Health Benefits of Nutritional Supplements

Selected Readings from the Last 20 Years (1990-2010)

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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, 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 20 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 health-care 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 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

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Cardiovascular Health


“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. (#65)

“Mg2+ [magnesium] deficiency or a reduction in dietary intake of Mg2+ 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. (#22)
“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 to 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. (#110)

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**EB Rimm, et al. (#121)**

“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).”
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)

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

-DS Kelley, et al. (#75)


“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. (#10)

“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 (#128)
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. (#36)


“We conclude that CoQ10 administration can improve recovery of the mitochondria and the cardiac 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. (#124)

“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. (#97)
115. 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 al-

“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. (#167)

“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. (#92)
134. Skyrme-Jones RA, O’Brien RC, Berry KL, Meredith IT. Vitamin E supplementation improves endothelial function in
152. Venn BJ, Green TJ, Moser R, Mann JI. Comparison of the effect of low-dose supplementation with L-

"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. (#174)


“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. (#162)
“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. (#168)
Cancer


“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 (#215)
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. (#256)

“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, micronutrients, or other micronutrients and bladder cancer risk.”

-DS Michaud (#251)


219. Gorham ED, Garland CF, Garland FC, Grant WB, Mohr

“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. (#250)

“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 (#187)
“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. (#245)

“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. (#285)


“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. (#252)
“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. (#243)


263. Peters U, Littman AJ, Kristal AR, Patterson RE, Potter
“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. (#196)

“...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. (#180)
“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. (#231)
Bone and Joint Health

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

- SL Meacham, et al. (#351)

“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 Cholecalciferol], 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...”

- DA Greene, et al. (#327)

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

- SL Meacham, et al. (#351)

“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 suggested by previous reports.”

- C Bolton-Smith, et al. (#300)

“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. (#371)


327. 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].


"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 (#358)

"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 (#334)
“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. (#338)


372. Sato Y, Honda Y, Iwamoto J, Kanoko T, Satoh K. Effect of folate and mecobalamin on hip fractures in patients with

“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 (#324)

“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. (#352)


“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. (#314)

“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. (#377)
Healthy Pregnancies and Healthy Babies


“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 percent) 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. (#491)

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. (#476)
“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 (#448)


“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 Bhaté, et al. (#393)

“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 over-consumption 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. (#426)
“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 (#401)
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. (#424)


“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 (#439)


“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. (456)
Immune Function

“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. (#502)

513. Boardley D, Fahlman M. Micronutrient supplementation does not attenuate seasonal decline of immune system indexes in well-nourished elderly women: A placebo-


530. El-Kadiki A, Sutton AJ. Role of multivitamins and mineral supplements in preventing infections in elderly people: systematic review and meta-analysis of randomised

*“Inadequate intake and status of vitamins and trace elements may lead to suppressed immunity, which predisposes to infections and aggravates undemutrition. 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. (#564)

*“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. (#559)


536. 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 (#560)


“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 naïve 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. (#565)
“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. (#568)

“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. (#598)
564. Maggini S, Wintergerst ES, Beveridge S, Hornig DH. 
Selected vitamins and trace elements support immune function 
by strengthening epithelial barriers and cellular and humoral 
565. 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 
566. McKay DL, Perrone G, Rasmussen H, Dallal G, Hart- 
man 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 
567. Merchant AT, Curhan G, Bendich A, Singh VN, Willett 
WC, Fawzi WW. Vitamin intake is not associated with commun-
568. 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 
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RD, Stollar BD. Vitamin E supplementation and in vivo immune 
response in healthy elderly subjects: a randomized 
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573. 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 under-
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mitamin A supplementation enhances infants' immune responses to 
hepatitis B vaccine but does not affect responses to Haemo-
575. Nieman DC. Exercise immunology: future directions 
for research related to athletes, nutrition, and the elderly. 2000. 
576. Nieman DC, Henson DA, Gross SJ, Jenkins DP, Davis 
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ulty SR, McAnulty LS, Mayer EP. Quercetin reduces illness but 
not immune perturbations after intensive exercise. 2007. Med 
577. Nugent AP, Roche HM, Noone EJ, Long A, Kelleher DK, 
Gibney MJ. The effects of conjugated linoleic acid supplemen-
578. Overbeck S, Rink L, Haase H. Modulating the immune 
response by oral zinc supplementation: a single approach for 

“In conclusion, our double-blind, place-
bo-controlled study shows that levels of 
vitamin E higher than currently recom-
ended enhance in vivo indexes of T 
cell-mediated function in healthy elder-
ly. The enhancement of cell-mediated 
immunity by vitamin E was not asso-
ciated with any adverse effects. Since 
age-associated decline in immune re-
response is associated with increased 
morbidity and mortality in the elderly 
and is widely observed, recommenda-
tions to increase the intake of vitamin E 
for elderly should be considered.”

- EG Pallast, et al. (#580)
“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)2VD3 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 Treg cells.”

- JR Mora, et al. (#570)

“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. (#605)


“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. (#540)

“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 (#520)
Healthy Vision


619. Bursell SE, Clermont AC, Aiello LP, Aiello LM, Schlossman DF, Feener EP, Laffel L, King GL. High-dose vitamin E supplementation normalizes retinal blood flow and

“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. (#673)


“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. (#618)

“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. (#672)
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 (#664)
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. (#635)


“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. (#669)
Other References


