Gluch M, Fraumeni JF Jr. Vitamin supplement use and reduced risk of oral and pharyngeal cancer. 1992. Am J Epidemiol 135(10):1083-92.

"Total vitamin B6 intake was also statistically significantly inversely associated with risk of colorectal cancer. We observed 59 cases of colorectal cancer among the 25% of women (approximately 8200) with the lowest plasma vitamin B6 concentrations over the 10-year follow-up, compared with 33 cases of colorectal cancer in the 25% of women with the highest plasma vitamin B6 concentrations."

-EK Wei, et al.

233. Hatfield DL, Gladyshev VN. The Outcome of Selenium and Vitamin E Cancer Prevention Trial (SELECT) Reveals the Need for Better Understanding of Selenium Biology. 2009. Mol Interv 9(1):18-21.

234. Heather Eliassen et al. Plasma carotenoids and risk of breast cancer over 20 y of follow-up. Am J Clin Nutr doi: 10.3945/ajcn.114.105080

235. Heinonen OP, Albanes D, Virtamo J, Taylor PR, Huttunen JK, Hartman AM, Haapakoski J, Malila N, Rautalahti M, Ripatti S, Maenpaa H, Teerenhovi L, Koss L, Virolainen M, Edwards BK. Prostate cancer and supplementation with alpha-tocopherol and beta-carotene: incidence and mortality in a controlled trial. 1998. J Natl Cancer Inst 90(6):440-6.

236. Hennekens CH, Buring JE, Manson JE, Stampfer M, Rosner B, Cook NR, Belanger C, LaMotte F, Gaziano JM, Ridker PM, Willett W, Peto R. Lack of effect of long-term supplementation with beta carotene on the incidence of malignant neoplasms and cardiovascular disease. 1996. N Engl J Med 334(18):1150-5.

237. Hercberg S, Galan P, Preziosi P, Bertrais S, Mennen L, Malvy D, Roussel AM, Favier A, Briancon S. The SU.VI. MAX Study: a randomized, placebo-controlled trial of the health effects of antioxidant vitamins and minerals. 2004. Arch Intern Med 164(21):2335-42.

238. Hernaandez J, Syed S, Weiss G, Fernandes G, von Merveldt Dl, Troyer DA, Basler JW, Thompson IM Jr. The modulation of prostate cancer risk with alpha-tocopherol: a pilot randomized, controlled clinical trial. 2005. J Urol 174(2):519-22.

239. Hoenjet KM, Dagnelie PC, Delaere KP, Wijckmans NE, Zambon JV, Oosterhof GO. Effect of a nutritional supplement containing vitamin E, selenium, vitamin c and coenzyme Q10 on serum PSA in patients with hormonally untreated carcinoma of the prostate: a randomized placebo-controlled study. 2005. Eur Urol 47(4):433-9.

240. Ishitani K, Lin J, Mason JE, Buring JE, Zhang SM. A Prospective Study of Multivitamin Supplement Use and Risk of Breast Cancer. 2008. Am J Epidemiol 167(10):1197-206.

"Our study of nearly 1100 incident cases of cancer is one of the largest prospective studies of serum selenium levels and cancer risk and has more site-specific cancers than any previous study. We found highly significant ($p < 10^{-4}$) inverse associations of serum selenium levels with the incidence of both esophageal and gastric cardia cancers over a period of 5.25 years of follow-up. Individuals in the highest quartile of selenium developed these cancers at approximately half the rate as individuals in the lowest quartile."

-SD Mark, et al.

241. Jian L et al. Do dietary lycopene and other carotenoids protect against prostate cancer? Int J Cancer. 2005 Mar 1;113(6):1010-4.

242. Johansson M, Appleby PN, Allen NE, Travis RC, Roddam AW, Egevad L, Jenab M, Rinaldi S, Kiemeney LA, Bueno-de-Mesquita HB, Vollset SE, Ueland PM, Sánchez MJ, Quirós JR, González CA, Larrañaga N, Chirlaque MD, Ardanaz E, Sieri S, Palli D, Vineis P, Tumino R, Linseisen J, Kaaks R, Boeing H, Pischon T, Psaltopoulou T, Trichopoulou A, Trichopoulos D, Khaw KT, Bingham S, Hallmans G, Riboli E, Stattin P, Key TJ. Circulating concentrations of folate and vitamin B12 in relation to prostate cancer risk: results from the European Prospective Investigation into Cancer and Nutrition study. 2008. Cancer Epidemiol Biomarkers Prev 17(2):279-85.

243. Kilkkinen A, Knekt P, Heliövaara M, Rissanen H, Marniemi J, Hakulinen T, Aromaa A. Vitamin D Status and the Risk of Lung Cancer: A Cohort Study in Finland. 2008. Cancer Epidem Biomarkers Prev 17:3274.

244. Kirsh VA, Hayes RB, Mayne ST, Chatterjee N, Subar AF, Dixon LB, Albanes D, Andriole GL, Urban DA, Peters U; PLCO Trial. Supplemental and dietary vitamin E, beta-carotene, and vitamin C intakes and prostate cancer risk. 2006. J Natl Cancer Inst 98(4):245-54.

"Based on overall consideration of results from observational and laboratory studies, the existing evidence is consistent with the hypothesis that increasing vitamin D3 intake to 1000–2000 IU per day or raising the serum level of 25(OH)D to 33 ng/mL or higher would be associated with substantially lower incidence rates of colorectal cancer, with only minimal risks."

-ED Gorham, et al.

245. Klein EA. The Selenium and Vitamin E Cancer Prevention Trial. 2009. Cur Clin Urol 6:349-60.

246. Kranse R, Dagnelie PC, van Kemenade MC, de Jong FH, Blom JH, Tijburg LB, Weststrate JA, Schroder FH. Dietary intervention in prostate cancer patients: PSA response in a randomized double-blind placebo-controlled study. 2005. Int J Cancer 113(5):835-40.

247. Kristal AR, Stanford JL, Cohen JH, Wicklund K, Patterson RE. Vitamin and mineral supplement use is associated with reduced risk of prostate cancer. 1999. Cancer Epidemiol Biomarkers Prev 8(10):887-92.

248. Lamm DL, Riggs DR, Shriver JS, vanGilder PF, Rach JF, DeHaven JI. Megadose vitamins in bladder cancer: a double-blind clinical trial. 1994. J Urol 151(1):21-6.

249. Larsson SC, Giovannucci E, Wolk A. Vitamin B6 intake, alcohol consumption, and colorectal cancer: a longitudinal population-based cohort of women. 2005. Gastroenterology 128(7):1830-7.

250. Larsson SC, Orsini N, Wolk A. Vitamin B6 and risk of colorectal cancer: a meta-analysis of prospective studies. 2010. JAMA 303(11):1077-83.

251. Le Marchand L, White KK, Nomura AM, Wilkens LR, Selhub JS, Tiirikainen M, Goodman MT, Murphy SP, Henderson BE, Kolonel LN. Plasma levels of B vitamins and colorectal cancer risk: the multiethnic cohort study. 2009. Cancer Epidemiol Biomarkers Prev 18(8):2195-201.

252. Lee IM, Cook NR, Manson JE, Buring JE, Hennekens CH. Beta-carotene supplementation and incidence of cancer and cardiovascular disease: the Women's Health Study. 1999. J Natl Cancer Inst 91(24):2102-6.

253. Leitzmann MF, Stampfer MJ, Wu K, Colditz GA, Willett WC, Giovannucci EL. Zinc supplement use and risk of prostate cancer. 2003. J Natl Cancer Inst 95(13)1004-7.

254. Li JY, Taylor PR, Li B, Dawsey S, Wang GQ, Ershow AG, Guo W, Liu SF, Yang CS, Shen Q, et al. Nutrition intervention trials in Linxian, China: multiple vitamin/mineral supplementation, cancer incidence, and disease-specific mortality among adults with esophageal dysplasia. 1993. J Natl Cancer Inst 85(18):1492-8.

255. Lin J, Cook NR, Albert C, Zaharris E, Gaziano JM, Denburgh MV, Burin JE, Manson JE. Vitamins C and E and Beta Carotene Supplementation and Cancer Risk: A Randomized Controlled Trial. 2008. J Natl Cancer Inst 101(1):14-23.

256. Lin J, Zhang SM, Cook NR, Manson JE, Lee IM, Buring JE. Intakes of calcium and vitamin D and risk of colorectal cancer in women. 2005. Am J Epidemiol 161(8):755-64.

257. Lippman SM, Klein EA, Goodman PJ, Lucia MS, Thompson IM, Ford LG, Parnes HL, Minasian LM, Gaziano JM, Hartline JA, Parsons JK, Bearden JD 3rd, Crawford ED, Goodman GE, Claudio J, Winquist E, Cook ED, Karp DD, Walther P, Lieber MM, Kristal AR, Darke AK, Arnold KB, Ganz PA, Santella RM, Albanes D, Taylor PR, Probstfield JL, Jagpal TJ, Crowley JJ, Meyskens FL Jr, Baker LH, Coltman CA Jr. Effect of selenium and vitamin E on risk of prostate cancer and other cancers: the Selenium and Vitamin E Cancer Prevention Trial (SELECT). 2009. JAMA 301(1):39-51.

"So far, epidemiological data for cancer argue for an overall positive role of sun-induced vitamin D. There may be more beneficial than adverse effects of moderately increased sun exposure, even for total cancer mortality. This message should be addressed to populations at risk for vitamin D deficiency."

- J Moan, et al.

258. Maalmi H. et al., Serum 25-hydroxyvitamin D levels and survival in colorectal and breast cancer patients: Systematic review and meta-analysis of prospective cohort studies. Eur J Cancer (2014).

259. Mark SD, Qiao YL, Dawsey SM, Wu YP, Katki H, Gunter EW, Fraumeni JF Jr, Blot WJ, Dong ZW, Taylor PR. Prospective study of serum selenium levels and incident esophageal and gastric cancers. 2000. J Natl Cancer Inst 92(21):1753-63.

260. Martinez ME, Giovannucci EL, Colditz GA, Stampfer MJ, Hunter DJ, Speizer FE, Wing A, Willett WC. Calcium, vitamin D, and the occurrence of colorectal cancer among women. 1996. J Natl Cancer Inst 88(19):1375-82.

261. McCullough ML, Bandera EV, Moore DF, Kushi LH. Vitamin D and calcium intake in relation to risk of endometrial cancer: a systematic review of the literature. 2008. Prev Med 46(4):298-302.

262. McCullough ML, Robertson AS, Rodriguez C, Jacobs EJ, Chao A, Carolyn J, Calle EE, Willett WC, Thun MJ. Calcium, vitamin D, dairy products, and risk of colorectal cancer in the Cancer Prevention Study II Nutrition Cohort (United States). 2003. Cancer Causes Control 14(1):1-12.

263. Meyer F, Bairati I, Fortin A, Gélinas M, Nabid A, Brochet F, Têtu B. Interaction between antioxidant vitamin supplementation and cigarette smoking during radiation therapy in relation to long-term effects on recurrence and mortality: a randomized trial among head and neck cancer patients. 2008. Int J Cancer 122(7):1679-83.

"Optimizing micronutrient intake (through better diets, fortification of foods, or multivitamin-mineral pills) can have a major impact on public health at low cost. Other micronutrients are likely to be added to the list of those whose deficiency causes DNA damage in the coming years. Tuning-up human metabolism, which varies with genetic constitution and changes with age, is likely to be a major way to minimize DNA damage, improve health and prolong healthy lifespan."

- BN Ames

264. Meyer F, Galan P, Douvillel P, Bairati I, Kegle P, Bertrais S, Estaquio C, Hercberg S. Antioxidant vitamin and mineral supplementation and prostate cancer prevention in the SU.VI.MAX trial. 2005. Int J Cancer 116(2):182-6.

265. Michaud DS, Spiegelman D, Clinton SK, Rimm EB, Willett WC, Giovannucci E. Prospective study of dietary supplements, macronutrients, micronutrients, and risk of bladder cancer in US men. 2000. Am J Epidemiol 152:1145-53.

266. Moan J, Porojnicu AC, Dahlback A, Setlow RB. Addressing the health benefits and risks, involving vitamin D or skin cancer, of increased sun exposure. 2008. PNAS 105(2):668-73.

267. Mondul AM, Weinstein SJ, Männistö S, Synder K, Horst RL, Virtamo J, Albanes D. Serum Vitamin D and Risk of Bladder Cancer. 2010. Cancer Res; ePub ahead of print. Retrieved online 8 November 2010. doi: 10.1158/0008-5472.CAN-10-0985.

268. Mohr SB. A brief history of vitamin D and cancer prevention. 2009. Ann Epidemiol 19(2):79-83.

269. Mohr SB, Garland CF, Gorham ED, Grant WB, Garland FC. Could ultraviolet B irradiance and vitamin D be associated with lower incidence rates of lung cancer?. 2008. J Epidemiol Community Health 62:69-74.

270. Moorman PG, Ricciuti MF, Millikan RC, Newman B. Vitamin supplement use and breast cancer in a North Carolina population. 2001. Public Health Nutr 4(3):821-7.

271. Moyad MA. Selenium and vitamin E supplements for prostate cancer: evidence or embellishment?. 2002. Urology 59(4 Suppl 1):9-19.

"In conclusion, our findings do not support a protective role of calcium and vitamin D intakes against colorectal cancer incidence. However, given the strong evidence from both animal studies and in vitro studies, the benefits of these two nutrients cannot be ruled out. More detailed investigation of the interaction of calcium with other nutrients, including vitamin D, and additional questions better characterizing vitamin D status may be necessary to elucidate the true associations of calcium and vitamin D with risk of colorectal cancer."

-J Lin, et al.

272. Neuhouser ML, Sorensen B, Hollis BW, Ambs A, Ulrich CM, McTiernan A, Bernstein L, Wayne S, Gilliland F, Baumgartner K, Baumgartner R, Ballard-Barbash R. Vitamin D insufficiency in a multiethnic cohort of breast cancer survivors. 2008. Am J Clin Nutr 88(1):133-9.

273. Ng K, Wolpin BM, Meyerhardt JA, Wu K, Chan AT, Hollis BW, Giovannucci EL, Stampfer MJ, Willett WC, Fuchs CS. Prospective study of predictors of vitamin D status and survival in patients with colorectal cancer. 2009. Br J Cancer 101:916-23.

274. Omenn GS, Goodman GE, Thornquist MD, Balmes J, Cullen MR, Glass A, Keogh JP, Meyskens FL, Valanis B, Williams JH, Barnhart S, Hammar S. Effects of a combination of beta carotene and vitamin A on lung cancer and cardiovascular disease. 1996. N Engl J Med 334(18):1150-5.

275. Patterson RE, White E, Kristal AR, Neuhouser ML, Potter JD. Vitamin supplements and cancer risk: the epidemiologic evidence. 1997. Cancer Causes Control 8(5):786-802.

276. Peters U, Chatterjee N, McGlynn KA, Schoen RE Church TR, Bresalier RS, Gaudet MM, Flood A, Schatzkin A, Hayes RB. Calcium intake and colorectal adenoma in a US colorectal cancer early detection program. 2004. Am J Clin Nutr 80(5):1358-65.

277. Peters U, Littman AJ, Kristal AR, Patterson RE, Potter JD, White E. Vitamin E and selenium supplementation and risk of prostate cancer in the Vitamins and lifestyle (VITAL) study cohort. 2008. Cancer Causes and Control 19(1):75-87.

278. Poole EM et al. Postdiagnosis supplement use and breast cancer prognosis in the After Breast Cancer Pooling Project. Breast Cancer Res Treat. 2013 May 10.

279. Pufulete M, Al-Ghnaniem R, Khushal A, Appleby P, Harris N, Gout S, Emery PW, Sanders TA. Effect of folic acid supplementation on genomic DNA methylation in patients with colorectal adenoma. 2005. Gut 54(5):648-53.

"On a very simplistic level, cancer is thought to arise because of an excess of DNA damage and/or the inappropriate expression of critical genes. Folate has consequently been of particular interest as a potential cancer protective agent because of the important roles it plays in nucleotide synthesis, as well as in the biological methylation of molecules such as DNA, RNA, proteins, and the phospholipids."

- SW Choi, et al.

280. Pryor WA, Stahl W, Rock CL. Beta carotene: from biochemistry to clinical trials. 2000. Nutr Rev 58(2 Pt 1):39-53.

281. Qiao YL, Dawsey SM, Kamangar F, Fan JH, Abnet CC, Sun XD, Johnson LL, Gail MH, Dong ZW, Yu B, Mark SD, Taylor PR. Total and Cancer Mortality after Supplementation with Vitamins and Minerals: Follow-up of the Linxian General Population Nutrition Intervention Trial. 2009. J Natl Cancer Inst 101(7):507-18.

282. Rodriguez C, Jacobs EJ, Mondul AM, Calle EE, McCullough ML, Thur MJ. Vitamin E supplements and risk of prostate cancer in U.S. men. 2004. Cancer Epidemiol Biomarkers Prev 13(3):378-82.

283. Rodriguez C, McCullough ML, Mondul AM, Jacobs EJ, Fakhrabadi-Shokoohi d, Giovannucci EL, Thun MJ, Calle EE. Calcium, dairy products, and risk of prostate cancer in a prospective cohort of United States men. 2003. Cancer Epidemiol Biomarkers Prev 12(7):597-603.

284. Schatzkin A, Lanza E, Corle D, Lance P, Iber F, Caan B, Shike M, Weissfeld J, Burt R, Cooper MR, Kikendall JW, Cahill J, Polyp Prevention Trial Study Group. Lack of effect of a low-fat, high-fiber diet on the recurrence of colorectal adenomas. 2000. N Engl J Med 342(16):1149-55.

285. Schroder FH, Roobol MJ, Boeve ER, de Mutsert R, Zuijdgeest-van Leeuwen SD, Kersten I, Wildhagen M, van Helvoort A. Randomized, double-blind, placebo-controlled crossover study in men with prostate cancer and rising PSA: effectiveness of a dietary supplement. 2005. Eur Urol 48(6):922-30.

286. Sharp L, Little J, Brockton NT, Cotton SC, Masson LF, Haites NE, Cassidy J. Polymorphisms in the methylenetetrahydrofolate reductase (MTHFR) gene, intakes of folate and related B vitamins and colorectal cancer: a case–control study in a population with relatively low folate intake. 2008. Br J Nutr 99:379-89.

287. Shklar G, Oh SK. Experimental basis for cancer prevention by vitamin E. 2000. Cancer Invest 18(3):214-22.

288. Song Y, Chung CS, Bruno RS, Traber MG, Brown KH, King JC, Ho E. 2009. Dietary zinc restriction and repletion affects DNA integrity in healthy men. AJCN 90(2):321-8.

"In our study, vitamin E showed no overall effect on lung cancer; however, preliminary analyses indicate possible efficacy with longer duration of intervention. Prostate cancer incidence was 34% lower in the vitamin E group and colorectal cancer was 16% lower, the latter being consistent with recent observational data suggesting such a protective association. Such effects, if corroborated by other studies, would have substantial public health consequences on two common malignancies."

- D Albanes, et al.

289. Stolzenberg-Solomon RZ, Hayes RB, Horst RL, Anderson KE, Hollis BW, Silverman DT. Serum Vitamin D and Risk of Pancreatic Cancer in the Prostate, Lung, Colorectal, and Ovarian Screening Trial. 2009. Cancer Res 69:1439.

290. Taylor PR, Wang GQ, Dawsey SM, Guo W, Mark SD, Li JY, Blot WJ, Li B. Effect of nutrition intervention on intermediate endpoints in esophageal and gastric carcinogenesis. 1995. Am J Clin Nutr 62(6 Suppl):1420S-3S.

291. Terry P, Baron JA, Bergkvist L, Holmberg L, Wolk A. Dietary calcium and vitamin D intake and risk of colorectal cancer: a prospective cohort study in women. 2002. Nutr Cancer 43(1):39-46.

292. The Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group. The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. 1994. N Engl J Med 330(15):1029-35

293. Thompson JR, Fitz Gerald P, Willoughby MLN, Arm-

strong BK. Maternal folate supplementation in pregnancy and protection against acute lymphoblastic leukaemia in childhood: a case-control study. 2001. Lancet 358:1935-40.

294. Travis RC, Crowe FL, Allen NE, Appleby PN, Roddam AW, Tjønneland A, Olsen A, Linseisen J, Kaaks R, Boeing H, Kröger J, Trichopoulou A, Dilis V, Trichopoulos D, Vineis P, Palli D, Tumino R, Sieri S, Bueno-de-Mesquita HB, van Duijnhoven FJ, Chirlaque MD, Barricarte A, Larrañaga N, González CA, Argüelles MV, Sánchez MJ, Stattin P, Hallmans G, Khaw KT, Bingham S, Rinaldi S, Slimani N, Jenab M, Riboli E, Key TJ. Serum vitamin D and risk of prostate cancer in a case-control analysis nested within the European Prospective Investigation into Cancer and Nutrition (EPIC). 2009. Am J Epidemiol 169(10):1223-32.

"Our study, performed in individuals not selected for risk factors, indicates that a 7.5-year low-dose antioxidant supplementation lowered total cancer incidence in men but not in women. A similar tendency was observed for all-cause mortality."

-S Hercberg

295. Tsavachidou D, McDonnell TJ, Wen S, Wang X, Vakar-Lopez F, Pisters LL, Pettaway CA, Wood CG, Do KA, Thall PF, Stephens C, Efstathiou E, Taylor R, Menter DG, Troncoso P, Lippman SM, Logothetis CJ, Kim J. Selenium and vitamin E: cell type- and intervention-specific tissue effects in prostate cancer. 2009. J Natl Cancer Inst 101(5):306-20.

296. U.S. Preventive Services Task Force. Routine vitamin supplementation to prevent cancer and cardiovascular disease: recommendations and rationale. 2003. Ann Intern Med 139:51-5.

297. Velicer CM, Ulrich CM. Vitamin and Mineral Supplement Use Among US Adults After Cancer Diagnosis: A Systematic Review. 2008. J Clin Oncology 26(4):665-73.

298. Virtamo J, Pietinen P, Huttunen JK, Korhonen P, Malila N, Virtanen MJ, Albanes D, Taylor PR, Albert P; ATBC Study Group. Incidence of cancer and mortality following alpha-tocopherol and beta-carotene supplementation: a postintervention follow-up. 2003. JAMA 290(4):476-85.

299. Wactawski-Wende J, Kotchen JM, Anderson FL, Assaf AR, Brunner RL, O'Sullivan MJ, Margolis KL, Ockene JK, Phillips L, Pottern L, Prentice RL, Robbins J, Rohan TE, Sarto FE, Sharma S, Stefanick ML, Van Horn L, Wallace RB, Whitlock E, Bassford T, Beresford SA, Black HR, Bonds DE, Brzyski RG, Caan B, Chlebowski RT, Cochrane B, Garland C, Gass M, Hays J, Heiss G, Hendrix SL, Howard BV, Hsia J, Hubbell FA, Jackson RD, Johnson KC, Judd H, Kooperberg CL, Kuller LH, LaCroix AZ, Lane DS, Langer RD, Lasser NL, Lewis CE, Limacher MC, Manson JE; Women's Health Initiative Investigators. Calcium plus vitamin D supplementation and the risk of colorectal cancer. 2006. N Engl J Med 354(7):684-96.

300. Wei EK, Giovannucci E, Selhub J, Fuchs CS, Hankinson SE, Ma J. Plasma vitamin B6 and the risk of colorectal cancer and adenoma in women. 2005. J Natl Cancer Inst 97(9):684-92.

301. Wu K, Willett WC, Chan JM, Fuchs CS, Colditz GA, Rimm EB, Giovannucci EL. A prospective study on supplemental vitamin E intake and risk of colon cancer in women and men. 2002. Cancer Epidemiol Biomarkers Prev 11(11):1298-304.

302. Xu Q, Parks CG, DeRoo LA, Cawthon RM, Sandler DP, Chen H. Multivitamin use and telomere length in women. 2009. Am J Clin Nutr 89:1857–63.

303. Zhang SM, Cook NR, Albert CM, Gaziano JM, Buring JE, Manson JE. Effect of combined folic acid, vitamin B6, and vitamin B12 on cancer risk in women: a randomized trial. 2008. JAMA 300(17):2012-21.

304. Zhang SM, Giovannucci EL, Hunter DJ, Rimm EB, Ascherio A, Colditz GA, Speizer FE, Willett WC. Vitamin supplement use and the risk of non-Hodgkin's lymphoma among women and men. 2001. Am J Epidemiol 153(11):1056-63.

"In summary, overall risks for prostate cancer were unaffected by supplemental dietary antioxidant use among participants in the PLCO Trial; however, vitamin E supplementation in smokers and β-carotene supplementation in men with low dietary β-carotene were associated with reduced risks of this disease."

-VA Kirsh, et al.

305. Zhang SM, Moore SC, Lin J, Cook NR, Manson JE, Lee IM, Buring JE. Folate, vitamin B6, multivitamin supplements, and colorectal cancer risk in women. 2006. Am J Epidemiol 163(2):108-15.

306. Zheng W, Anderson KE, Kushi LH, Sellers TA, Greenstein J, Hong CP, Cerhan JR, Bostick RM, Folsom AR. A prospective cohort study of intake of calcium, vitamin D, and other micronutrients in relation to incidence of rectal cancer among postmenopausal women. 1998. Cancer Epidemiol Biomarkers Prev 7(3):221-5.

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307. Adams J, Pepping J. Vitamin K in the treatment and prevention of osteoporosis and arterial calcification. 2005. Am J Health Syst Pharm 62(15):1574-81.

308. Alekel DL, St Germain A, Peterson CT, Hanson KB, Stewart JW, Toda T. Isoflavone-rich soy protein isolate attenuates bone loss in the lumbar spine of perimenopausal women. 2000. AJCN 72(3):844-52.

309. Allen SC, Raut S. Biochemical recovery time scales in elderly patients with osteomalacia. 2004. J R Soc Med 97(11): 527-30

310. Barnes MS, Robson PJ, Bonham MP, Strain JJ, Wallace JM. Effect of vitamin D supplementation on vitamin D status and bone turnover markers in young adults. 2006. Eur J Clin Nutr 60:727-33.

311. Bikle DD. Role of vitamin D, its metabolites, and analogs in the management of osteoporosis. 1994. Rheum Dis Clin North Am 20(3):759-75.

312. Binkley NC, Krueger DC, Kawahara TN, Engelke JA, Chappell RJ, Suttie JW. A high phylloquinone intake is required to achieve maximal osteocalcin gamma-carboxylation. 2002. Am J Clin Nutr 76(5):1055-60.

313. Binkley NC, Suttie JW. Vitamin K nutrition and osteoporosis. 1995. J Nutr 125(7):1812-21.

314. Bischoff-Ferrari HA, Willett WC, Wong JB, Giovannucci E, Dietrich T, Dawson-Hughes B. Fracture prevention with vitamin D supplementation: a meta-analysis of randomized controlled trials. 2005. JAMA 293(18):2257-64.

315. Bolton-Smith C, McMurdo MET, Paterson CR, Mole PA, Harvey JM, Fenton ST, Prynne CJ, Mishra GD, Shearer MJ. Two-Year Randomized Controlled Trial of Vitamin K1 (Phylloquinone) and Vitamin D3 Plus Calcium on the Bone Health of Older Women. 2007. J Bone Min Res 22(4):509-19.

"One member in each twin pair was randomly assigned using computer-generated numbers to receive 800 mg of elemental Calcium from citrate and carbonate, 400 IU of vitamin D3 (as Cholecaliferol), 400 mg of Magnesium from citrate, and amino acid chelate and oxide in four orange-flavoured chewable tablets (Active Calcium™ Chewable); the other twin was given a matched placebo in a double-blinded manner. The placebo tablet was identical in appearance, taste and composition but contained no active ingredient. All tablets were supplied by USANA Health Sciences, Inc., Sydney, Australia…

"Our findings indicate that supplementation with 800 mg calcium and 400 IU vitamin D3 per day for a period of 6 months was associated with increased trabecular area, trabecular density and strength strain index at the ultra-distal tibia and radius and increased cortical area at tibial mid-shaft."

- DA Greene, et al.

316. Bonjour JP, Chevalley T, Ammann P, Slosman D, Rizzoli R. Gain in bone mineral mass in prepubertal girls 3-5 years after discontinuation of calcium supplementation: a follow-up study. 2001. Lancet 358:1208-12.

317. Braham R, Dawson B, Goodman C, McNaughton L. The effect of glucosamine supplementation on people experiencing regular knee pain. 2003. Br J Sports Med 37(1):45–9.

318. Brownbill RA, Petrosian M, Ilich JZ. Association between dietary conjugated linoleic acid and bone mineral density in postmenopausal women. 2005. J Am Coll Nutr 24(3):177-81.

319. Bruyere O, Pavelka K, Rovati LC, Deroisy R, Olejarova M, Gatterova J, Giacovelli G, Reginster JY. Glucosamine sulfate reduces osteoarthritis progression in postmenopausal women with knee osteoarthritis: evidence from two 3-year studies. 2004. Menopause 11(2):138-43.

"[Boron] may have a preventive or therapeutic effect that helps to diminish bone mineral loss in susceptible populations."

- SL Meacham, et al.

320. Buckley LM, Hillner BE. A cost effectiveness analysis of calcium and vitamin D supplementation, etidronate, and alendronate in the prevention of vertebral fractures in women treated with glucocorticoids. 2003. J Rheumatol 30(1):132-8.

321. Cameron MA, Paton LM, Nowson CA, Margerison C, Frame M, Wark JD. The effect of calcium supplementation on bone density in premenarcheal females: a co-twin approach. 2004. J Clin Endocrinol Metab 89(10):4916-22.

322. Chapuy MC, Arlot ME, Duboeuf F, Brun J, Crouzet B, Arnaud S, Delmas PD, Meunier PJ. Vitamin D3 and calcium to prevent hip fractures in the elderly women. 1992. N Engl J Med 327(23):1637-42.
323. Chapuy MC, Pamphile R, Paris E, Kempf C, Schlichting M, Arnaud S, Garnero P, Meunier PJ. Combined calcium and vitamin D3 supplementation in elderly women: confirmation of reversal of secondary hyperparathyroidism and hip fracture risk: the Decalyos II study. 2002. Osteoporos Int 13(3):257-64.
324. Cheng S, Lyytikäinen A, Kröger H, Lamberg-Allardt C, Alén, Koistinen A, Wang QJ, Suuriniemi M, Suominen H, Mahonen A, Nicholson PHF, Ivaska KK, Korpela R, Ohlsson C, Väänänen KH, Tylavsky F. Effects of calcium, dairy product, and vitamin D supplementation on bone mass accrual and body composition in 10-12 year old girls: a 2-y randomized trial. 2005. Am J Clin Nutr 82:1115-26.

"Our particular contribution has been to extend from animal models to humans the essentiality of Cu, Mn and Zn in the development and maintenance of BMD [bone mineral density]... Through understanding the value of trace elements from food or supplements, and through sensible dietary strategies, we can slow the rate of bone loss, thus delaying or preventing osteoporosis, in a simple and inexpensive manner."

- PD Saltman, et al.

325. Chevalley T, Bonjour JP, Ferrari S, Hans D, Rizzoli R. Skeletal site selectivity in the effects of calcium supplementation on areal bone mineral density gain: a randomized, double-blind, placebo-controlled trial in prepubertal boys. 2005. J Clin Endocrinol Metab 90(6):3342-9.
326. Cooper L, Clifton-Bligh PB, Nery ML, Figtree G, Twigg S, Hibbert E, Robinson BG. Vitamin D supplementation and bone mineral density in early postmenopausal women. 2003. Am J Clin Nutr 77(5):1324-9.
327. Cumming RG, Nevitt MC. Calcium for prevention of osteoporotic fractures in postmenopausal women. 1997. J Bone Miner Res 12(9):1321-9.
328. Curtis CL, Hughes CE, Flannery CR, Little CB, Harwood JL, Caterson B. n-3 Fatty Acids Specifically Modulate Catabolic Factors Involved in Articular Cartilage Degradation. 2000. J Biol Chem 275(2):721-4.
329. Curtis CL, Rees SG, Cramp J, Flannery CR, Hughes CE, Little CB, Williams R, Wilson C, Dent CM, Harwood JL, Caterson B. Effects of n-3 fatty acids on cartilage metabolism. 2002. Proc Nutr Soc 61(3):381-9.
330. Dawson-Hughes B, Harris SS, Krall EA, Dallal GE. Effect of calcium and vitamin D supplementation on bone density in men and women 65 years of age or older. 1997. N Engl J Med 337(10):670-6.
331. Dawson-Hughes B, Harris SS, Krall EA, Dallal GE, Falconer G, Green CL. Rates of bone loss in postmenopausal women randomly assigned to one of two dosages of vitamin D. 1995. Am J Clin Nutr 61(5):1140-5.
332. Dawson-Hughes B, Dallal GE, Krall EA, Harris S, Sokoll LJ, Falconer G. Effect of vitamin D supplementation on wintertime and overall bone loss in healthy postmenopausal women. 1991. Ann Intern Med 115(7):505-12.
333. Dawson-Hughes B, Dallal GE, Krall EA, Sadowski L, Sahyoun N, Tannenbaum S. A controlled trial of the effect of calcium supplementation on bone density in postmenopausal women. 1990. N Engl J Med 323(13):878-83.
334. Dietrich T, Joshipura KJ, Dawson-Hughes B, Bischoff-Ferrari HA. Association between serum concentrations of 25-hydroxyvitamin D3 and periodontal disease in the US population. 2004. Am J Clin Nutr 80:108–13.

"In summary, dietary supplementation with a combination of nutritionally relevant amounts of vitamin K with vitamin D and calcium in healthy older women was associated with a modest but significant increase in BMC at one site, consisting predominantly of trabecular bone. Similar changes were not observed in either the vitamin K group alone or in the calcium plus vitamin D group, suggesting a synergistic role of the combination as sugggested by previous reports."

- C Bolton-Smith, et al.

335. Dodiuk-Gad RP, Rozen GS, Rennert G, Rennert HS, Ish-Shalom S. Sustained effect of short-term calcium supplementation on bone mass in adolescent girls with low calcium intake. 2005. AJCN 81(1):168-74.
336. Fang Fang Zhang and Sarah Booth. Low Vitamin D Linked to Osteoarthritis. AgResearch Magazine July 2015. Vol. 63 No. 7.
337. Farina EK, Kiel DP, Roubenoff R, Schaefer EJ, Cupples LA, Tucker KL. Protective effects of fish intake and interactive effects of long-chain polyunsaturated fatty acid intakes on hip bone mineral density in older adults: the Framingham Osteoporosis Study. Am J Clin Nutr. 2011;93(5):1142-51.
338. Feskanich D, Singh V, Willett WC, Colditz GA. Vitamin A intake and hip fractures among postmenopausal women. 2002. JAMA 287(1):47-54.

339. Feskanich D, Willett WC, Colditz GA. Calcium, vitamin D, milk consumption, and hip fractures: a prospective study among postmenopausal women. 2003. Am J Clin Nutr 77(2):504-11.
340. Fraser DR. Vitamin D-deficiency in Asia. 2004. J Steroid Biochem Mol Biol 89-90(1-5):491-5.
341. Gennari C. Calcium and vitamin D nutrition and bone disease of the elderly. 2001. Public Health Nutr 4(2B):547-59.
342. Going S, Lohman T, Houtkooper L, Metcalfe L, Flint-Wagner H, Blew R, Stanford V, Cussler E, Martin J, Teixeira P, Harris M, Milliken L, Figueroa-Galvez A, Weber J. Effects of exercise on bone mineral density in calcium-replete postmenopausal women with and without hormone replacement therapy. 2003. Osteoporos Int 14(8):637-43.
343. Grant AM, Avenell A, Campbell MK, McDonald AM, MacLennan GS, McPherson GC, Anderson FH, Cooper C, Francis RM, Donaldson C, Gillespie WJ, Robinson CM, Torgerson DJ, Wallace WA, RECORD Trial Group. Oral vitamin D3 and calcium for secondary prevention of low-trauma fractures in elderly people (Randomised Evaluation of Calcium Or vitamin D, RECORD): a randomized placebo-controlled trial. 2005. Lancet 365(9471):1621-8.

"Adequate nutrition plays a major role in the prevention and treatment of osteoporosis; the nutrients of greatest importance are calcium and vitamin D. Numerous studies have shown that higher calcium intake at various ages are associated with higher bone mineral density compared with the bone mass of those with lower calcium intakes. In older postmenopausal women, the benefits of vitamin D and calcium supplementation in preventing bone loss, decreasing bone turnover, and decreasing nonvertebral fractures are clear."

- JW Nieves

344. Greene DA, Naughton GA. Calcium and vitamin-D supplementation on bone structural properties in peripubertal female identical twins: a randomised controlled trial. 2010. Osteoporos Int [Epub ahead of print].
345. Greenspan SL, Resnick NM, Parker RA. Vitamin D supplementation in older women. 2005. J Gerontol A Biol Sci Med Sci 60(6):754-9.
346. Gulati S, Sharma RK, Gulati K, Singh U, Srivastava A. Longitudinal follow-up of bone mineral density in children with nephritic syndrome and the role of calcium and vitamin D supplements. 2005. Nephrol Dial Transplant 20(8):1598-603.
347. Haney EM, Stadler D, Bliziotes MM. Vitamin D insufficiency in internal medicine residents. 2005. Calcif Tissue Int 76(1):11-6.
348. Hanley DA, Cranney A, Jones G, Whiting SJ, Leslie WD, Cole DEC, Atkinson SA, Josse RG, Feldman S, Kline GA, Rosen C. Vitamin D in adult health and disease: a review and guideline statement from Osteoporosis Canada. 2010. CMAJ 182(12):E610-8.
349. Harris S, Dawson-Hughes B. Rates of change in bone mineral density of the spine, heel, femoral, neck and radius in healthy postmenopausal women. 1992. Bone Miner 17(1):87-95.

"Much evidence indicates that both calcium and vitamin D are efficacious in protecting the skeleton, particularly when these 2 nutrients are used in combination. Each nutrient is necessary for the full expression of the effect of the other, and where their actions are independent, their effects on skeletal health are complementary. Nutrient status for both tends to be deficient in the adult population of the industrialized nations. Hence, supplementation or food fortification with both nutrients is appropriate and, given contemporary diets and sun exposure, probably necessary."

- RP Heaney

350. Harwood RH, Sahota O, Gaynor K, Masud T, Hosking DJ, The Nottingham Neck of Femur (NONOF) Study. A randomized, controlled comparison of different calcium and vitamin D supplementation regimens in elderly women after hip fracture: The Nottingham Neck of Femur (NONOF) Study. 2004. Age Ageing 33(1):45-51.
351. Heaney RP. Bone health. 2007. Am J Clin Nutr 85(suppl):300S-3S.
352. Heaney RP. Nutritional factors in osteoporosis. 1993. Annu Rev Nutr 13:287-316.
353. Hunter D, Major P, Arden N, Swaminathan R, Andrew T, MacGregor AJ, Keen R, Snieder H, Spector TD. A randomized controlled trial of vitamin D supplementation on preventing postmenopausal bone loss and modifying bone metabolism using identical twin pairs. 2000. J Bone Miner Res 15(11):2276-83.
354. Hyun TH, Barrett-Connor E, Milne DB. Zinc intakes and plasma concentrations in men with osteoporosis: the Rancho Bernardo Study. 2004. AJCN 80(3):715-21.

355. Ilich JZ, Kerstetter JE. Nutrition in Bone Health Revisited: A Story Beyond Calcium. 2000. JACN 19(6):715-37.
356. Jackson RD, LaCroix AZ, Gass M, Wallace RB, Robbins J, Lewis CE, Bassford T, Beresford SAA, Black HR, Blanchette P, Bonds DE, Brunner RL, Brzyski RG, Caan B, Cauley JA, Chlebowski RT, Cummings SR, Granek I, Hays J, Heiss G, Hendrix SL, Howard BV, Hsia J, Hubbell FA, Johnson KC, Judd H, Kotchen JM, Kuller LH, Langer RD, Lasser NL, Limacher MC, Ludlam S, Manson JE, Margolis KL, McGowan J, Ockene JK, O'Sullivan MJ, Phillips L, Prentice RL, Sarto GE, Stefanick ML, Van Horn L, Wactawski-Wende J, Whitlock E, Anderson GL, Assaf AR, Barad D. Calcium plus vitamin D supplementation and the risk of fractures. 2006. N Engl J Med 354(7):669-83.

"Numerous studies have demonstrated the importance of vitamin K in bone health. Cell studies have helped delineate the mechanism by which menaquinone promotes bone mineralization and inhibits resorption. Human and animal studies have clearly demonstrated that vitamin K can improve bone health by increasing bone mass and reducing bone loss."

- J Adams, et al.

357. Javaid MK, Crozier SR, Harvey NC, Gale CR, Dennison EM, Boucher BJ, Arden NK, Godfrey KM, Cooper C; Princess Anne Hospital Study Group. Maternal vitamin D status during pregnancy and childhood bone mass at age 9 years: a longitudinal study. 2006. Lancet 367(9504):36-43.
358. Johnston CC Jr, Miller JZ, Slemenda CW, Reister TK, Hui S, Christian JC, Peacock M. Calcium supplementation and increases in bone mineral density in children. 1992. N Engl J Med 327(2):82-7.
359. Jugdaohsingh R, Tucker KL, Qiao N, Cupples LA, Kiel DP, Powell JJ. Dietary silicon intake is positively associated with bone mineral density in men and premenopausal women of the Framingham Offspring Cohort. 2004. Journal of Bone and Mineral Research 19(2):297-307.
360. Lambert HL, Eastell R, Karnik K, Russell JM, Barker ME. Calcium supplementation and bone mineral accretion in adolescent girls: an 18-mo randomized controlled trial with 2-y follow-up. 2008. Am J Clin Nutr 87(2):455-62.
361. Larsen ER, Mosekilde L, Foldspang A. Vitamin D and calcium supplementation prevents osteoporotic fractures in elderly community dwelling residents: a pragmatic population-based 3-year intervention study. 2004. J Bone Miner Res 19(3):370-8.
362. Lee WTK, Leung SSF, Leung DMY, Cheng JCY. A follow-up study on the effects of calcium-supplement withdrawal and puberty on bone acquisition of children. 1996. Am J Clin Nutr 64:71-7.
363. Lee WTK, Leung SSF, Leung DMY, Tsang HSY, Lau J, Cheng JCY. A randomized double-blind controlled calcium supplementation trial, and bone and height acquisition in children. 1995. Br J Nutr 74:125-39.
364. Lee WTK, Leung SSF, Leung DMY, Wang SH, Xu YC, Zeng WP, Cheng JCY. Bone mineral acquisition in low calcium intake children following the withdrawal of calcium supplement. 1997. Acta Paediatr 86:570-6.
365. Lee WTK, Leung SSF, Wang SH, Xu YC, Zeng WP, Lau J, Oppenheimer SJ, Cheng JCY. Double-blind, controlled calcium supplementation and bone mineral accretion in children accustomed to a low-calcium diet. 1994. Am J Clin Nutr 60:744-50.

"Osteoporosis is a multifactorial disorder, and, despite the considerable influence of heredity, bone health depends on the whole range of other nutrients and foods as well as the environmental factors. The prolonged deficiency or excess of one or the combination of several, as well as the changes in requirements of those nutrients caused by physiological and metabolic changes, might contribute to osteoporosis."

- JZ Ilich, et al.

366. Lips P, Graafmans WC, Ooms ME, Bezemer PD, Bouter LM. Vitamin D supplementation and fracture incidence in elderly persons: a randomized, placebo-controlled clinical trial. 1996. Ann Intern Med 124(4):400-6.
367. Lloyd T, Andon MB, Rollings N, Martel JK, Landis JR, Demers LM, Eggli DF, Kieselhorst K, Kulin HE. Calcium supplementation and bone mineral density in adolescent girls. 1993. JAMA 270(7):841-4.
368. Meacham SL, Taper LJ, Volpe SL. Effect of boron supplementation on blood and urinary calcium, magnesium, and phosphorus, and urinary boron in athletic and sedentary women. 1995. AJCN 61(2):341-5.
369. Meacham SL, Taper LJ, Volpe SL. Effects of boron supplementation on bone mineral density and dietary, blood, and urinary calcium, phosphorus, magnesium, and boron in female athletes. 1994. Environ Health Perspect 102(Suppl 7):79-82.

370. Meier C, Woitge HW, Witte K, Lemmer B, Seibel MJ. Supplementation with oral vitamin D3 and calcium during winter prevents seasonal bone loss: a randomized controlled open-label prospective trial. 2004. J Bone Miner Res 19(8):1221-30.
371. Meunier P. Prevention of hip fractures by correcting calcium and vitamin D insufficiencies in elderly people. 1996. Scand J Rheumatol Suppl 103:75-8.
372. Meyer HE, Smedshaug GB, Kvaavik E, Falch JA, Tverdal A, Pedersen JI. Can vitamin D supplementation reduce the risk of fracture in the elderly? A randomized controlled trial. 2002. J Bone Miner Res 17(4):709-15.
373. Michaëlsson K, Lithell H, Vessby B, Melhus H. Serum retinol levels and the risk of fracture. 2003. N Engl J Med 348:287-94.
374. Ng NTM, Heesch KC, Brown WJ. Efficacy of a progressive walking program and glucosamine sulphate supplementation on osteoarthritic symptoms of the hip and knee: a feasibility trial. 2010. Arthrit Res Ther 12(1):R25.
375. Nieves JW. Osteoporosis: the role of micronutrients. 2005. AJCN 81(5):1232S-9S.

"The effects of low intakes of minerals important to normal bone metabolism need further investigation. An inadequate intake or imbalance of one or several of the minerals critical to bone development may jeopardize normal bone metabolism. There has been widespread interest over the years in assuring adequate calcium intakes at critical stages of the female life cycle. This interest should be extended to emphasize optimal intakes of all minerals known or suspected to affect bone mineral density, such as calcium, phosphorus, magnesium, and boron."

- SL Meacham, et al.

376. Nowson CA, Green RM, Hopper JL, Sherwin AJ, Young D, Kaymakci B, Guest CS, Smid M, Larkins RG, Wark JD. A co-twin study of the effect of calcium supplementation on bone density during adolescence. 1997. Osteoporos Int 7(3):219-25.
377. Papadimitropoulos E, Wells G, Shea B, Gillespie W, Weaver B, Zytaruk N, Cranney A, Adachi J, Tugwell P, Josse R, Greenwood C, Guyatt G; Osteoporosis Methodology Group and The Osteoporosis Research Advisory Group. Meta-analyses of therapies for postmenopausal osteoporosis. VIII: Meta-analysis of the efficacy of vitamin D treatment in preventing osteoporosis in postmenopausal women. 2002. Endocr Rev 23(4):560-9.
378. Peacock M, Liu G, Carey M, McClintock R, Ambrosius W, Hui S, Johnston CC. Effect of calcium or 25OH vitamin D3 dietary supplementation on bone loss at the hip in men and women over the age of 60. 2000. J Clin Endocrinol Metab 85(9):3011-9.
379. Porthouse J, Cockayne S, King C, Saxon L, Steele E, Aspray T, Baverstock M, Birks Y, Dumville J, Francis R, Iglesias C, Puffer S, Sutcliffe A, Watt I, Tortrson DJ. Randomised controlled trial of calcium and supplementation with cholecalciferol (vitamin D3) for prevention of fractures in primary care. 2005. BMJ 330(7498):1003.
380. Potter SM, Baum JA, Teng H, Stillman RJ, Shay NF, Erdman JW Jr. Soy protein and isoflavones: their effects on blood lipids and bone density in postmenopausal women. 1998. Am J Clin Nutr 68(6 Suppl):1375S-9S.
381. Prentice A, Ginty F, Stear SJ, Jones SC, Laskey MA, Cole TJ. Calcium Supplementation Increases Stature and Bone Mineral Mass of 16- to 18-Year-Old Boys. 2005. J Clin Endocrinol Metab 90(6):3153-61.
382. Raiten DJ, Picciano MF. Vitamin D and health in the 21st century: bone and beyond. Executive summary. 2004. Am J Clin Nutr 80(suppl):1673S–7S.
383. Recker RR, Hinders S, Davies KM, Heaney RP, Stegman MR, Lappe JM, Kimmel DB. Correcting calcium nutritional deficiency prevents spine fractures in elderly women. 1996. J Bone Miner Res 11(12):1961-6.

"In the presence of osteoporosis, vitamin D insufficiency may amplify bone loss and thus enhance fracture risk. It follows that at any age, but particularly in the elderly, an adequate intake of both calcium and vitamin D is important for the preservation of bone mass and prevention of osteoporosis."

- C Gennari

384. Reid IR, Ames RW, Evans MC, Gamble GD, Sharpe SJ. Long-term effects of calcium supplementation on bone loss and fractures in postmenopausal women: a randomized controlled trial. 1995. Am J Med 98(4):331-5.
385. Reid IR, Ames RW, Evans MC, Gamble GD, Sharpe SJ. Effect of calcium supplementation on bone loss in postmenopausal women. 1993. N Engl J Med 328(7):460-4.
386. Ricci TA, Chowdhury HA, Heymsfield SB, Stahl T, Pierson RN, Jr., Shapses SA. Calcium supplementation suppresses bone turnover during weight reduction in postmenopausal women. 1998. J Bone Miner Res 13:1045-50.

387. Ryder KM, Shorr RI, Bush AJ, Kritchevsky SB, Harris T, Stone K, Cauley J, Tylavsky FA. Magnesium intake from food and supplements is associated with bone mineral density in healthy older white subjects. 2005. J Am Geriatr Soc 53(11):1875-80.
388. Saltman PD, Strause LG. The Role of Trace Minerals in Osteoporosis. 1993. JACN 12(4):384-9.
389. Sato Y, Honda Y, Iwamoto J, Kanoko T, Satoh K. Effect of folate and mecobalamin on hip fractures in patients with stroke: a randomized controlled trial. 2005. JAMA 293(9):1082-8.
390. Shea B, Wells G, Cranney A, Zytaruk N, Robinson V, Griffith L, Ortiz Z, Peterson J, Adachi J, Tugwell P, Guyatt G, Osteoporosis Methodology Group, Osteoporosis Research Advisory Group. Meta-analyses of therapies for postmenopausal osteoporosis. VII. Meta-analysis of calcium supplementation for the prevention of postmenopausal osteoporosis. 2002. Endocr Rev 23(4):552-9.
391. Shearer MJ. The roles of vitamins D and K in bone health and osteoporosis prevention. 1997. Proc Nutr Soc 56(3):915-937.

"In summary, spinal bone loss in a small group of older postmenopausal women was slowed by supplementation with calcium as CCM [calcium citrate malate] and was halted by supplementation with a mineral cocktail composed of CCM along with zinc, manganese and copper. Only the group supplemented with calcium plus trace minerals differed from the placebo group, which, as expected, lost a significant amount of bone density."

- L Strause, et al.

392. Shearer MJ, Bach A, Kohlmeier M. Chemistry, nutritional sources, tissue distribution and metabolism of vitamin K with special reference to bone health. 1996. J Nutr 126(4 Suppl):1181S-6S.
393. Stear SJ, Prentice A, Jones SC, Cole TJ. Effect of a calcium and exercise intervention on the bone mineral status of 16-18-y-old adolescent girls. 2003. Am J Clin Nutr 77:985-92.
394. Strause L, Saltman P, Smith KT, Bracker M, Andon MB. Spinal bone loss in postmenopausal women supplemented with calcium and trace minerals. 1994. J Nutr 124:1060-4.
395. Thie NM, Prasad NG, Major PW. Evaluation of glucosamine sulfate compared to ibuprofen for the treatment of temporomandibular joint osteoarthritis: a randomized double blind controlled 3 month clinical trial. 2001. J Rheumatol 28(6):1347-55.
396. Thomas MK, Lloyd-Jones DM, Thadhani RI, Shaw AC, Deraska DJ, Kitch BT, Vamvakas EC, Dick IM, Prince RL, Finkelstein JS. Hypovitaminosis D in medical inpatients. 1998. N Engl J Med 338(12):777-83.
397. Trivedi DP, Doll R, Khaw KT. Effect of four monthly oral vitamin D3 (cholecalciferol) supplementation on fractures and mortality in men and women living in the community; randomized double blind controlled trial. 2003. BMJ 326(7387):469.
398. Utiger RD. The need for more vitamin D. 1998. N Engl J Med 338(12):828-9.
399. von Hurst PR, Stonehouse W, Kruger MC, Coad J. Vitamin D supplementation suppresses age-induced bone turnover in older women who are vitamin D deficient. 2010. J Steroid Biochem Mol Biol 121(1-2):293-6.

"Collectively, our data provide evidence supporting dietary supplementation of n-3 PUFA [omega-3 polyunsaturated fatty acids], which in turn may have a beneficial effect of slowing and reducing inflammation in the pathogenesis of degenerative joint diseases in man."

- CL Curtis, et al.

400. Winters-Stone KM, Snow CM. One year of oral calcium supplementation maintains cortical bone density in young adult female distance runners. 2004. Int J Sport Nutr Exerc Metab 14(1):7-17.
401. Yasui T, Miyatani Y, Tomita J, Yamada M, Uemura H, Miura M, Irahara M. Effect of vitamin K2 treatment on carboxylation of osteocalcin in early postmenopausal women. 2006. Gynecological Endocrinology 22(8):455-9.
402. Zamora SA, Rizzoli R, Belli DC, Slosman DO, Bonjour JP. Vitamin D supplementation during infancy is associated with higher bone mineral mass in prepubertal girls. 1999. J Clin Endocrinol Metab 84:4541-4.

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403. Abrams SA. In utero physiology: role in nutrient delivery and fetal development for calcium, phosphorus, and vitamin D. 2007. Am J Clin Nutr 85(2):604S-7S.

404. Amirlak I, Ezimokhai M, Dawodu A, Dawson KP, Kochiyil J, Thomas L, Abdulle AM. Current maternal-infant micronutrient status and the effects on birth weight in the United Arab Emirates. 2009. East Mediterr Health J 15(6):1399-406.

405. Auestad N, Halter R, Hall RT, Blatter M, Bogle ML, Burks W, Erickson JR, Fitzgerald KM, Dobson V, Innis SM, Singer LT, Montalto MB, Jacobs JR, Qiu W, Bornstein MH. Growth and development in term infants fed long-chain polyunsaturated fatty acids: a double-masked, randomized, parallel, prospective, multivariate study. 2001. Pediatrics 108(2):372-81.

406. Auestad N, Scott DT, Janowsky JS, Jacobsen C, Carroll RE, Montalto MB, Halter R, Qiu W, Jacobs JR, Connor WE, Connor SL, Taylor JA, Neuringer M, Fitzgerald KM, Hall RT. Visual, cognitive, and language assessments at 39 months: a follow-up study of children fed formulas containing long-chain polyunsaturated fatty acids to 1 year of age. 2003. Pediatrics 112(3 Pt 1):e177-83.

407. Bailey LB, Berry RJ. Folic acid supplementation and the occurrence of congenital heart defects, orofacial clefts, multiple births, and miscarriage. 2005. Am J Clin Nutr 81(suppl):1213S-7S.

"We have demonstrated for the first time in a purposeful, community-based prospective study an association between maternal nutritional measurements in pregnancy and two major risk factors for type 2 diabetes in the offspring... Maternal macronutrient intakes were unrelated to adiposity and insulin resistance in the offspring. However, higher maternal folate concentrations predicted greater adiposity (fat mass and body fat per cent) and higher insulin resistance, and lower vitamin B12 concentrations predicted higher insulin resistance. Children born to mothers with low vitamin B12 concentrations but high folate concentrations were the most insulin resistant."

- CS Yajnik, et al.

408. Bath SC et al. Effect of inadequate iodine status in UK pregnant women on cognitive outcomes in their children: results from the Avon Longitudinal Study of Parents and Children (ALSPAC). Lancet. 2013 May 21. pii: S0140-6736(13)60436-5.

409. Belizan JM, Villar J, Gonzalez L, Campodonico L, Bergei E. Calcium supplementation to prevent hypertensive disorders of pregnancy. 1991. N Engl J Med 325:1399-405.

410. Berry RJ, Li Z, Erickson JD, Li S, Moore CA, Wang H, Mulinare J, Zhao P, Wong LY, Gindler J, Hong SX, Correa A. Prevention of neural-tube defects with folic acid in China. China-U.S. Collaborative Project for Neural Tube Defect Prevention. 1999. N Engl J Med 341(20):1485-90.

411. Bhate V, Deshpande S, Bhat D, Joshi N, Ladkat R, Watve S, Fall C, de Jager CA, Refsum H, Yajnik C. Vitamin B12 status of pregnant Indian women and cognitive function in their 9-year-old children. 2008. Food Nutr Bull 29(4):249-54.

412. Birch EE, Birch DG, Hoffman DR, Uauy R. Dietary essential fatty acid supply and visual acuity development. 1992. Invest Ophthalmol Vis Sci 33:3242-53.

413. Birch EE, Carlson SE, Hoffman DR, Fitzgerald-Gustafson KM, Fu VLN, Drover JR, Castañeda YS, Minns L, Wheaton DKH, Mundy D, Marunycz J, Diersen-Schade DA. The DIAMOND (DHA Intake And Measurement Of Neural Development) Study: a double-masked, randomized controlled clinical trial of the maturation of infant visual acuity as a function of the dietary level of docosahexaenoic acid. 2010. AJCN 91(4):848-59.

"In conclusion, relatively modest amounts of dietary docosahexaenoic acid during pregnancy appear to extend gestational age and may lead to enhanced fetal growth."

- CM Smuts, et al.

414. Birch EE, Garfield S, Hoffman DR, Uauy R, Birch DG. A randomized controlled trial of early dietary supply of long-chain polyunsaturated fatty acids and mental development in term infants. 2000. Dev Med Child Neurol 42(3):174-181.

415. Bodnar LM, Krohn MA, Simhan HN. Maternal Vitamin D Deficiency Is Associated with Bacterial Vaginosis in the First Trimester of Pregnancy. 2009. J Nutr 139(6):1157-61.

416. Bodnar LM, Simhan HN, Powers RW, Frank MP, Cooperstein E, Roberts JM. High Prevalence of Vitamin D Insufficiency in

Black and White Pregnant Women Residing in the Northern United States and Their Neonates. 2007. J Nutr 137:447-52.
417. Botto LD, Mulinare J, Erickson JD. Occurrence of omphalocele in relation to maternal multivitamin use: a population-based study. 2002. Pediatrics 109(5):904-8.
418. Botto LD, Mulinare J, Erickson JD. Occurrence of congenital heart defects in relation to maternal multivitamin use. 2000. Am J Epidemiol 151(9):878-84.
419. Bourre JM. Dietary omega-3 fatty acids for women. 2007. Biomedicine & Pharmacotherapy 61:105-12.
420. Brehm JM, Celedón JC, Soto-Quiros ME, Avila L, Hunninghake GM, Forno E, Laskey D, Sylvia JS, Hollis BW, Weiss ST, Litonjua AA. Serum vitamin D levels and markers of severity of childhood asthma in Costa Rica. 2009. Am J Respir Crit Care Med 179(9):765-71.
421. Bucher HC, Guyatt GH, Cook RJ, Hatala R, Cook DJ, Lang JD, Hunt D. Effect of calcium supplementation on pregnancy-induced hypertension and preeclampsia: a meta-analysis of randomized controlled trials. 1996. JAMA 276(17):1388.

"Dosing recommendations for mothers during pregnancy should be aimed at preventing problems in neonates and infants, and a vitamin D dose sufficient for the mother during pregnancy should produce normal cord blood 25(OH)D concentrations at birth. Giving relatively small doses of vitamin D directly to the infant or supplementing the mother with 100 µg (4000 IU) vitamin D daily should maintain normal 25(OH)D concentrations in exclusively breastfed infants without harming the mother."

- CS Kovacs

422. Camargo CA Jr, Rifas-Shiman SL, Litonjua AA, Rich-Edwards JW, Weiss ST, Gold DR, Kleinman K, Gillman MW. Maternal intake of vitamin D during pregnancy and risk of recurrent wheeze in children at 3 y of age. 2007. Am J Clin Nutr 85(3):788-95.
423. Carlson SE, Werkman SH, Rhodes PG, Tolley EA. Visual-acuity development in healthy preterm infants: effect of marine-oil supplementation. 1993. Am J Clin Nutr 58(1):35-42.
424. Chappell LC, Seed PT, Briley AL, Kelly FJ, Lee R, Hunt BJ, Parmar K, Bewley SJ, Shennan AH, Steer PJ, Poston L. Effect of antioxidants on the occurrence of pre-eclampsia in women at increased risk: a randomized trial. 1999. Lancet 354(9181):810-6.
425. Chappell LC, Seed PT, Kelly FJ, Briley A, Hunt BJ, Charnock-Jones DS, Mallet A, Poston L. Vitamin C and E supplementation in women at risk of preeclampsia is associated with changes in indices of oxidative stress and placental function. 2002. Am J Obstet Gynecol 187(3):777-84.
426. Chen K, Zhang X, Wei XP, Qu P, Liu YX, Li TY. Antioxidant vitamin status during pregnancy in relation to cognitive development in the first two years of life. 2009. Early Hum Dev 85(7):421-7.
427. Christian P, Stewart CP. Maternal micronutrient deficiency, fetal development, and the risk of chronic disease. 2010. J Nutr 140(3):437-45.
428. Clifton-Bligh RJ, McElduff P, McElduff A. Maternal vitamin D deficiency, ethnicity and gestational diabetes. 2008. Diabet Med 25(6):678-84.
429. Cooper C, Javaid K, Westlake S, Harvey N, Dennison E. Developmental origins of osteoporotic fracture: the role of maternal vitamin D insufficiency. 2005. J Nutr 135(11):2728S-34S.
430. Correa A, Botto L, Liu Y, Mulinare J, Erickson JD. Do multivitamin supplements attenuate the risk for diabetes-associated birth defects?. 2003. Pediatrics 111(5):1146-51.
431. Czeizel AE, Dudas I. Prevention of the first occurrence of neural-tube defects by periconceptional vitamin supplementation. 1992. N Engl J Med 327(26):1832-5.
432. Dahle LO, Berg G, Hammar M, Hurtig M, Larsson L. The effect of oral magnesium substitution on pregnancy induce leg cramps. 1995. Am J Obstet Gynecol 173(1):175-80.
433. Daly LE, Kirke PN, Molloy A, Weir DG, Scott JM. Folate levels and neural tube defects: implications for prevention. 1995. JAMA 274(21):1698-702.

"Given the results of this study, we think that all women planning pregnancy should receive a vitamin supplement containing folic acid."

- AE Czeizel, et al.

434. Dawodu A, Wagner CL. Mother-child vitamin D deficiency: an international perspective. 2007. Arch Dis Child 92(9):737-40.
435. Denise HM Heppe et al. Maternal first-trimester diet and childhood bone mass: the Generation R Study. Am J Clin Nutr doi: 10.3945/ajcn.112.051052.

436. Devereux G, Litonjua AA, Turner SW, Craig LC, McNeill G, Martindale S, Helms PJ, Seaton A, Weiss ST. Maternal vitamin D intake during pregnancy and early childhood wheezing. 2007. Am J Clin Nutr 85(3):853-9.
437. Devereux G, Turner SW, Craig LC, McNeill G, Martindale S, Harbour PJ, Helms PJ, Seaton A. Low maternal vitamin E intake during pregnancy is associated with asthma in 5-year-old children. 2006. Am J Respir Crit Care Med 174(5):499-507.
438. Dijkstra SH, van Beek A, Janssen JW, de Vleeschouwer LH, Huysman WA, van den Akker EL. High prevalence of vitamin D deficiency in newborn infants of high-risk mothers. 2007. Arch Dis Child 92(9):750-3.
439. Erkkola M, Kaila M, Nwaru BI, Kronberg-Kippilä C, Ahonen S, Nevalainen J, Veijola R, Pekkanen J, Ilonen J, Simell O, Knip M, Virtanen SM. Maternal vitamin D intake during pregnancy is inversely associated with asthma and allergic rhinitis in 5-year-old children. 2009. Clin Exp Allergy 39(6):875-82.
440. Gaber KR, Farag MK, Soliman SE, El-Bassyouni HT, El-Kamah G. Maternal vitamin B12 and the risk of fetal neural tube defects in Egyptian patients. Clin Lab 53(1-2):69-75.
441. Gale CR, Robinson SM, Harvey NC, Javaid MK, Jiang B, Martyn CN, Godfrey KM, Cooper C; Princess Anne Hospital Study Group. Maternal vitamin D status during pregnancy and child outcomes. 2008. Eur J Clin Nutr 62(1):68-77.
442. Gernand AD, Simhan HN, Klebanoff MA, Bodnar LM. Maternal serum 25-hydroxyvitamin d and measures of newborn and placental weight in a U.S. Multicenter cohort study. J Clin Endocrinol Metab. 2013 Jan;98(1):398-404.
443. Gibson RA, Neumann MA, Makrides M. Effect of increasing breast milk docosahexaenoic acid on plasma and erythrocyte phospholipids fatty acids and neural indices of exclusively breast fed infants. 1997. Eur J Clin Nutr 51(9):578-84.
444. Goldenberg RL, Tamura T, Neggers Y, Copper RL, Johnston KE, DuBard MB, Hauth JC. The effect of zinc supplementation on pregnancy outcome. 1995. JAMA 274(6):463-8.
445. Goodyer P, Kurpad A, Rekha S, Muthayya S, Dwarkanath P, Iyengar A, Philip B, Mhaskar A, Benjamin A, Maharaj S, Laforte D, Raju C, Phadke K. Effects of maternal vitamin A status on kidney development: a pilot study. 2007. Pediatr Nephrol 22(2):209-14.
446. Greenberg JA, Bell SJ, Ausdal WV. Omega-3 Fatty Acid Supplementation During Pregnancy. 2008. Rev Obstet Gynecol 1(4):162–9.
447. Håberg SE, London SJ, Stigum H, Nafstad P, Nystad W. Folic acid supplements in pregnancy and early childhood respiratory health. 2009. Arch Dis Child 94(3):180-4.
448. Haugen M, Brantsaeter AL, Trogstad L, Alexander J, Roth C, Magnus P, Meltzer HM. Vitamin D supplementation and reduced risk of preeclampsia in nulliparous women. 2009. Epidemiology 20(5):720-6.
449. Hay G, Clausen T, Whitelaw A, Trygg K, Johnston C, Henriksen T, Refsum H. Maternal folate and cobalamin status predicts vitamin status in newborns and 6-month-old infants. 2010. J Nutr 140(3):557-64.
450. Heird WC. The role of polyunsaturated fatty acids in term and preterm infants and breastfeeding mothers. 2001. Pediatr Clin North Am 48(1):173-88.
451. Helland IB, Smith L, Saarem K, Saugstad OD, Drevon CA. Maternal Supplementation with Very-Long-Chain n-3 Fatty Acids during Pregnancy and Lactation Augments Children's IQ at 4 Years of Age. 2003. Pediatrics 111:e39-44.
452. Helland IB, Saugstad OD, Smith L, Saarem K, Solvoll K, Ganes T, Drevon CA. Similar effects on infants of n-3 and n-6 fatty acids supplementation to pregnant and lactating women. 2001. Pediatrics 108(5):E82.

"Our study demonstrates an association between maternal vitamin B12 status during pregnancy and children's cognitive functioning. Higher maternal plasma vitamin B12 concentration in pregnancy was an independent predictor of the child's cognitive performance on the CTT-A and Digit Span Backward tests, after controlling for a number of possible confounders, including the child's own vitamin B12 status at 6 years of age."

- V Bhate, et al.

"The recommendations for dietary omega-3 fatty acids should be adopted at the onset of pregnancy, but there may be benefits for all women who are considering becoming pregnant. Given concerns for mercury toxicity with overconsumption of certain fish, in order to meet these recommendations, pregnant women will need to consume omega-3 fatty acids from 3 sources: vegetable oils, 2 servings of seafood per week, and omega-3 fatty acid supplements containing EPA and DHA or DHA alone."

- JA Greenberg, et al.

453. Herrera JA, Arevalo-Herrera M, Herrera S. Prevention of preeclampsia by linoleic acid and calcium supplementation: a randomized controlled trial. 1998. Obstet Gynecol 91(4):585-90.
454. Hoffman DR, Birch EE, Birch DG, Uauy RD. Effects of supplementation with omega 3 long-chain polyunsaturated fatty acids on retinal and cortical development in premature infants. 1993. Am J Clin Nutr 57(5 Suppl):807S-12S.
455. Hoffman DR, Theuer RC, Castañeda YS, Wheaton DH, Bosworth RG, O'Connor AR, Morale SE, Wiedemann LE, Birch EE. Maturation of Visual Acuity is Accelerated in Breast-Fed Term Infants Fed Baby Food Containing DHA-Enriched Egg Yolk. 2004. J Nutr 134:2307-13.
456. Hollis BW. Vitamin D requirement during pregnancy and lactation. 2007. J Bone Miner Res 22(Suppl 2):V39-44.
457. Hollis BW, Wagner CL. Nutritional vitamin D status during pregnancy: reasons for concern. 2006. CMAJ 174(9):1287-90.
458. Holmes VA, Barnes MS, Alexander HD, McFaul P, Wallace JM. Vitamin D deficiency and insufficiency in pregnant women: a longitudinal study. 2009. Br J Nutr 102(6):876-81.
459. Hornstra G. Essential fatty acids in mothers and their neonates. 2000. AJCN 71(suppl):1262S-9S.
460. Hübner U, Alwan A, Jouma M, Tabbaa M, Schorr H, Herrmann W. Low serum vitamin B12 is associated with recurrent pregnancy loss in Syrian women. 2008. Clin Chem Lab Med 46(9):1265-9.
461. Hyppönen E, Boucher BJ. Avoidance of vitamin D deficiency in pregnancy in the United Kingdom: the case for a unified approach in National policy. 2010. Br J Nutr 104(3):309-14.
462. Jain SK, Wise R, Yanamandra K, Dhanireddy R, Bocchini JA Jr. The effect of maternal and cord-blood vitamin C, vitamin E and lipid peroxide levels on newborn birth weight. 2008. Mol Cell Biochem 309(1-2):217-21.
463. Javaid MK, Crozier SR, Harvey NC, Gale CR, Dennison EM, Boucher BJ, Arden NK, Godfrey KM, Cooper C; Princess Anne Hospital Study Group. Maternal vitamin D status during pregnancy and childhood bone mass at age 9 years: a longitudinal study. 2006. Lancet 367(9504):36-43.
464. Jensen CL, Voigt RG, Prager TC, Zou YL, Fraley JK, Rozelle JC, Turcich MR, Llorente AM, Anderson RE, Heird WC. Effects of maternal docosahexaenoic acid intake on visual function and neurodevelopment in breastfed term infants. 2005. Am J Clin Nutr 82(1):125-32.
465. Johansen AM, Lie RT, Wilcox AJ, Andersen LF, Drevon CA. Maternal dietary intake of vitamin A and risk of orofacial clefts: a population-based case-control study in Norway. 2008. Am J Epidemiol 167(10):1164-70.
466. Kaitlin M March et al. Maternal vitamin D3 supplementation at 50 µg/d protects against low serum 25-hydroxyvitamin D in infants at 8 wk of age: a randomized controlled trial of 3 doses of vitamin D beginning in gestation and continued in lactation. First published July 8, 2015, doi: 10.3945/ajcn.114.106385.
467. Klemmensen A, Tabor A, Østerdal ML, Knudsen VK, Halldorsson TI, Mikkelsen TB, Olsen SF. Intake of vitamin C and E in pregnancy and risk of pre-eclampsia: prospective study among 57346 women. 2009. BJOG 116(7):964-74.
468. Koc A, Kocyigit A, Soran M, Demir N, Sevinc E, Erel O, Mil Z. High frequency of maternal vitamin B12 deficiency as an important cause of infantile vitamin B12 deficiency in Sanliurfa province of Turkey. 2006. Eur J Nutr 45(5):291-7.
469. Kovacs CS. Vitamin D in pregnancy and lactation: maternal, fetal, and neonatal outcomes from human and animal studies. 2008. AJCN 88(2):520S-8S.
470. Lauritzen L, Jorgensen MH, Mikkelsen TB, Skovgaard M, Straarup EM, Olsen SF, Hoy CE, Michaelsen KF. Maternal fish oil supplementation in lactation: effect on visual acuity and n-3 fatty acid content of infant erythrocytes. 2004. Lipids 39(3):195-206.
471. Lee JM, Smith JR, Philipp BL, Chen TC, Mathieu J, Holick MF. Vitamin D deficiency in a healthy group of mothers and newborn infants. 2007. Clin Pediatr 46(1):42-4.
472. Levine RJ, Hauth JC, Curet LB, Sibai BM, Catalano PM, Morris CD, DerSimonian R, Esterlitz JR, Raymond EG, Bild DE, Clemens JD, Cutler JA. Trial of calcium to prevent preeclampsia. 1997. N Engl J Med 337(2):69-76.

"This trial demonstrates that the visual maturation of healthy infants is improved by continued supplies of DHA from both human milk and DHA-enriched baby foods well into 1 y of life."

- DR Hoffman, et al.

"Omega-3 fatty acid (dietary or in capsules) ensures that a woman's adipose tissue contains a reserve of these fatty acids for the developing fetus and the breast-fed newborn infant. This ensures the optimal cerebral and cognitive development of the infant. The presence of large quantities of EPA and DHA in the diet slightly lengthens pregnancy, and improves its quality."

- JM Bourre

473. Luoto R, Laitinen K, Nermes M, Isolauri E. Impact of maternal probiotic-supplemented dietary counselling on pregnancy outcome and prenatal and postnatal growth: a double-blind, placebo-controlled study. 2010. Br J Nutr 103(12):1792-9.
474. Mahon P, Harvey N, Crozier S, Inskip H, Robinson S, Arden N, Swaminathan R, Cooper C, Godfrey K, SWS Study Group. Low maternal vitamin D status and fetal bone development: cohort study. 2010. J Bone Miner Res 25(1):14-9.
475. Makrides M, Neumann M, Simmer K, Pater J, Gibson R. Are long-chain polyunsaturated fatty acids essential nutrients in infancy?. 1995. Lancet 345:1463-8.

"In summary, our data strongly suggest that zinc supplementation improves pregnancy outcome in at least some pregnant women, and we support the inclusion of zinc in prenatal multivitamin/mineral tablets."

- RL Goldenberg, et al.

476. Mehta S, Hunter DJ, Mugusi FM, Spiegelman D, Manji KP, Giovannucci EL, Hertzmark E, Msamanga GI, Fawzi WW. Perinatal outcomes, including mother-to-child transmission of HIV, and child mortality and their association with maternal vitamin D status in Tanzania. 2009. J Infect Dis 200(7):1022-30.
477. Merewood A, Mehta SD, Chen TC, Bauchner H, Holick MF. Association between vitamin D deficiency and primary cesarean section. 2009. J Clin Endocrinol Metab 94(3):940-5.
478. Miller RL. Prenatal maternal diet affects asthma risk in offspring. 2008. J Clin Invest 118(10):3265-8.
479. Minami H, Furuhashi M, Minami K, Miyazaki K, Yoshida K, Ishikawa K. Fetal intraventricular bleeding possibly due to maternal vitamin K deficiency. 2008. Fetal Diagn Ther 24(4):357-60.
480. Molloy AM, Kirke PN, Troendle JF, Burke H, Sutton M, Brody LC, Scott JM, Mills JL. Maternal vitamin B12 status and risk of neural tube defects in a population with high neural tube defect prevalence and no folic acid fortification. 2009. Pediatrics 123(3):917-23.
481. MRC Vitamin Study Research Group. Prevention of neural tube defects: results of the Medical Research Council Vitamin Study. 1991. Lancet 338(8760):131-7.
482. Mulligan ML, Felton SK, Riek AE, Bernal-Mizrachi C. Implications of vitamin D deficiency in pregnancy and lactation. 2010. Am J Obstet Gynecol 202(5):429-30.
483. Muthayya S, Kurpad AV, Duggan CP, Bosch RJ, Dwarkanath P, Mhaskar A, Mhaskar R, Thomas A, Vaz M, Bhat S, Fawzi WW. Low maternal vitamin B12 status is associated with intrauterine growth retardation in urban South Indians. 2006. Eur J Clin Nutr 60(6):791-801.
484. Newhook LA, Sloka S, Grant M, Randell E, Kovacs CS, Twells LK. Vitamin D insufficiency common in newborns, children and pregnant women living in Newfoundland and Labrador, Canada. 2009. Matern Child Nutr 5(2):186-91.
485. Nisreen A. Alwan, Janet E. Cade, Harry J. McArdle, Darren C. Greenwood, Helen E. Hayes and Nigel A. B. Simpson. Maternal iron status in early pregnancy and birth outcomes: insights from the Baby's Vascular health and Iron in Pregnancy study. British Journal of Nutrition, available on CJO2015. doi:10.1017/S0007114515001166.
486. O'Riordan MN, Kiely M, Higgins JR, Cashman KD. Prevalence of suboptimal vitamin D status during pregnancy. 2008. Ir Med J 101(8):240, 242-3.
487. Ortega RM, Martinez RM, Lopez-Sobaler AM, Andres P, Quintas ME. Influence of calcium intake on gestational hypertension. 1999. Ann Nutr Metab 43:37-46.
488. Pasco JA, Wark JD, Carlin JB, Ponsonby AL, Vuillermin PJ, Morley R. Maternal vitamin D in pregnancy may influence not only offspring bone mass but other aspects of musculoskeletal health and adiposity. 2008. Med Hypotheses 71(2):266-9.
489. Preston-Martin S, Pogoda JM, Mueller BA, Lubin F, Modan B, Holly EA, Filippini G, Cordier S, Peris-Bonet R, Choi W, Little J, Arslan A. Prenatal vitamin supplementation and pediatric brain tumors: huge international variation in use and possible reduction in risk. 1998. Childs Nerv Syst 14(10):551-7.

"This study indicates that maternal supplementation with very-long-chain n-3 PUFAs during pregnancy and lactation improves the intelligence of children at 4 years of age."

- IB Helland, et al.

490. Roberts JM, Myatt L, Spong CY, Thom EA, Hauth JC, Leveno KJ, Pearson GD, Wapner RJ, Varner MW, Thorp JM Jr, Mercer BM, Peaceman AM, Ramin SM, Carpenter MW, Samuels P, Sciscione A, Harper M, Smith WJ, Saade G, Sorokin Y, Anderson GB, Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Vitamins C and E to prevent complications of pregnancy-associated hypertension. 2010. N Engl J Med 362(14):1282-91.

491. Rochat MK, Ege MJ, Plabst D, Steinle J, Bitter S, Braun-Fahrländer C, Dalphin JC, Riedler J, Roponen M, Hirvonen MR, Büchele G, Renz H, Lauener R, Krauss-Etschmann S, von Mutius E; PASTURE Study group. Maternal vitamin D intake during pregnancy increases gene expression of ILT3 and ILT4 in cord blood. 2010. Clin Exp Allergy 40(5):786-94.

492. Sabour H, Hossein-Nezhad A, Maghbooli Z, Madani F, Mir E, Larijani B. Relationship between pregnancy outcomes and maternal vitamin D and calcium intake: A cross-sectional study. 2006. Gynecol Endocrinol 22(10):585-9.

"Because the neonatal DHA status correlates positively with birth weight, birth length, and head circumference, maternal DHA supplementation during pregnancy may improve the prognosis of preterm infants."

- G Hornstra

493. Samia A. Nossier, Noha E. Naeim, Nawal A. El-Sayed and Azza A. Abu Zeid. The effect of zinc supplementation on pregnancy outcomes: a double-blind, randomised controlled trial, Egypt. British Journal of Nutrition, available on CJO2015. doi:10.1017/S000711451500166X.

494. Sanchez-Ramos L, Adair CD, Kaunitz AM, Briones DK, Del Valle GO, Delke I. Calcium supplementation in mild preeclampsia remote from term: a randomized double-blind clinical trial. 1995. Obstet Gynecol 85(6):915-8.

495. Scholl TO, Hediger ML, Bendich A, Schall JI, Smith WK, Krueger PM. Use of multivitamin/mineral prenatal supplements: influence on the outcome of pregnancy. 1997. Am J Epidemiol 146(2):134-41.

496. Shaw GM, Lammer EJ, Wasserman CR, O'Malley CD, Tolarova MM. Risks of orofacial clefts in children born to women using multivitamins containing folic acid periconceptionally. 1995. Lancet 346(8972):393-6.

497. Sinclair KD, Allegrucci C, Singh R, Gardner DS, Sebastian S, Bispham J, Thurston A, Huntley JF, Rees WD, Maloney CA, Lea RG, Craigon J, McEvoy TG, Young LE. DNA methylation, insulin resistance, and blood pressure in offspring determined by maternal periconceptional B vitamin and methionine status. 2007. Proc Natl Acad Sci 104(49):19351-6.

498. Slovis TL, Chapman S. Evaluating the data concerning vitamin D insufficiency/deficiency and child abuse. 2008. Pediatr Radiol 38(11):1221-4.

499. Smuts CM, Huang M, Mundy D, Plasse T, Major S, Carlson SE. A Randomized Trial of Docosahexaenoic Acid Supplementation During the Third Trimester of Pregnancy. 2003. Amer Coll Obstet Gynecol 101(3):469-79.

500. Stallings VA. Childhood cancer and vitamins: prevention and treatment. 2008. Pediatr Blood Cancer 50(2 Suppl):442-4; discussion 451.

501. Stene LC, Joner G, Norwegian Childhood Diabetes Study Group. Use of cod liver oil during the first year of life is associated with lower risk of childhood-onset type 1 diabetes: a large, population-based, case-control study year of life is associated with lower risk of childhood-onset type 1 diabetes: a large, population-based, case-control study. 2003. Am J Clin Nutr 78:1128-34.

502. Surén P, Roth C, Bresnahan M, et al. Association between maternal use of folic acid supplements and risk of autism spectrum disorders in children. JAMA. 2013 Feb 13;309(6):570-7.

503. Thompson MD, Cole DE, Ray JG. Vitamin B-12 and neural tube defects: the Canadian experience. 2009. Am J Clin Nutr 89(2):697S-701S.

504. Turner SW, Campbell D, Smith N, Craig LCA, McNeill G, Forbes SH, Harbour PJ, Seaton A, Helms PJ, Devereux GS. Associations between fetal size, maternal α-tocopherol and childhood asthma. 2010. Thorax 65:391-7.

505. Uauy R, Hoffman DR, Peirano P, Birch DG, Birch EE. Essential fatty acids in visual and brain development. 2001. Lipids 36(9):885-95.

506. Vahratian A, Siega-Riz AM, Savitz DA, Thorp JM Jr. Multivitamin use and the risk of preterm birth. 2004. Am J Epidemiol 160:886-92.

507. van den Elzen HJ, Wladimiroff JW, Overbeek TE, Morris DC, Grobbee DE. Calcium metabolism, calcium supplementation and hypertensive disorders of pregnancy. 1995. Eur J Obstet Gynecol Reprod Biol 59(1):5-16.

"Studies summarized in this review provide evidence supporting the view that dietary EFA supply affects visual development of preterm and term infants."

- R Uauy, et al.

508. Verkleij-Hagoort AC, van Driel LM, Lindemans J, Isaacs A, Steegers EA, Helbing WA, Uitterlinden AG, Steegers-Theunissen RP. Genetic and lifestyle factors related to the periconception vitamin B12 status and congenital heart defects: a Dutch case-control study. 2008. Mol Genet Metab 94(1):112-9.

509. Villamor E, Msamanga G, Saathoff E, Fataki M, Manji K, Fawzi WW. Effects of maternal vitamin supplements on malaria in children born to HIV-infected women. 2007. Am J Trop

Med Hyg 76(6):1066-71.
510. Wagner CL, Hulsey TC, Fanning D, Ebeling M, Hollis BW. High-dose vitamin D3 supplementation in a cohort of breastfeeding mothers and their infants: a 6-month follow-up pilot study. 2006. Breastfeed Med 1(2):59-70.
511. Werler MM, Shapiro S, Mitchell AA. Periconceptional folic acid exposure and risk of occurrent neural tube defects. 1993. JAMA 269(10):1257-61.
512. Willatts P, Forsyth JS, DiModugno MK, Varma S, Colvin M. Effect of long-chain polyunsaturated fatty acids in infant formula on problem solving at 10 months of age. 1998. Lancet 352:688-91.
513. Winsloe C, Earl S, Dennison EM, Cooper C, Harvey NC. Early life factors in the pathogenesis of osteoporosis. 2009. Curr Osteoporos Rep 7(4):140-4.
514. Yajnik C. Nutritional control of fetal growth. 2006. Nutr Rev 64(5 Pt 2):S50-1; discussion S72-91.
515. Yajnik CS, Deshpande SS, Jackson AA, Refsum H, Rao S, Fisher DJ, Bhat DS, Naik Ss, Coyaji KJ, Joglekar CV, Joshi N, Lubree HG, Deshpande VU, Rege SS, Fall CHD. Vitamin B12 and folate concentrations during pregnancy and insulin resistance in the offspring: the Pune Maternal Nutrition Study. 2008. Diabetologia 51(1):29-38.
516. Young GL, Jewell D. Interventions for leg cramps in pregnancy. 2002. Cochrane Database Syst Rev (1):CD000121
517. Yu CK, Sykes L, Sethi M, Teoh TG, Robinson S. Vitamin D deficiency and supplementation during pregnancy. 2009. Clin Endocrinol (Oxf) 70(5):685-90.
518. Zatollah Asemi et al. Magnesium supplementation affects metabolic status and pregnancy outcomes in gestational diabetes: a randomized, double-blind, placebo-controlled trial. First published May 27, 2015, doi: 10.3945/ajcn.114.098616
519. Zengin E, Sarper N, Kılıç C. Clinical manifestations of infants with nutritional vitamin B12 deficiency due to maternal dietary deficiency. 2009. Acta Pædiatrica 98(1):98-102.
520. Zhang C, Qiu C, Hu FB, David RM, van Dam RM, Bralley A, Williams MA. Maternal plasma 25-hydroxyvitamin D concentrations and the risk for gestational diabetes mellitus. 2008. PLoS One 3(11):e3753.

"In our analysis, women who were severely vitamin D deficient [25(OH)D <37.5 nmol/liter] at the time of delivery had almost 4 times the odds of cesarean birth than women who were not deficient. One explanation for our findings is the fact that skeletal muscle contains the vitamin D receptor. Vitamin D deficiency has been associated with proximal muscle weakness as well as suboptimal muscle performance and strength."

- A Merewood, et al.

Immune Function

521. Abate A, Yang G, Dennery PA, Oberle S, Schroder H. Synergistic inhibition of cyclooxygenase-2 expression by vitamin E and aspirin. 2000. Free Rad Bio Med 29(11):1135-42.

522. Adams JS, Hewison M. Unexpected actions of vitamin D: new perspectives on the regulation of innate and adaptive immunity. 2008. Nat Clin Pract Endocrinol Metab 4(2):80-90.

523. Adams JS, Liu PT, Chun R, Modlin RL, Hewison M. Vitamin D in defense of the human immune response. 2007. Ann N Y Acad Sci 1117:94-105.

524. Adams JS, Ren S, Liu PT, Chun RF, Lagishetty V, Gombart AF, Borregaard N, Modlin RL, Hewison M. Vitamin D-directed rheostatic regulation of monocyte antibacterial responses. 2009. J Immunol 182(7):4289-95.

"The common denominator that rises from these studies is that vitamin D affects the immune system at many levels and by a number of mechanisms. It takes part in the genetic regulation of cytokine production, VDR expression and affects important biological processes by which these cells interact."

- Y Arnson, et al.

525. Adorini L, Penna G. Control of autoimmune diseases by the vitamin D endocrine system. 2008. Nat Clin Pract Rheumatol 4(8):404-12.

526. Aggarwal R, Sentz J, Miller MA. Role of zinc administration in prevention of childhood diarrhea and respiratory illnesses: a meta-analysis. 2007. Pediatrics 119(6):1120-30.

527. Arnson Y, Amital H, Shoenfeld Y. Vitamin D and autoimmunity: new aetiological and therapeutic considerations. 2007. Ann Rheum Dis 66(9):1137-42.

528. Avenell A, Campbell MK, Cook JA, Hannaford PC, Kilonzo MM, McNeill G, Milne AC, Ramsay CR, Seymour DG, Stephen AI, Vale LD, Writing Group of the MAVIS trial.Effect of multivitamin and multimineral supplements on morbidity from infections in older people (MAVIS trial): pragmatic, randomised, double blind, placebo controlled trial. 2005. BMJ 331(7512):324-9.

529. Avenell A, Cook JA, Maclennan GS, Macpherson GC. Vitamin D supplementation to prevent infections: a substudy of a randomised placebo-controlled trial in older people (RECORD trial, ISRCTN 51647438). 2007. Age Ageing 36(5):574-7.

530. Baeke F, van Etten E, Gysemans C, Overbergh L, Mathieu C. Vitamin D signaling in immune-mediated disorders: Evolving insights and therapeutic opportunities. 2008. Mol Aspects Med 29(6):376-87.

531. Baeke F, van Etten E, Overbergh L, Mathieu C. Vitamin D3 and the immune system: maintaining the balance in health and disease. 2007. Nutr Res Rev 20(1):106-18.

532. Barasch A, Elad S, Altman A, Damato K, Epstein J. Antimicrobials, mucosal coating agents, anesthetics, analgesics, and nutritional supplements for alimentary tract mucositis. 2006. Support Care Cancer 14(6):528-32.

533. Barringer TA, Kirk JK, Santaniello AC, Foley KL, Michielutte R. Effect of a multivitamin and mineral supplement on infection and quality of life. A randomized, double-blind, placebo-controlled trial. 2003. Ann Intern Med 138(5):365-71.

534. Beck MA. Selenium and vitamin E status: impact on viral pathogenicity. 2007. J Nutr 137(5):1338-40.

535. Beveridge S, Wintergerst ES, Maggini S, Hornig D. Immune-enhancing role of vitamin C and zinc and effect on clinical conditions. 2008. Proc Nutr Soc 67:E83.

"Our findings suggest that in certain diabetic samples, perhaps those with a high prevalence of micronutrient deficiency, daily use of a multivitamin and mineral supplement can decrease infection frequency."

- TA Barringer, et al.

536. Bikle DD. Vitamin D and the immune system: role in protection against bacterial infection. 2008. Curr Opin Nephrol Hypertens 17(4):348-52.

537. Bishop NC, Blannin AK, Walsh NP, Robson PJ, Gleeson M. Nutritional aspects of immunosuppression in athletes. 1999. Sports Med 28(3):151-76.

538. Boardley D, Fahlman M. Micronutrient supplementation does not attenuate seasonal decline of immune system indexes in well-nourished elderly women: A placebo-controlled study. 2000. J Am Diet Assoc 100(3):356-9.

539. Bogden JD, Bendich A, Kemp FW, Bruening KS, Shurnick JH, Denny T, Baker H, Louria DB. Daily micronutrient supplements enhance delayed-hypersensitivity skin test responses in older people. 1994. Am J Clin Nutr 60(3):437-47.

540. Bodgen JD, Oleske JM, Lavenhar MA, Munves EM, Kemp FW, Bruening KS, Holding KJ, Denny TN, Guarino MA, Holland BK. Effects of one year of supplementation with zinc and other micronutrients on cellular immunity in the elderly. 1990. J Am Coll Nutr 9(3):214-25.

541. Bonham M, O'Connor JM, Alexander HD, Coulter J, Walsh PM, McAnena LB, Downes CS, Hannigan BM, Strain JJ. Zinc supplementation has no effect on circulating levels of peripheral blood leucocytes and lymphocyte subsets in healthy adult men. 2003. Br J Nutr 89(5):695-703.

542. Cantorna MT. Vitamin D and its role in immunology: multiple sclerosis, and inflammatory bowel disease. 2006. Prog Biophys Mol Biol 92(1):60-4.

543. Cantorna MT, Yu S, Bruce D. The paradoxical effects of vitamin D on type 1 mediated immunity. 2008. Mol Aspects Med 29(6):369-75.

544. Carrillo-Vico A, Reiter RJ, Lardone PJ, Herrera JL, Fernández-Montesinos R, Guerrero JM, Pozo D. The modulatory role of melatonin on immune responsiveness. 2006. Curr Opin Investig Drugs 7(5):423-31.

545. Chandra RK. Effect of vitamin and trace-element supplementation on immune responses and infection in elderly subjects. 1992. Lancet 340(8828):1124-7.

546. Chandra RK. Influence of multinutrient supplement on immune responses and infection-related illness in 50-65 year old individuals. 2002. Nutr Res 22:5-11.

"Inadequate intake and status of vitamins and trace elements may lead to suppressed immunity, which predisposes to infections and aggravates undernutrition. Evidence has accumulated that in humans certain nutrients selectively influence the immune response, induce dysregulation of a coordinated host response to infections in cases of deficiency and oversupply, and that deficiency may impact virulence of otherwise harmless pathogens. Thus, micronutrients are required at appropriate intakes for the immune system to function optimally. Available data indicate a role of vitamins (A, D, E, B6, B12, folate, and C), and trace elements (selenium, zinc, copper, and iron) on the immune response... Overall, inadequate intake and status of these vitamins and trace elements may lead to suppressed immunity, which predisposes to infections and aggravates malnutrition. Therefore, supplementation with these selected micronutrients can support the body's natural defence system by enhancing all three levels of immunity."

- S Maggini, et al.

547. Chavance M, Herbeth B, Lemoine A, Zhu BP. Does multivitamin supplementation prevent infections in healthy elderly subjects? A controlled trial. 1993. Int J Vitam Nutr Res 63(1):11-6.

548. Sally N Adebamowo, Donna Spiegelman, Walter C Willett, and Kathryn M Rexrode. Association between intakes of magnesium, potassium, and calcium and risk of stroke: 2 cohorts of US women and updated meta-analyses. Am J Clin Nutr June 2015 vol. 101 no. 6 1269-1277.

549. Collins CE, Kershaw J, Brockington S. Effect of nutritional supplements on wound healing in home-nursed elderly: a randomized trial. 2005. Nutrition 21(2):147-55.

550. Corthésy B, Gaskins HR, Mercenier A. Cross-talk between probiotic bacteria and the host immune system. 2007. J Nutr 137(3 Suppl 2):781S-90S.

551. Cutolo M, Otsa K. Review: vitamin D, immunity and lupus. 2008. Lupus 17(1):6-10.

552. Damsgaard CT, Lauritzen L, Kjaer TM, Holm PM, Fruekilde MB, Michaelsen KF, Frøkiaer H. Fish oil supplementation modulates immune function in healthy infants. 2007. J Nutr 137(4):1031-6.

"The elucidation of the precise roles of vitamin D in the immune system and in the pathogenesis of multiple diseases has the potential to have profound effects on our ability to prevent and treat these disorders."

- NE Lange, et al.

553. De la Fuente M, Hernanz A, Guayerbas N, Victor VM, Arnalich F. Vitamin E ingestion improves several immune functions in elderly men and women. 2008. Free Radic Res 42(3):272-80.

554. De la Fuente M, Hernanz A, Vallejo MC. The immune system in the oxidative stress conditions of aging and hypertension: favorable effects of antioxidants and physical exercise. 2005. Antioxid Redox Signal 7(9-10):1356-66.

555. Dreyfuss ML, Fawzi WW. Micronutrients and vertical transmission of HIV-1. 2002. AJCN 75(6):959-70.

556. El-Kadiki A, Sutton AJ. Role of multivitamins and mineral supplements in preventing infections in elderly people: systematic review and meta-analysis of randomised controlled trials. 2005. BMJ 330(7496):871.
557. Enioutina EY, Bareyan D, Daynes RA. TLR-induced local metabolism of vitamin D3 plays an important role in the diversification of adaptive immune responses. 2009. J Immunol 182(7):4296-305.
558. Fawzi WW, Villamor E, Msamanga GI, Antelman G, Aboud S, Urassa W, Hunter D. Trial of zinc supplements in relation to pregnancy outcomes, hematologic indicators, and T cell counts among HIV-1-infected women in Tanzania. 2005. Am J Clin Nutr 81(1):161-7.
559. Ferguson LR, Philpott M. Cancer prevention by dietary bioactive components that target the immune response. 2007. Curr Cancer Drug Targets 7(5):459-64.
560. Fogarty A, Lewis S, Weiss S, Britton J. Dietary vitamin E, IgE concentrations, and atopy. 2000. Lancet 356(9241):1573-4.
561. Fritsche K. Fatty acids as modulators of the immune response. 2006. Annu Rev Nutr 26:45-73.
562. Froicu M, Cantorna MT. Vitamin D and the vitamin D receptor are critical for control of the innate immune response to colonic injury. 2007. BMC Immunol 8:5.

"Because aging and malnutrition exert cumulative influences on immune responses, many elderly people have poor cell-mediated immune responses and are therefore at a high risk of infection. Nutritional therapy may improve immune responses of elderly patients with protein-energy malnutrition. Supplementation with high pharmacologic doses of a single nutrient (zinc or vitamin E) may be useful for improving immune responses of self-sufficient elderly people living at home. Therefore, nutritional deficiency must be treated in the elderly to reduce infectious risk and possibly slow the aging process."

- BM Lesourd

563. Fuller CJ, Faulkner H, Bendich A, Parker RS, Roe DA. Effect of beta-carotene supplementation on photosuppression of delayed-type hypersensitivity in normal young men. 1992. Am J Clin Nutr 56(4):684-90.
564. Gariballa S. Vitamin and mineral supplements for preventing infections in older people. 2005. BMJ 331(7512):304-5.
565. Gariballa S, Forster S, Walters S, Powers H. A randomized, double-blind, placebo-controlled trial of nutritional supplementation during acute illness. 2006. Am J Med 119(8):693-9.
566. Girodon F, Galan P, Monget AL, Boutron-Ruault MC, Brunet-Lecomte P, Preziosi P, Arnaud J, Manuguerra JC, Herchberg S, MIN. VIT. AOX. geriatric network. Impact of trace elements and vitamin supplementation on immunity and infections in institutionalized elderly patients: a randomized controlled trial. 1999. Arch Intern Med 159(7):748-54.
567. Girodon F, Lombard M, Galan P, Brunet-Lecomte P, Monget AL, Arnaud J, Preziosi P, Hercberg S. Effect of micronutrient supplementation on infection in institutionalized elderly subjects: a controlled trial. 1997. Ann Nutr Metab 41(2):98-107.
568. Gleeson M. Can nutrition limit exercise-induced immunodepression?. 2006. Nutr Rev 64(3):119-31.
569. Gleeson M, Bishop NC. Elite athlete immunology: importance of nutrition. 2000. Int J Sports Med 21 Suppl 1:S4450.
570. Gottrand F. Long-chain polyunsaturated fatty acids influence the immune system of infants. 2008. J Nutr 138(9):1807S-12S.
571. Graat JM, Schouten EG, Kok FJ. Effect of daily vitamin E and multivitamin-mineral supplementation on acute respiratory tract infections in elderly persons: a randomized controlled trial. 2002. JAMA 288(6):715-21.
572. Haase H, Mocchegiani E, Rink L. Correlation between zinc status and immune function in the elderly. 2006. Biogerontology 7(5-6):421-8.
573. Håberg SE, London SJ, Stigum H, Nafstad P, Nystad W. Folic acid supplements in pregnancy and early childhood respiratory health. 2009. Arch Dis Child 94(3):180-4.
574. Hara M, Tanaka K, Hirota Y. Immune response to influenza vaccine in healthy adults and the elderly: association with nutritional status. 2005. Vaccine 23(12):1457-63.

"In summary, our results show that the age-associated defect in the redistribution of signaling molecules to the immunological synapse is reversed by vitamin E. This effect is strongest in naive T cells, which exhibit the age-related defects in protein recruitment and T cell activation. This is the first demonstration of a reversal of a key early signaling defect in aged T cells by a nutrient. These findings have important implications for the development of preventive and therapeutic strategies to reduce age-associated defects in T cells."

- MG Marko, et al.

575. Herraiz LA, Hsieh WC, Parker RS, Swanson JE, Bendich A, Roe DA. Effect of UV exposure and beta-carotene supplementation on delayed-type hypersensitivity response in healthy older men. 1998. J Am Coll Nutr 17(6):617-24.
576. Hewison M. Vitamin D and the immune system: new perspectives on an old theme. 2010. Endocrinol Metab Clin North Am 39(2):365-79.
577. High KP. Micronutrient supplementation and immune function in the elderly. 1999. Clin Infect Dis 28(4):717-22.
578. High KP. Nutritional strategies to boost immunity and prevent infection in elderly individuals. 2001. Clin Infect Dis 33:1892-900.
579. Hoffmann PR, Berry MJ. The influence of selenium on immune responses. 2008. Mol Nutr Food Res 52(11):1273-80.
580. Hojsak I, Snovak N, Abdović S, Szajewska H, Mišak Z, Kolače S. Lactobacillus GG in the prevention of gastrointestinal and respiratory tract infections in children who attend day care centres: a randomized, double-blind, placebo-controlled trial. 2010. Clin Nutr 29(3):312-6.
581. Holmøy T. Vitamin D status modulates the immune response to Epstein Barr virus: Synergistic effect of risk factors in multiple sclerosis. 2008. Med Hypotheses 70(1):66-9.

"Investigators have demonstrated how appropriate serum concentrations of vitamin D facilitate the ability of immune cells to defend against bacterial and viral infections. Ongoing research in this area has provided new ways of understanding the immune system and how the pleiotropic actions of vitamin D serve an important immunoregulatory role in proper immune function. With the increasing evidence of vitamin D insufficiency's detrimental effects beyond the classically defined cause of rickets, the full story behind the role of vitamin D insufficiency/deficiency in pediatric infection and immune function awaits full elucidation."

- VP Walker, et al.

582. Hughes DA, Wright AJA, Finglas PM, Perrless ACJ, Bailey AL, Astley SB, Pinder AC, Southon S. The effect of b-carotene supplementation on the immune function of blood monocytes from healthy male nonsmokers. 1997. J Lab Clin Med 129:309-17.
583. Hurwitz BE, Klaus JR, Llabre MM, Gonzalez A, Lawrence PJ, Maher KJ, Greeson JM, Baum MK, Shor-Posner G, Skyler JS, Schneiderman N. Suppression of human immunodeficiency virus type 1 viral load with selenium supplementation: a randomized controlled trial. 2007. Arch Intern Med 167(2):148-54.

"Although our study suggests that many elderly individuals might benefit from a supplementary intake of vitamin E, such public health recommendations can only be considered after longer-term studies with lower amounts of tocopherol are completed. This point will be especially important in determining if the immunostimulatory effect observed is due to pharmacologic or physiologic effect of vitamin E. Nevertheless, it is encouraging to note that a single nutrient supplement can enhance immune responsiveness in healthy elderly subjects consuming the recommended amounts of all nutrients. This is especially significant because dietary intervention represents the most practical approach for delaying or reversing the rate of decline of immune function with age."

- SN Meydani, et al.

584. Kaiser JD, Campa AM, Ondercin JP, Leoung GS, Pless RF, Baum MK. Micronutrient supplementation increases CD4 count in HIV-infected individuals on highly active antiretroviral therapy: a prospective, double-blinded, placebo-controlled trial. 2006. J Acquir Immune Defic Syndr 42(5):523-8.
585. Lange NE, Litonjua A, Hawrylowicz CM, Weiss S. Vitamin D, the immune system and asthma. 2009. Expert Rev Clin Immunol 5(6):693-702.
586. Lesourd BM. Nutrition and immunity in the elderly: modification of immune responses with nutritional treatments. 1997. Am J Clin Nutr 66(2):478S-84S.
587. Leyes P, Martínez E, Forga MT. Use of diet, nutritional supplements and exercise in HIV-infected patients receiving combination antiretroviral therapies: a systematic review. 2008. Antivir Ther 13(2):149-59.
588. Li-Ng M, Aloia JF, Pollack S, Cunha BA, Mikhail M, Yeh J, Berbari N. A randomized controlled trial of vitamin D3 supplementation for the prevention of symptomatic upper respiratory tract infections. 2009. Epidemiol Infect 137(10):1396-404.
589. Long KZ, Estrada-Garcia T, Rosado JL, Ignacio Santos J, Haas M, Firestone M, Bhagwat J, Young C, DuPont HL, Hertzmark E, Nanthakumar NN. The effect of vitamin A supplementation on the intestinal immune response in Mexican children is modified by pathogen infections and diarrhea. 2006. J Nutr 136(5):1365-70.

590. Maggini S, Wintergerst ES, Beveridge S, Hornig DH. Selected vitamins and trace elements support immune function by strengthening epithelial barriers and cellular and humoral immune responses. 2007. BJN 98(Suppl 1):S29-35.
591. Marko MG, Ahmed T, Bunnell SC, We Dayong, Chung H, Huber BT, Meydani SN. Age-Associated Decline in Effective Immune Synapse Formation of CDR+ T Cells is Reversed by Vitamin E Supplementation. 2007. J Immunol 178:1443-9.
592. McKay DL, Perrone G, Rasmussen H, Dallal G, Hartman W, Cao G, Prior RL, Roubenoff R, Blumberg JB. The effects of a multivitamin/mineral supplement on micronutrient status, antioxidant capacity and cytokine production in healthy older adults consuming a fortified diet. 2000. J Am Coll Nutr 19(5):613-21.
593. Merchant AT, Curhan G, Bendich A, Singh VN, Willett WC, Fawzi WW. Vitamin intake is not associated with community-acquired pneumonia in U.S. men. 2004. J Nutr 134:439-44.
594. Meydani SN, Barklund MP, Liu S, Meydani M, Miller RA, Cannon JG, Morrow FD, Rocklin R, Blumberg JB. Vitamin E supplementation enhances cell-mediated immunity in healthy elderly subjects. 1990. Am J Clin Nutr 52(3):557-63.

"In conclusion, our double-blind, placebo-controlled study shows that levels of vitamin E higher than currently recommended enhance in vivo indexes of T cell-mediated function in healthy elderly. The enhancement of cell-mediated immunity by vitamin E was not associated with any adverse effects. Since age-associated decline in immune response is associated with increased morbidity and mortality in the elderly and is widely observed, recommendations to increase the intake of vitamin E for elderly should be considered."

- EG Pallast, et al.

595. Meydani SN, Meydani M, Blumberg JB, Leka LS, Siber G, Loszewski R, Thompson C, Pedrosa MC, Diamond RD, Stollar BD. Vitamin E supplementation and in vivo immune response in healthy elderly subjects: a randomized controlled trial. 1997. JAMA 277(17):1380-6.
596. Mora JR, Iwata M, von Andrian UH. Vitamin effects on the immune system: vitamins A and D take centre stage. 2008. Nat Rev Immunol 8(9):685-98.
597. Moreira A, Kekkonen RA, Delgado L, Fonseca J, Korpela R, Haahtela T. Nutritional modulation of exercise-induced immunodepression in athletes: a systematic review and meta-analysis. 2007. Eur J Clin Nutr 61(4):443-60.
598. Muñoz C, Rios E, Olivos J, Brunser O, Olivares M. Iron, copper and immunocompetence. 2007. Br J Nutr 98(Suppl 1):S24-8.
599. Nakamura K, Kariyazono H, Komokata T, Hamada N, Sakata R, Yamada K. Influence of preoperative administration of omega-3 fatty acid-enriched supplement on inflammatory and immune responses in patients undergoing major surgery for cancer. 2005. Nutrition 21(6):639-49.
600. Newton S, Owusu-Agyei S, Ampofo W, Zandoh C, Adjuik M, Adjei G, Tchum S, Filteau S, Kirkwood BR. Vitamin A supplementation enhances infants' immune responses to hepatitis B vaccine but does not affect responses to Haemophilus influenzae type b vaccine. 2007. J Nutr 137(5):1272-7.
601. Nieman DC. Exercise immunology: future directions for research related to athletes, nutrition, and the elderly. 2000. Int J Sports Med 21 Suppl 1:S61-8.

"In summary, the present study demonstrates that modest daily doses of micronutrients given for 1 y can enhance cellular immunity and can also prevent the development of biochemical evidence of micronutrient deficiencies in healthy, independently living older people. These results suggest that the dietary micronutrient intake of older people and/or the current RDAs for one or more micronutnients may be too low to support optimal immunity in older individuals."

- JD Bogden, et al.

602. Nieman DC, Henson DA, Gross SJ, Jenkins DP, Davis JM, Murphy EA, Carmichael MD, Dumke CL, Utter AC, McAnulty SR, McAnulty LS, Mayer EP. Quercetin reduces illness but not immune perturbations after intensive exercise. 2007. Med Sci Sports Exerc 39(9):1561-9.
603. Nugent AP, Roche HM, Noone EJ, Long A, Kelleher DK, Gibney MJ. The effects of conjugated linoleic acid supplementation on immune function in healthy volunteers. 2005. Eur J Clin Nutr 59(6):742-50.
604. Overbeck S, Rink L, Haase H. Modulating the immune response by oral zinc supplementation: a single approach for multiple diseases. 2008. Arch Immunol Ther Exp 56(1):15-30.

605. Pagmantidis V, Méplan C, van Schothorst EM, Keijer J, Hesketh JE. Supplementation of healthy volunteers with nutritionally relevant amounts of selenium increases the expression of lymphocyte protein biosynthesis genes. 2008. Am J Clin Nutr 87(1):181-9.
606. Pallast EG, Schouten EG, de Waart FG, Fonk HC, Doekes G, von Blomberg BM, Kok FJ. Effect of 50-and 100mg vitamin E supplements on cellular immune function in non-institutionalized elderly persons. 1999. Am J Clin Nutr 69(6):1273-81.
607. Penn ND, Purkins L, Kelleher J, Heatley RV, Mascie-Taylor BH, Belfield PW. The effect of dietary supplementation with vitamins A, C and E on cell-mediated immune function in elderly long-stay patients: a randomized controlled trial. 1991. Age Aging 20(3):169-74.
608. Pichard C, Sudre P, Karsegard V, Yerly S, Slosman DO, Delley V, Perrin L, Hirschel B, Swiss HIV Cohort Study. A randomized double-blind controlled study of 6 months of oral nutritional supplementation with arginine and omega-3 fatty acids in HIV-infected patients. 1998. AIDS 12(1):53-63.
609. Prasad AS. Zinc: mechanisms of host defense. 2007. J Nutr 137(5):1345-9.

"Nutritional intervention has proven to be a practical approach in modulating dysregulated immune and inflammatory responses. The efficacy of such intervention, as with vitamin E, for example, has been demonstrated in clinical trials using infections as an endpoint. At the same time, mechanistic studies have deciphered how vitamin E affects T cell functions at cellular and molecular levels and thus, lend further support to the efficacy of nutrient supplementation in modulating the age-related immune dysregulation."

- D Wu, et al.

610. Prasad AS, Beck FW, Bao B, Fitzgerald JT, Snell DC, Steinberg JD, Cardozo LJ. Zinc supplementation decreases incidence of infections in the elderly: effect of zinc on generation of cytokines and oxidative stress. 2007. Am J Clin Nutr 85(3):837-44.
611. Rahman MJ, Sarker P, Roy SK, Ahmad SM, Chisti J, Azim T, Mathan M, Sack D, Andersson J, Raqib R. Effects of zinc supplementation as adjunct therapy on the systemic immune responses in shigellosis. 2005. Am J Clin Nutr 81(2):495-502.
612. Richard SA, Zavaleta N, Caulfield LE, Black RE, Witzig RS, Shankar AH. Zinc and iron supplementation and malaria, diarrhea, and respiratory infections in children in the Peruvian Amazon. 2006. Am J Trop Med Hyg 75(1):126-32.

"Although many open questions remain, there is promise that vitamin A and D metabolites or their analogues have the potential to be used in clinical settings for therapeutic benefit. In particular, it will be important to assess the impact of using $1,25(OH)_2VD_3$ analogues as an adjuvant immunomodulatory therapy in the setting of autoimmune diseases and in transplant recipients. It will also be important to determine the net effects of retinoic acid or synthetic RAR-agonists, especially in the intestine, where these agents appear to have a role in enhancing immune responses. The capacity of vitamin A metabolites to foster gut-homing T cells might improve strategies of mucosal vaccination or aid in decreasing pathogenic immunity by potentiating the induction of T_{Reg} cells."

- JR Mora, et al.

613. Richards JB, Valdes AM, Gardner JP, Paximadas D, Kimura M, Nessa A, Lu X, Surdulescu GL, Swaminathan R, Spector TD, Aviv A. Higher serum vitamin D concentrations are associated with longer leukocyte telomere length in women. 2007. Am J Clin Nutr 86(5):1420-5.
614. Roth DE, Caulfield LE, Ezzati M, Black RE. Acute lower respiratory infections in childhood: opportunities for reducing the global burden through nutritional interventions. 2008. Bull World Health Organ 86(5):356-64.
615. Ryan-Borchers TA, Park JS, Chew BP, McGuire MK, Fournier LR, Beerman KA. Soy isoflavones modulate immune function in healthy postmenopausal women. 2006. Am J Clin Nutr 83(5):1118-25.
616. Ryan-Harshman M, Aldoori W. The relevance of selenium to immunity, cancer, and infectious/inflammatory diseases. 2005. Can J Diet Pract Res 66(2):98-102.
617. Santos MS, Leka LS, Ribaya-Mercado JD, Russell RM, Meydani M, Hennekens CH, Gaziano JM, Meydani SN. Short-and long-term beta-carotene supplementation do not influence T cell-mediated immunity in healthy elderly persons. 1997. Am J Clin Nutr 66(4):917-24.
618. Schauber J, Gallo RL. The vitamin D pathway: a new target for control of the skin's immune response?. 2008. Exp Dermatol 17(8):633-9.

619. Smolders J, Damoiseaux J, Menheere P, Hupperts R. Vitamin D as an immune modulator in multiple sclerosis, a review. 2008. J Neuroimmunol 194(1-2):7-17.
620. Stephen AI, Avenell A. A systematic review of multivitamin and multimineral supplementation for infection. 2006. J Hum Nutr Diet 19(3):179-90.
621. Taylor AL, Hale J, Wiltschut J, Lehmann H, Dunstan JA, Prescott SL. Effects of probiotic supplementation for the first 6 months of life on allergen- and vaccine-specific immune responses. 2006. Clin Exp Allergy 36(10):1227-35.
622. van Etten E, Stoffels K, Gysemans C, Mathieu C, Overbergh L. Regulation of vitamin D homeostasis: implications for the immune system. 2008. Nutr Rev 66(10 Suppl 2):S125-34.
623. Villamor E, Fawzi WW. Effects of vitamin a supplementation on immune responses and correlation with clinical outcomes. 2005. Clin Microbiol Rev 18(3):446-64.
624. Walker VP, Modlin RL. The Vitamin D Connection to Pediatric Infections and Immune Function. 2009. Pediatr Res 65(5 Pt 2):106R-13R.

"In our study, patients who received zinc and selenium had a better antibody response after influenza vaccine, and the percentage of patients without respiratory tract infections was higher in the T [trace elements: zinc, selenium] and VT [vitamin and trace elements: zinc, selenium, ascorbic acid, beta carotene, alpha-tocopherol] groups. Our results suggest a beneficial effect of these nutrients on the immunity of elderly persons by improving their resistance to infections. Larger trials will be required to confirm our findings, which may have considerable impact on the health of the institutionalized elderly."

- F Girodon, et al.

625. Wang TT, Dabbas B, Laperriere D, Bitton AJ, Soualhine H, Tavera-Mendoza LE, Dionne S, Servant MJ, Bitton A, Seidman EG, Mader S, Behr MA, White JH. Direct and indirect induction by 1,25-dihydroxyvitamin D3 of the NOD2/CARD15-defensin beta2 innate immune pathway defective in Crohn disease. 2010. J Biol Chem 285(4):2227-31.
626. Webb AL, Villamor E. Update: effects of antioxidant and non-antioxidant vitamin supplementation on immune function. 2007. Nutr Rev 65(5):181-217.
627. White JH. Vitamin D signaling, infectious diseases, and regulation of innate immunity. 2008. Infect Immun 76(9):3837-43.
628. Winkler P, de Vrese M, Laue Ch, Schrezenmeir J. Effect of a dietary supplement containing probiotic bacteria plus vitamins and minerals on common cold infections and cellular immune parameters. 2005. Int J Clin Pharmacol Ther 43(7):318-26.
629. Wintergerst ES, Maggini S, Hornig DH. Contribution of selected vitamins and trace elements to immune function. 2007. Ann Nutr Metab 51(4):301-23.
630. Wintergerst ES, Maggini S, Hornig DH. Immune-enhancing role of vitamin C and zinc and effect on clinical conditions. 2006. Ann Nutr Metab 50(2):85-94.
631. Wong CP, Rinaldi NA, Ho E. Zinc deficiency enhanced inflammatory response by increasing immune cell activation and inducing IL6 promoter demethylation. Mol Nutr Food Res. 2015 Feb 5.

"The results of this study substantiate the hypothesis that nutritional status is an important determinant of immunocompetence in old age and that an optimum intake of micronutrients is needed for enhanced immune responses in elderly subjects. Such an intervention led to a striking reduction in illness, a finding that is of considerable clinical and public-health importance."

- RK Chandra

632. Wu D, Meydani SN. Age-associated changes in immune and inflammatory responses: impact of vitamin E intervention. 2008. J Leukoc Biol 84:900-14.
633. Yamshchikov AV, Desai NS, Blumberg Hm, Ziegler TR, Tangpricha V. Vitamin D for treatment and prevention of infectious diseases: a systematic review of randomized controlled trials. 2009. Endocr Pract 15(5):438-49.

Healthy Vision

634. Age-Related Eye Disease Study Research Group. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss. 2001. Arch Ophthalmol 119:1417-36.

635. Age-related Eye Disease Study Research Group. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E and beta carotene for age-related cataract and vision loss. 2001. Arch Ophthalmol 119:1439-52.

636. Age-Related Eye Disease Study Research Group. The Relationship of Dietary Carotenoid and Vitamin A, E, and C Intake With Age-Related Macular Degeneration in a Case-Control Study: AREDS Report No. 22. 2007. Arch Ophthalmol 125(9):1225-32.

637. AREDS Research Group. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss. 2001. Arch Ophthalmol 119:1417-36.

"A daily dose of 10 mg lutein supplementation induced an increase in mean plasma lutein by a factor of 5 and a linear 4-week increase in relative MP [macular pigment] density of 4% to 5%. To our knowledge, this is the first study in which the effects of intake of lutein have been assessed with objective measurement techniques. In particular, the SLO-based technique provided very reliable results. With this technique all subjects showed a significant increase in MP density."

- TTJM Berendschot, et al.

638. AREDS Research Group. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E and beta carotene for age-related cataract and vision loss. 2001. Arch Ophthamol 119:1439-52.

639. Bamini Gopinath et al. Homocysteine, folate, vitamin B-12, and 10-y incidence of age-related macular degeneration. Am J Clin Nutr. 2013 May 1.

640. Berendschot TTJM, Goldbohm RA, Klopping WAA, van de Kraats J, van Norel J, van Norren D. Influence of lutein supplementation on macular pigment, assessed with two objective techniques. 2000. Invest Opthamol Vis Sci 41(11):3322-6.

641. Bernstein PS, Zhao DY, Wintch SW, Ermakov IV, McClane RW, Gellermann W. Resonance Raman measurement of macular carotenoids in normal subjects and in age related macular degeneration patients. 2002. Ophthalmology 109(10):1780-1787.

642. Berson EL, Rosner B, Sandberg MA, Weigel-DiFranco C, Brockhurst RJ, Hayes KC, Johnson EJ, Anderson EJ, Johnson CA, Gaudio AR, Willett WC, Schaefer EJ. Clinical trial of lutein in patients with retinitis pigmentosa receiving vitamin A. 2010. Arch Ophthalmol 128(4):403-11.

643. Birch EE, Carlson SE, Hoffman DR, Fitzgerald-Gustafson KM, Fu VLN, Drover JR, Castañeda YS, Minns L, Wheaton DKH, Mundy D, Marunycz J, Diersen-Schade DA. The DIAMOND (DHA Intake And Measurement Of Neural Development) Study: a double-masked, randomized controlled clinical trial of the maturation of infant visual acuity as a function of the dietary level of docosahexaenoic acid. 2010. AJCN 91(4):848-59.

"We found that high dietary intake of vitamin E and zinc was associated with a lower risk of incident AMD [age-related macular degeneration]. An above-median intake of the combination of vitamins C and E, beta carotene, and zinc was associated with a 35% lower risk of incident AMD."

- R van Leeuwen, et al.

644. Bone RA, Landrum JT. Distribution of macular pigment components, zeaxanthin and lutein, in human retina. 1992. Methods in Enzymology 213:360-6.

645. Bone RA, Landrum JT, Mayne ST, Gomez CM, Tibor SE, Twaroska EE. Macular pigment in donor eyes with and without AMD: a case control study. 2001. Investigative Ophthalmology and Visual Science 42(1):135-240.

646. Brown L, Rimm EB, Seddon JM, Giovannucci EL, Chasan-Taber L, Spiegelman D, Willett WC, Hankinson SE. A prospective study of carotenoid intake and risk of cataract extraction in US men. 1999. Am J Clin Nutr 70(4):517-24.

647. Bursell SE, Clermont AC, Aiello LP, Aiello LM, Schlossman DK, Feener EP, Laffel L, King GL. High-dose vitamin E supplementa-

tion normalizes retinal blood flow and creatinine clearance in patients with type 1 diabetes. 1999. Diabetes Care 22(8):1245-51.

648. Carpentier S, Knaus M, Suh M. Associations between lutein, zeaxanthin, and age-related macular degeneration: an overview. 2009. Crit Rev Food Sci Nutr 49(4):313-26.

649. Chasan-Taber L, Willett WC, Seddon JM, Stampfer MJ, Rosner B, Colditz GA, Speizer FE, Hankinson SE. A prospective study of carotenoid and vitamin A intakes and risk of cataract extraction in US women. 1999. Am J Clin Nutr 70:509-16.

650. Chasan-Taber L, Willett WC, Seddon JM, Stampfer MJ, Rosner B, Colditz GA, Hankinson SE. A prospective study of vitamin supplement intake and cataract extraction among U.S. women. 1999. Epidemiology 10(6):679-84.

651. Cho E, Stampfer MJ, Seddon JM, Hung S, Spiegelman D, Rimm EB, Willett WC, Hankinson SE. Prospective study of zinc intake and the risk of age-related macular degeneration. 2001. Ann Epidemiol 11(5):328-36.

652. Chong EWT, Wong TY, Kreis AJ, Simpson JA, Guymer RH. Dietary antioxidants and primary prevention of age related macular degeneration: systematic review and meta-analysis. 2007. BMJ 335(7623):755.

653. Christen WG, Ajani UA, Glynn RJ, Manson JE, Schaumberg DA, Chew EC, Buring JE, Hennekens CH. Prospective cohort study of antioxidant vitamin supplement use and the risk of age-related maculopathy. 1999. Am J Epidemiol 149(5):476-84.

654. Chylack LT Jr, Brown NP, Bron A, Hurst M, Kopcke W, Thien U, Schalch W. The Roche European American Cataract Trial (REACT): a randomized clinical trial to investigate the efficacy of an oral antioxidant micronutrient mixture to slow progression of age-related cataract. 2002. Ophthalmic Epidemiol 9(1):49-80.

655. Coleman H, Chew E. Nutritional supplementation in age-related macular degeneration. 2007. Curr Opin Ophthalmol 18(3):220-3.

656. Delcourt C, Cristol J, Tessier F, Leger CL, Descomps B, Papox L, POLA Study Group. Age-related macular degeneration and antioxidant status in the POLA study. 1999. Arch Ophthalmol 117(10):1384-90.

657. Fletcher E, Bentham GC, Agnew M, Young IS, Augood C, Chakravarthy U, de Jong PT, Rahu M, Seland J, Soubrane G, Tomazzoli L, Topouzis F, Vingerling JR, Vioque J. Sunlight exposure, antioxidants, and age-related macular degeneration. 2008. Arch Ophthalmol 126(10):1396-1403.

"In this large prospective study, we observed a modest inverse association between intake of lutein and zeaxanthin and extraction of cataracts. Men in the highest fifth of lutein and zeaxanthin intake had a 19% lower risk of cataract extraction compared with those in the lowest fifth of intake. There was no significant association between intake of vitamin A or other carotenoids and risk of cataract in multivariate analyses. Increased consumption of some foods high in lutein, including broccoli and spinach, was associated with a lower risk of cataract extraction. The finding that increased intake of other fruit and vegetables was not associated with a decreased risk suggests that the relation may be specifically due to lutein and zeaxanthin and not simply to a healthy lifestyle."

-L Brown, et al.

"In summary, data from the present short term prospective study are consistent with potentially protective influences of vitamins E and C and lutein on the development of cataract in the lens nucleus. However, strong inverse relations for intake of these nutrients were not observed. Data from longer term prospective studies and from clinical trials currently under way will be useful in further evaluating these associations."

-PR Trumbo, et al.

658. Flood V, Smith W, Wang JJ, Manzi F, Webb K, Mitchell P. Dietary antioxidant intake and incidence of early age-related maculopathy: the Blue Mountains Eye Study. 2002. Ophthalmology 109(12):2272-8.

659. Hammond R Jr, Johnson EZ, Russell RM, Krinsky MI, Yeum KJ, Edwards RM, Snodderly DM. Dietary modification of human macular pigment density. 1997. Invest Ophthalmol Vis Sci 38(9):1795-1801.

660. Hammond R Jr, Wooten BR, Snodderly DM. Density of the human crystalline lens is related to the macular pigment carotenoids, lutein and zeaxanthin. 1997. Optom Vis Sci 74(7):499-504.

661. Hammond BR et al. A double-blind, placebo-controlled study on the effects of lutein and zeaxanthin on photostress recovery, glare disability, and chromatic contrast. Invest Ophthalmol Vis Sci. 2014 Dec 2;55(12):8583-9.

662. Hankinson SE, Stampfer MJ, Seddon JM, Colditz GA, Rosner B, Speizer FE, Willett WC. Nutrient intake and cataract extraction in women: a prospective study. 1992. BMJ 305(6849):335-9.
663. Hawkins WR. Zinc supplementation for macular degeneration. 1991. Arch Ophthalmol 109:1345.
664. Jacques PF, Taylor A, Moeller S, Hankinson SE, Rogers G, Tung W, Ludovico J, Willett WC, Chylack LT Jr. Long-term nutrient intake and 5-year change in nuclear lens opacities. 2005. Arch Ophthalmol 123(4):517-26.
665. Jacques PF, Chylack LT Jr, Hankinson SE, Khu PM, Rogers G, Friend J, Tung W, Wolfe JK, Padhye N. Willett WC, Taylor A. Long-term nutrient intake and early age-related nuclear lens opacities. 2001. Arch Ophthalmol 119(7):1009-19.
666. Jacques PF, Taylor A, Hankinson SE, Willett WC, Mahnken B, Lee Y, Vaid K, Lahav M. Long-term vitamin C supplement use and prevalence of early age-related lens opacities. 1997. Am J Clin Nutr 66(4):911-6.
667. Jampol LM. Antioxidants, zinc and age-related macular degeneration results and recommendations. 2001. Arch Ophthalmol 119(10):1533-4.
668. Jampol LM, Ferris FL III. Antioxidants and zinc to prevent progression of age related macular degeneration. 2001. JAMA 286(19):2466-8.

"The results of our LAST [Lutein Antioxidant Supplementation Trial] study support the results of our pilot spinach data that lutein may be useful in the nutritional intervention of atrophic ARMD [age-related macular degeneration] in midwestern male subjects. In LAST, lutein enhanced macular pigment and visual function with AREDS stages II, III, and IV. Thus lutein supplementation may be beneficial at all stages of ARMD. Further studies with more patients of both genders are needed to determine the long-term effect of lutein alone or lutein together with a broad spectrum of antioxidants, vitamins, and minerals on patients with atrophic age-related macular degeneration."

-S Richer, et al.

669. Johnson J, Hammond BR, Yeum K, Qin J, Wang XD, Castaneda C, Snodderly DM, Russell RM. Relation among serum and tissue concentrations of lutein and zeaxanthin and macular pigment density. 2000. Am J Clin Nutr 71(6):1555-62.
670. Juan Wu, MS; Eunyoung Cho, ScD; Walter C. Willett, MD, MPH, DrPH; Srinivas M. Sastry, MD, MPH; Debra A. Schaumberg, ScD, OD, MPH JAMA Ophthalmol. Published online October 08, 2015. doi:10.1001/jamaophthalmol.2015.3590
671. Koh HH, Murray IJ, Nolan D, Carden D, Feather J, Beatty S. Plasma and macular responses to lutein supplement in subjects with and without age-related maculopathy: a pilot study. 2004. Exp Eye Res 79(1):21-7.
672. Kowluru RA, Tang J, Kern TS. Abnormalities of retinal metabolism in diabetes and experimental galactosemia. VII. Effect of long-term administration of antioxidants on the development of retinopathy. 2001. Diabetes 50(8):1938-42.
673. Krishnadev N, Meleth AD, Chew EY. Nutritional supplements for age-related macular degeneration. 2010. Curr Opin Ophthalmol 21(3):184-9.
674. Kuzniarz M, Mitchell P, Cumming RG, Flood VM. Use of vitamin supplements and cataract: the Blue Mountains Eye Study. 2001. Am J Ophthalmol 132(1):19-26.

"In summary, a multivitamin-multimineral supplement with a combination of vitamin C, vitamin E, β-carotene, and zinc (with cupric oxide) is recommended for AMD but not cataract. Observational studies for cataract provide only weak support for multivitamins or other vitamin supplements. The results of observational studies suggest that a healthy lifestyle with a diet containing foods rich in antioxidants, especially lutein and zeaxanthin, and n–3 fatty acids appears beneficial for AMD and possibly cataract."

-JM Seddon

675. Landrum JT, Bone RA. Lutein, zeaxanthin, and the macular pigment. 2001. Arch Biochem Biophys 385(1):28-40.
676. Landrum JT, Bone RA, Joa H, Kilburn MD, Moore LL, Sprague KE. A one year study of the macular pigment: the effect of 140 days of a lutein supplement. 1997. Exp Eye Res 65(1):57-62.
677. Laplaud PM, Lelubre A, Chapman MJ. Antioxidant action of Vaccinium myrtillus extract on human low density lipoproteins in vitro: initial observations. 1997. Fundam Clin Pharmacol 11(1):35-40.
678. Larkin M. Vitamins reduce risk of vision loss from macular degeneration. 2001. Lancet 358(9290):1347.
679. Leske MC, Chylack LT Jr, He Q, Wu SY, Schoenfeld E, Friend J, Wolfe J. Antioxidant vitamins and nuclear opacities: the longitudinal study of cataract. 1998. Ophthalmology 105(5):831-6.

680. Leske MC, Wu SY, Connell AM, Hyman L, Schachat AP. Lens opacities, demographic factors and nutritional supplements in the Barbados Eye Study. 1997. Int J Epidemiol 26(6):1314-22.
681. Lyle BJ, Mares-Perlman JA, Klein BE, Klein R, Greger JL. Antioxidant intake and risk of incident age-related nuclear cataracts in the Beaver Dam Eye Study. 1999. Am J Epidemiol 149(9):801-9.
682. Lyle BJ, Mares-Perlman JA, Klein BE, Klein R, Palta M, Bowen PE, Greger JL. Serum carotenoids and tocopherols and incidence of age-related nuclear cataract. 1999. Am J Clin Nutr 69(2):272-7.
683. Mares-Perlman JA, Brady WE, Klein R, Klein BE, Bowen P, Stacewicz-Sapuntzakis M, Palta M. Serum antioxidants and age-related macular degeneration in a population-based case-control study. 1995. Arch Ophthalmol 113(12):1518-23.
684. Mares-Perlman JA, Klein BE, Klein R, Ritter LL. Relation between lens opacities and vitamin and mineral supplement use. 1994. Ophthalmology 101(2):315-25.
685. Mares-Perlman JA, Lyle BJ, Klein R, Fisher AI, Brady WE, VandenLangenberg GM, Trabulsi JN, Palta M. Vitamin supplement use and incident cataracts in a population-based study. 2000. Arch Ophthalmol 118(11):1556-63.
686. McNeil JJ, Robman L, Tikellis G, Sinclair MI, McCarty CA, Taylor HR. Vitamin E supplementation and cataract: randomized controlled trial. 2004. Ophthalmology 111(1):75-84.
687. Moeller SM, Parekh N, Tinker L, Ritenbaugh C, Blodi B, Wallace RB, Mares JA. Associations between intermediate age-related macular degeneration and lutein and zeaxanthin in the Carotenoids in Age-related Eye Disease Study (CAREDS): ancillary study of the Women's Health Initiative. 2006. Arch Ophthalmol 124(8):1151-62.
688. Moeller SM, Voland R, Tinker L, Blodi BA, Klein ML, Gehrs KM, Johnson EJ, Snodderly DM, Wallace RB, Chappell RJ, Parekh N, Ritenbaugh C, Mares JA. Associations Between Age-Related Nuclear Cataract and Lutein and Zeaxanthin in the Diet and Serum in the Carotenoids in the Age-Related Eye Disease Study (CAREDS), an Ancillary Study of the Women's Health Initiative. 2008. Arch Ophthalmology 126(3):354-64.

"In this large prospective study, those with the highest intake of lutein and zeaxanthin had a 22% lower risk of cataract extraction than did those in the lowest quintile of intake (RR: 0.78; 95% CI:0.63, 0.95; P for trend = 0.04) after age, smoking, and other potential cataract risk factors were controlled for. Other specific carotenoids (a-carotene, b-carotene, lycopene, and b-cryptoxanthin), vitamin A, and retinol were not associated with cataract in multivariate analysis. Increasing frequency of intake of spinach and kale, foods rich in lutein, was associated with a moderate decrease in risk. The observation that other fruit and vegetables were not associated with decreased risk suggests that the relation may be due to lutein, a specific carotenoid predominantly found in spinach and kale, and not to a healthy lifestyle per se."

- L Chasan-Taber, et al.

689. Olmedilla B, Granado F, Blanco I, Vaquero M. Lutein, but not alpha-tocopherol, supplementation improves visual function in patients with age-related cataracts: a 2-y double-blind, placebo-controlled pilot study. 2003. Nutrition 19(1):21-4.
690. Parekh N, Chappell RJ, Millen AE, Albert DM, Mares JA. Association between vitamin D and age-related macular degeneration in the Third National Health and Nutrition Examination Survey, 1988 through 1994. 2007. Arch Ophthalmol 125(5):661-9.
691. Richer S, Stiles W, Statkute L, Pulido J, Frankowski J, Rudy D, Pei K, Tsipursky M, Nyland J. Double-masked, placebo-controlled, randomized trial of lutein and antioxidant supplementation in the intervention of atrophic age-related macular degeneration: the Veterans Last study (Lutein Antioxidant Supplementation Trial). 2004. Optometry 75:216-30.
692. Robertson JM, Donner AP, Trevithick JR. A possible role for vitamins C and E in cataract prevention. 1991. Am J Clin Nutr 53(1 Suppl):346S-51S.

"In summary, the results of the present study provide added support for a relation between nutrient intake and nuclear opacification. Our observation that vitamin E intake is associated with a reduction in nuclear opacification is consistent with other longitudinal studies, strengthening the hypothesized role for this specific nutrient in nuclear cataract formation, and the associations with riboflavin, thiamin, and niacin should serve to focus added effort on examining the role of these nutrients in the development of nuclear cataract."

- PF Jacques, et al.

693. Sangiovanni JP, Agrón E, Meleth AD, Reed GF, Sperduto RD, Clemons TE, Chew EY; Age-Related Eye Disease Study Research Group. {omega}-3 Long-chain polyunsaturated fatty acid intake and 12-y incidence of neovascular age-related macular degeneration and central geographic atrophy: AREDS report 30, a prospective cohort study from the Age-Related Eye Disease Study. 2009. Am J Clin Nutr 90(6):1601-7.
694. Seddon JM. Multivitamin-multimineral supplements and eye disease: age-related macular degeneration and cataract. 2007. AJCN 85(1):304S-7S.
695. Seddon JM, Christen WG, Manson JE, LaMotte FS, Glynn RJ, Buring JE, Hennekens CH. The use of vitamin supplements and the risk of cataract among US male physicians. 1994. Am J Public Health 84(5):788-92.
696. Smith W, Mitchell P, Webb K, Leeder SR. Dietary antioxidant and age-related maculopathy: the Blue Mountains Eye Study. 1999. Ophthalmology 106(4):761-7.
697. Sperduto RD, Hu TS, Milton RC, Zhao JL, Everett DF, Cheng QF, Blot WJ, Bing L, Taylor PR, Li JY, et al. The Linxian cataract studies: two nutrition intervention trials. 1993. Arch Ophthalmol 111(9):1246-53.
698. Stur M, Tittl M, Reitner A, Meisinger V. Oral zinc and the second eye in age-related macular degeneration. 1996. Invest Ophthalmol Vis Sci 37(7):1225-35.

"In the overall sample we observed no associations between antioxidant nutrient intake and either cortical or PSC [posterior subcapsular] opacities, but we noted significant and provocative associations in selected subgroups. The inverse association observed in the present study between vitamin C intake and the prevalence of cortical opacities in women aged <60 y and the fact that significantly decreased odds of cortical opacities were found only with a duration of vitamin C supplement use >=10 y provide added support for a protective role for vitamin C against the formation of lens opacities. We also found that for PSC opacities there were decreased odds for nonsmokers with higher intakes of carotenoids."

- A Taylor, et al.

699. Tanya S. Glaser, MD et al. The Association of Dietary Lutein plus Zeaxanthin and B Vitamins with Cataracts in the Age-Related Eye Disease Study. Ophthalmology July 2015 Volume 122, Issue 7, Pages 1471–1479.
700. Taylor A, Jacques PF, Chylack LT Jr, Hankinson SE, Khu PM, Rogers G, Friend J, Tung W, Wolfe JK, Padhye N, Willett WC. Long-term intake of vitamins and carotenoids and odds of early age-related cortical and posterior subcapsular lens opacities. 2002. Am J Clin Nutr 75(3):540-9.
701. Taylor HR, Tikellis G, Robman LD, McCarty CA, McNeil JJ. Vitamin E supplementation and macular degeneration: randomised controlled trial. 2002. BMJ 325(7354):11.
702. Teikari JM, Virtamo J, Rautalahti M, Palmgren J, Liesto K, Heinonen OP. Long-term supplementation with alpha-tocopherol and beta-carotene and age-related cataract. 1997. Acta Ophthalmol Scand 75(6):634-40.
703. Trumbo PR, Ellwood KC. Lutein and zeaxanthin intakes and risk of age-related macular degeneration and cataracts: an evaluation using the Food and Drug Administration's evidence-based review system for health claims. 2006. Am J Clin Nutr 84(5):971-4.
704. Van Leeuwen R, Boekhoorn S, Vingerling JR, Witteman JC, Klaver CC, Hofman A, de Jong PT. Dietary intake of antioxidants and risk of age-related macular degeneration. 2005. JAMA 294(24):3101-7.
705. Yao Y, Qiu QH, Wu XW, Cai ZY, Xu S, Liang XQ. Lutein supplementation improves visual performance in Chinese drivers: 1-year randomized, double-blind, placebo-controlled study. Nutrition 2013 Jan 26. pii: S0899-9007(12)00428-5.

Other References

706. Multivitamins in the Prevention of Cancer in Men: The Physicians' Health Study II Randomized Controlled Trial. JAMA. 2012;308(18).

707. Amieva H, Meillon C, Helmer C, Barberger-Gateau P, Dartigues JF (2013) Ginkgo Biloba Extract and Long-Term Cognitive Decline: A 20-Year Follow-Up Population-Based Study. PLoS ONE 8(1): e52755.

708. Argyriou AA, Chroni E, Koutras A, Ellul J, Papapetropoulos S, Katsoulas G, Iconomou G, Kalofonos HP. Vitamin E for prophylaxis against chemotherapy-induced neuropathy: a randomized controlled trial. 2005. Neurology 64(1):26-31.

709. Ascherio A. Weisskopf MG, O'Reilly EJ, Jacobs EJ, McCullough ML, Calle EE, Cudkowicz M, Thun MJ. Vitamin E intake and risk of amyotrophic lateral sclerosis. 2005. Ann Neurol 57(1):104-10.

710. Baker DE, Campbell RK. Vitamin and mineral supplementation in patients with diabetes mellitus. 1992. Diabetes Educ 18(5):420-7.

711. Belluzzi A, Brignola C, Campieri M, Pera A, Boschi S, Miglioli M. Effect of an enteric-coated fish-oil preparation on relapses in Crohn's disease. 1996. N Engl J Med 334(24):1557-60.

712. Bendich A. The potential for dietary supplements to reduce premenstrual syndrome (PMS) symptoms. 2000. J Am Coll Nutr 19(1):3-12.

713. Bendich A, Mallick R, Leader S. Potential health economic benefits of vitamin supplementation. 1997. West J Med 166(5):306-12.

714. Ben Schöttker et al. Strong associations of 25-hydroxyvitamin D concentrations with all-cause, cardiovascular, cancer, and respiratory disease mortality in a large cohort study. Am J Clin Nutr 2013 Apr; 97(4):782-793.

715. Benton D, Buts JP. Vitamin/mineral supplementation and intelligence. 1990. Lancet 335(8698):1158-60.

716. Bernstein WK, Khastgir T, Khastgir A, Hernandez E, Miller J, Schonfeld SA, Nissim JE, Chernow B. Lack of effectiveness of magnesium in chronic stable asthma. A prospective, randomized, double-blind, placebo-controlled, crossover trial in normal subjects and in patients with chronic stable asthma. 1995. Arch Intern Med 155(3):271-6.

717. Bertone-Johnson ER, Hankinson SE, Bendich A, Johnson SR, Willett WC, Manson JE. Calcium and vitamin D intake and risk of incident premenstrual syndrome. 2005. Arch Intern Med 165(11):1246-52.

718. Bischoff-Ferrari HA, Dawson-Hughes B, Willett WC, Staehelin HB, Bazemore MG, Zee RY, Wong JB. Effect of vitamin D on falls: a meta-analysis. 2004. JAMA 291(16):1999-2006.

719. Bischoff HA, Stahelin HB, Dick W, Akos R, Knecht M, Salis C, Nebiker M, Theiler R, Pfeifer M, Begerow B, Lew RA, Conzelmann M. Effects of vitamin D and calcium supplementation on falls: a randomized controlled trial. 2003. J Bone Miner Res 18(2):343-51.

720. Black PN, Scragg R. Relationship between serum 25-hydroxyvitamin d and pulmonary function in the third national health and nutrition examination survey. 2005. Chest 128(6):3792-8.

721. Blee TH, Cogbill TH, Lambert PJ. Hemorrhage associated with vitamin C deficiency in surgical patients. 2002. Surgery 131(4):408-12.

722. Brouwers FM, Van Der Werf S, Bleijenberg G, Van Der Zee L, Van Der Meer JW. The effect of a polynutrient supplement on fatigue and physical activity of patients with chronic fatigue syndrome: a double-blind randomized controlled trial. 2002. QJM 95(10):677-83.

723. Bryan J. Calvaresi E, Hughes D. Short-term folate, vitamin B-12 or vitamin B-6 supplementation slightly affects memory performance but not mood in women of various ages. 2002. J Nutr 132(6):1345-56.

724. Bursell SE, Clermont AC, Aiello LP, Aiello LM, Schlossman DK, Feener EP, Laffel. Mortality associated with low plasma concentration of beta carotene and the effect of oral supplementation. 1996. JAMA 275(9):699-703.

725. Bursell SE, Clermont AC, Aiello LP, Aiello LM, Schlossman DK, Feener EP, Laffel L, King GL. High-dose vitamin E supplementation normalizes retinal blood flow and creatinine clearance in patients with type 1 diabetes. 1999. Diabetes Care 22(8):1245-51.

726. Cangussu LM1, Nahas-Neto J, Orsatti CL, Bueloni-Dias FN, Nahas EA Effect of vitamin D supplementation alone on muscle function in postmenopausal women: a randomized, double-blind, placebo-controlled clinical trial. Osteoporos Int. 2015 May 9.

727. Carroll D, Ring C, Suter M, Willemsen G. The effects of an oral multivitamin combination with calcium, magnesium, and zinc on psychological well-being in healthy young male volunteers: a double-blind placebo-controlled trial. 2000. Psychopharmacology (Berl) 150(2):220-5.

728. Cerhan JR, Saag KG, Merlino LA, Mikuls TR, Criswell LA. Antioxidant micronutrients and risk of rheumatoid arthritis in a cohort of older women. 2003. Am J Epidemiol 157:345-54.
729. Chuang S-chun, Norat T, Murphy N, et al. Fiber intake and total and cause-specific mortality in the European Prospective Investigation into Cancer and Nutrition cohort. Am J Clin Nutr. 2012;96(1):164-74.
730. Clarke R, Smith AD, Jobst KA, Refsum H, Sutton L, Ueland PM. Folate, vitamin B12, and serum total homocysteine levels in confirmed Alzheimer disease. 1998. Arch Neurol 55(11):1449-55.
731. Cummingham JJ. Micronutrients as nutriceutical interventions in diabetes mellitus. 1998. J Am Coll Nutr 17(1):7.
732. Curhan GC, Willett WC, Speizer FE, Spiegelman D, Stampfer MJ. Comparison of dietary calcium with supplemental calcium and other nutrients as factors affecting the risk of kidney stones in women. 1997. Ann Intern Med 126(7):497-504.
733. Edmonds SE, Winyard PG, Guo R, Kidd B, Merry P, Langrish-Smith A, Hansen C, Ramm S, Blake DR. Putative analgesic activity of repeated oral doses of vitamin E in the treatment of rheumatoid arthritis. Results of a prospective placebo controlled double blind trial. 1997. Ann Rheum Dis 56(11):649-55.
734. Engelhart MJ, Geerlings MI, Ruitenberg A, van Swieten JC, Hofman A, Witteman JC, Breteler MM. Dietary intake of antioxidants and risk of Alzheimer disease. 2002. JAMA 287(24):3223-9.
735. Fairfield KM, Fletcher RH. Vitamins for chronic disease prevention in adults: scientific review. 2002. JAMA 287(23):3116-26.
736. Fenton WS, Dickerson F, Boronow J, Hibbein JR, Knable M. A placebo-controlled trial of omega-3 fatty acid (ethyl eicosapentaenoic acid) supplementation for residual symptoms and cognitive impairment in schizophrenia. 2001. Am J Psychiatry 158(12):2071-4.
737. Fletcher RH, Fairfield KM. Vitamins for chronic disease prevention in adults: clinical applications. 2002. JAMA 287(23):3127-9.
738. Flicker L, MacInnis RJ, Stein MS, Scherer SC, Mead KE, Nowson CA, Thomas J, Lowndes C, Hopper JL, Wark JD. Should older people in residential care receive vitamin D to prevent falls? Results of a randomized trial. 2005. J Am Geriatr Soc 53(11):1881-8.
739. Fogarty A, Lewis SA, Scrivener SL, Antoniak M, Pacey S, Pringle M, Britton J. Oral magnesium and vitamin C supplements in asthma: a parallel group randomized placebo-controlled trial. 2003. Clin Exp Allergy 33(10):1355-9.
740. Frusso R, Zarate M, Augustovski F, Rubinstein A. Magnesium for the treatment of nocturnal leg cramps: a crossover randomized trial. 1999. J Fam Pract 48(11):868-71.
741. Gopinath B, Flood VM, Rochtchina E, McMahon CM, Mitchell P. Consumption of omega-3 fatty acids and fish and risk of age-related hearing loss. 2010. Am J Clin Nutr 92(2):416-21.
742. Grodstein F, Chen J, Willett WC. High-dose antioxidant supplements and cognitive function in community-dwelling elderly women. 2003. Am J Clin Nutr 77(4):975-84.
743. Hasselmark L, Malmgren R, Zetterstrom O, Unge G. Selenium supplementation in intrinsic asthma. 1993. Allergy 48:30-36.
744. Helmy M, Shohyeb M, Helmy MH, el-Bassiouni EA. Antioxidants as adjuvant therapy in rheumatoid disease. A preliminary study. 2001. Arzneimittelforschung 51(4):293-8.
745. Hill J, Micklewright A, Lewis S, Britton J. Investigation of the effect of short-term change in dietary magnesium intake in asthma. 1997. Eur Respir J 10(10):2225-9.
746. Jackson MJ. Diagnosis and detection of deficiencies of micronutrients: minerals. 1999. Br Med Bull 55(3):634-42.
747. Jacob RA, Aiello GM, Stephensen CB, Blumberg JB, Milbury PE, Wallock LM, Ames BN. Moderate antioxidant supplementation has no effect on biomarkers of oxidant damage in healthy men with low fruit and vegetable intakes. 2003. J Nutr 133:740-3.
748. Janssen HC, Samson MM, Verhaar HJ. Vitamin D deficiency, muscle function, and falls in elderly people. 2002. Am J Clin Nutr 75(4):611-5.
749. Kennedy DO, Veasey R, Watson A, Dodd F, Jones E, Maggini S, Haskell CF. Effects of high-dose B vitamin complex with vitamin C and minerals on subjective mood and performance in healthy males. 2010. Psychopharmacology (Berl) 211(1):55-68.
750. Kenny AM, Biskup B, Robbins B, Marcella G, Burleson JA. Effects of vitamin D supplementation on strength, physical function, and health perception in older, community-dwelling men. 2003. J Am Geriatr Soc 51(12):1762-7.
751. Knekt P, Kilkkinen A, Rissanen H, Marniemi J, Sääksjärvi K, Heliövaara M. Serum vitamin D and the risk of Parkinson disease. 2010. Arch Neurol 67(7):808-11.
752. Kremer JM. n-3 Fatty acid supplements in rheumatoid arthritis. 2000. Am J Clin Nutr 71(suppl):349S-51S.

753. Kremer JM, Lawrence DA, Petrillo GF, Litts LL, Mullaly PM, Rynes RI, Stocker RP, Parhami N, Greenstein NS, Fuchs BR, Mathur A, Robinson DR, Sperling RI, Bigaouette J. Effects of high-dose fish oil on rheumatoid arthritis after stopping nonsteroidal antiinflammatory drugs. 1995. Arthritis Rheum 38(8):1107-14.
754. Latham NK, Anderson CS, Reid IR. Effects of vitamin D supplementation on strength, physical performance, and falls in older persons: a systematic review. 2003. J Am Geriatr Soc 51(9):1219-26.
755. Llewellyn DJ, Lang IA, Langa KM, Muniz-Terrera G, Phillips CL, Cherubini A, Ferrucci L, Melzer D. Vitamin D and risk of cognitive decline in elderly persons. 2010. Arch Intern Med 170(13):1135-41.
756. Luchsinger JA, Tang MX, Shea S, Mayeux R. Antioxidant vitamin intake and risk of Alzheimer disease. 2003. Arch Neurol 60(2):203-8.
757. Malouf M, Grimley EJ, Areosa SA. Folic acid with or without vitamin B12 for cognition and dementia. 2003. Cochrane Database Syst Rev (4):CD004514.
758. Masaki KH, Losonczy KG, Izmirlian G, Foley DJ, Ross GW, Petrovitch H, Havlik R, White LR. Association of vitamin E and C supplement use with cognitive function and dementia in elderly men. 2000. Neurology 54(6):1265-72.
759. Mendelsohn AB, Belle SH, Stoehr GP, Ganguli M. Use of antioxidant supplements and its association with cognitive function in a rural elderly cohort: the MoVIES Project. 1998. Am J Epidemiol 148(1):38-44.
760. Mithal A et al. Impact of nutrition on muscle mass, strength, and performance in older adults. Osteoporosis Int. 2012 Dec 18.
761. Morris MC, Beckett LA, Scherr PA, Hebert LE, Bennett DA, Field TS, Evans DA. Vitamin E and vitamin C supplement use and risk of incident Alzheimer disease. 1998. Alzheimer Dis Assoc Disord 12(3):121-6.
762. Morris MC, Evans DA, Bienias JL, Tangney CC, Wilson RS. Vitamin E and cognitive decline in older persons. 2002. Arch Neurol 59(7):1125-32.
763. Muller DP. Vitamin E and neurological function. 2010. Mol Nutr Food Res 54(5):710-8.
764. Munger KL, Zhang SM, O'Reilly E, Hernan MA, Olek MJ, Willett WC, Ascherio A. Vitamin D intake and incidence of multiple sclerosis. 2004. Neurology 62(1):60-5.
765. Murakami K, Miyake Y, Sasaki S, Tanaka K, Fukushima W, Kiyohara C, Tsuboi Y, Yamada T, Oeda T, Miki T, Kawamura N, Sakae N, Fukuyama H, Hirota Y, Nagai M; Fukuoka Kinki Parkinson's Disease Study Group. Dietary intake of folate, vitamin B6, vitamin B12 and riboflavin and risk of Parkinson's disease: a case-control study in Japan. 2010. Br J Nutr 104(5):757-64.
766. Nemets B, Stahl Z, Belmaker RH. Addition of omega-3 fatty acid to maintenance medication treatment for recurrent unipolar depressive disorder. 2002. Am J Psychiatry 159(3):477-9.
767. Opara EC. Oxidative stress, micronutrients, diabetes mellitus and its complications. 2002. J R Soc Health 122(1):28-34.
768. Pavelka K, Gatterova J, Olejarova M, Machacek S, Giacovelli G, Rovati LC. Glucosamine sulfate use and delay of progression of knee osteoarthritis: a 3-year, randomized, placebo-controlled, double-blind study. 2002. Arch Intern Med 162(18):2113-23.
769. Peacock JM, Folsom AR, Knopman DS, Mosley TH, Goff DC Jr, Szklo M. Dietary antioxidant intake and cognitive performance in middle-aged adults. The Atherosclerosis Risk in Communities (ARIC) Study investigators. 2000. Public Health Nutr 3(3):337-43.
770. Pearson PJ, Lewis SA, Britton J, Fogarty A. Vitamin E supplements in asthma: a parallel group randomized placebo controlled trial. 2005. Thorax 59(8):652-6.
771. Petersen RC, Thomas RG, Grundman M, Bennett D, Doody R, Ferris S, Galallsko D, Jin S, Kaye J, Levey A, Pfeiffer E, Sano M, van Dyck CH, Thal LJ, for the Alzheimer's Disease Cooperative Study Group. Vitamin E and Donepezil for the treatment of mild cognitive impairment. 2005. N Engl J Med 352:2379-88.
772. Pfeifer M, Begerow B, Minne HW, Abrams C, Nachtigall D, Hansen C. Effects of a short-term vitamin D and calcium supplementation on body sway and secondary hyperparathyroidism in elderly women. 2000. J Bone Miner Res 15(6):1113-8.
773. Phillipson T, et al. Impact of Oral Nutritional Supplementation on Hospital Outcomes. Am J Manag Care. 2013;19(2):121-128.
774. Rajiv Chowdhury et al. Vitamin D and risk of cause specific death: systematic review and meta-analysis of observational cohort and randomised intervention studies. BMJ 2014;348:g1903.
775. Romieu I, Meneses F, Ramirez M, Ruiz S, Padilla RP, Sienra JJ, Gerber M, Grievink L, Dekker R, Walda I, Brunekreef B. Antioxidant supplementation and respiratory functions among workers exposed to high levels of ozone. 1998. Am J Respir Crit Care Med 158:226-232.

776. Romieu I, Sienra-Monge JJ, Ramirez-Aguilar M, Tellez-Rojo MM, Moreno-Macias H, Reyes-Ruiz NI, del Rio-Navarro BE, Ruiz-Navarro MX, Hatch G, Slade R, Hernandez-Avila M. Antioxidant supplementation and lung functions among children with asthma exposed to high levels of air pollutants. 2002. Am J Respir Crit Care Med 166(5):703-9.
777. Sally N Adebamowo, Donna Spiegelman, Walter C Willett, and Kathryn M Rexrode. Association between intakes of magnesium, potassium, and calcium and risk of stroke: 2 cohorts of US women and updated meta-analyses. Am J Clin Nutr June 2015 vol. 101 no. 6 1269-1277.
778. Sano M, Ernesto C, Thomas RG, Klauber MR, Schafer K, Grundman M, Woodbury P, Growdon J, Cotman CW, Pfeiffer E, Schneider LS, Thal LJ. A controlled trial of selegiline, alpha-tocopherol, or both as treatment for Alzheimer's disease. 1997. N Engl J Med 336(17):1216-22.
779. Schlebusch L, Bosch BA, Polglase G, Kleinschmidt I, Pillay BJ, Cassimjee MH. A double-blind, placebo-controlled, double-centre study of the effects of an oral multivitamin-mineral combination on stress. 2000. S Afr Med J 90(12):1216-23.
780. Schmidt MC, Askew EW, Roberts DE, Prior RL, Ensign WY Jr, Hesslink RE Jr. Oxidative stress in humans training in a cold, moderate altitude environment and their response to a phytochemical antioxidant supplement. 2002. Wilderness Environ Med 13(2):94-105.
781. Schoenen J, Jacquy J, Lenaerts M. Effectiveness of high-dose riboflavin in migraine prophylaxis. A randomized controlled trial. 1998. Neurology 50(2):466-70.
782. Shen J, Lai CQ, Mattei J, Ordovas JM, Tucker KL. Association of vitamin B-6 status with inflammation, oxidative stress, and chronic inflammatory conditions: the Boston Puerto Rican Health Study. 2010. Am J Clin Nutr 91(2):337-42.
783. Shults CW, Oakes D, Kiebertz K, Beal MF, Haas R, Plumb S, Juncos JL, Nutt J, Shoulson I, Carter J, Kompoliti K, Perlmutter JS, Reich S, Stern M, Watts RL, Kurlan R, Molho E, Harrison M, Lew M, Parkinson Study Group. Effects of coenzyme Q10 in early Parkinson disease: evidence of slowing of the functional decline. 2002. Arch Neurol 59(10):1541-50.
784. Skarupski KA, Tangney C, Li H, Ouyang B, Evans DA, Morris MC. Longitudinal association of vitamin B6, folate, and vitamin B12 with depressive symptoms among older adults over time. 2010. AJCN 92(2):330-5.
785. Solomon PR, Adams F, Silver A, Zimmer J, DeVeaux R. Ginkgo for memory enhancement: a randomized controlled trial. 2002. JAMA 288(7):835-40.
786. Stoll AL, Locke CA, Marangell LB, Severus WE. Omega-3 fatty acids and bipolar disorder: a review. 1999. Prostaglandins Leukot Essent Fatty Acids 60(5-6):329-37.
787. Stoll AL, Severus WE, Freeman MP, Rueter S, Zboyan HA, Diamond E, Cress KK, Marangell LB. Omega 3 fatty acids in bipolar disorder: a preliminary double-blind, placebo-controlled trial. 1999. Arch Gen Psychiatry 56(5):407-12.
788. Studer M, Briel M, Leimenstoll B, Glass TR, Bucher HC. Effect of different antilipidemic agents and diets on mortality: a systematic review. 2005. Arch Intern Med 165(7):725-30.
789. Subakir SB, Setiadi E, Affandi B, Pringgoutomo S, Freisleben HJ. Benefits of vitamin E supplementation to Norplant users—in vitro and in vivo studies. 2000. Toxicology 148(2-3):173-8.
790. Thys-Jacobs S, Starkey P, Bernstein D, Tian J, The Premenstrual Syndrome Study Group. Calcium carbonate and the premenstrual syndrome: effects on premenstrual and menstrual symptoms. 1998. Am J Obstet Gynecol 179(2):444-52.
791. Tuija Jääskeläinen et al.. Higher serum 25-hydroxyvitamin D concentrations are related to a reduced risk of depression. British Journal of Nutrition, available on CJO2015.
792. Tutuncu NB, Bayraktar M, Varli K. Reversal of defective nerve conduction with vitamin E supplementation in type 2 diabetes: a preliminary study. 1998. Diabetes Care 21(11):1915-8.
793. Villeponteau B, Cockrell R, Feng J. Nutraceutical interventions may delay aging and the age-related diseases. 2000. Exp Gerontol 35(9-10):1405-17.
794. Ward KA, Das G, Berry JL, Roberts SA, Rawer R, Adams JE, Mughal Z. Vitamin D status and muscle function in post-menarchal adolescent girls. 2009. J Clin Endocrinol Metab 94(2):559-63.
795. Werbach MR. Nutritional strategies for treating chronic fatigue syndrome. 2000. Altern Med Rev 5(2):93-108.
796. Wong WY, Merkus HM, Thomas CM, Menkveld R, Zielhuis GA, Steegers-Theunissen RP. Effects of folic acid and zinc sulfate on male factor subfertility: a double-blind, randomized, placebo-controlled trial. 2002. Fertil Steril 77(3):491-8.
797. Zandi PP, Anthony JC, Khachaturian AS, Stone SV, Gustafson D, Tschanz JT, Norton MC, Welsh-Bohmer KA, Breitner JC, Cache County Study Group. Reduced risk of Alzheimer disease in users of antioxidant vitamin supplements: the Cache County Study. 2004. Arch Neurol 61(1):82-8.
798. Zhang SM, Hernan MA, Chen H, Spiegelman D, Willett WC, Ascherio A. Intakes of vitamins E and C, carotenoids, vitamin supplements, and PD risk. 2002. Neurology 59(8):1161-9.

799. Zhang SM, Hernan MA, Olek MJ, Spiegelman D, Willett WC, Ascherio A. Intakes of carotenoids, vitamin C, and vitamin E and MS risk among two large cohorts of women. 2001. Neurology 57(1):75-80.
800. Ziaei S, Faghihzadeh S, Sohrabvand F, Lmyian M, Emamgholy T. A randomized placebo-controlled trial to determine the effect of vitamin E in treatment of primary dysmenorrhoea. 2001. BJOG 108(11):1181-3.