Nutrient Supplements to Prolong Life

The scientific evidence to support life extension effects of nutritional supplements on humans

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Longevity, Life Extension

In medical publications on nutrients, terms such as lifespan, longevity and survival are rarely used. Much more frequently used are the terms mortality and death rate to describe if a nutritional treatment may prolong the life span of the subject(s) examined. Nutritional treatments that lower the all-cause mortality or the specific mortalities of potentially fatal diseases such as cardiovascular, cerebrovascular diseases and cancer generally tend to prolong life span.
In particular, nutritional treatments that may reduce the risk of coronary heart disease and cancer (the number one 'killer' in the western world), usually prolong a person's life span.[1]

Dietary Improvement

Eat Less to Live Longer

Low calorie diets and regularly fasting make animals live longer

Research has suggested that consumers of a **low calorie diet** may live longer as animal studies show that whenever the food intake is decreased by approximately 30 to 40 %, the average and maximal lifespan increases by + 15 to + 25% in different animal species from insects to primates[1-3]. However, **periodic fasting** may even yield **better results**. Fasting a whole day from time to time, for example, helps mice and rats to live longer, better even than a low-calorie diet with food restriction at each regular meal. The extension in lifespan reaches the + 35% in rodents that are periodically deprived of food, put into a two-day-per -week fasting or example [4-6]

Eat less to become a centenarian

A low calorie diet is a common dietary trait that is found in studies on centenarians. These long living people eat ten to twenty percent less than the average person[7-8].
Their diet is moderately low in calories with plenty of fruits and vegetables since their younger age. There was little weight gain with age in these long-living persons. They have in general a life-long low BMI (body mass index)[9]. Approximately 99% of all centenarians have been lean, not obese, throughout their life.

Several studies in humans and nonhuman primates have shown that the consumption of low calorie diets reduces the oxidative stress - the stress and damage caused by high levels of free radicals, improves biomarkers of longevity, reduces atherosclerosis, blood pressure, and disease markers[10-13].

The greater the food variation, the longer the life

Eat a great variety of food may also be necessary to live a long life. In the island of Okinawa, for example, where people live longer and there are three to four times more centenarians, the typical diet of elderly women consists of 100 biologically different foods per week. In diet of women living in Northern Japan, where life expectancy is shorter, the food variety is much lower, about 30 per week, which is the typical recommended minimal food variation and the food diversity consumed in most westernized countries (study on 200 elderly women)[14-15]. This finding confirms the importance of high food variation for longevity observed in another study that showed that mortality is decreased by 42% in people who vary their diet to a higher degree in comparison with people who eat a monotonous diet, rarely varying[16].

Drink More Water

Dehydration causes premature death

Dehydration is associated with high morbidity and mortality rates in elderly persons[17].
50% of elderly Medicare beneficiaries hospitalized with dehydration die within a year of admission. Hospitalization of elderly people with dehydration is a serious and costly medical problem[18].

Drinking more water may prolong life in mice

Calorie-restricted young and old mice live longer. The longer longevity may be due to their significant increase in water intake per gram of body weight compared to ad libitum fed counterparts[28].

Alcohol - A Dilemma?

Alcohol consumption can increase the risk of dying - the overall risk as well as the risk by cardiovascular and respiratory diseases

Alcohol consumption can shorten life by increasing the overall risk of dying as well as the risk of dying from cardiovascular and respiratory diseases. However, patients with a history of stroke and who drink alcohol, be it in small amounts (less than one drink per week) or daily (one drink or more per day), have been found to have -36% and -44% less overall and cardiovascular disease mortality respectively than never users of alcohol[20].

However, another more detailed investigation showed that ex-drinkers of alcohol have a considerably higher overall mortality rate than current drinkers or nondrinkers.
When the death risk of persons who never consume alcohol is taken into account, the results are entirely different. Real never drinkers have a significantly lower risk of dying by ischemic heart disease (-38%), respiratory disease (-31%) and all-cause (-12%) than both ex-drinkers and current drinkers calculated together. Moreover, men who start consuming alcohol on a regular basis have a -30% lower risk of developing major coronary heart disease, but that is the only benefit as they were shown to have a +40% higher risk of dying by diseases other than cardiovascular without any mortality compensation: no reduction in coronary heart

disease mortality (less coronary disease, but not a lower mortality by coronary disease), nor any reduction in overall cardiovascular mortality[21].

Furthermore, heavy alcohol drinkers have a considerably higher global risk of dying. British male doctors, for example, who drink at least three or more glasses of wine or beer per day (more than 21 units a week) have an increasingly greater risk of dying. In this category, there is a U-shaped relationship between allcause mortality and the mean amount of alcohol drunk.
The physicians who drank eight to 14 units per week, an average of one to two units a day, presented the lowest all-cause mortality[22].
The British physicians died easier from typical alcoholaugmented causes of death such as cirrhosis, liver cancer, pharynx and larynx cancers, and injury motor vehicle accidents[22]. In fact, a high number of these physicians died every year from alcohol-related deaths: an average of 6.4% per year with a male-to-female ratio 2 to 1! Car-related accidents are by far the main cause of alcohol-related years of life lost in men (51%) and in women (56%)[23].

Coffee: Good for the Longevity of Very Old People?

May coffee help very old persons to live a long life? In an Italian study on very old people, a high intake of espresso coffee was found to be associated with longevity in very old persons. This unexpected finding may possible be explained by the energy boost that coffee drinking provides for daily activities - it is known that being able to fulfil daily activities helps to live longer -and coffee's diuretic effect that helps elderly people whose kidney function is generally poor to better excrete into the urine toxins that come from the diet.

Eat Protein-Rich Foods

Eat animal foods to become a centenarian

A regular intake of animal foods rich in protein seems essential to live longer as the longest living humans, the centenarians, are never to our knowledge vegetarians, but eat fish, poultry and often meat. This is understandable as a vegan diet deprived of animal food produces deficiencies in B vitamins, iron, zinc, vitamin A, (essential) amino acids and fat[25].

Longer lifespans in patients who eat more protein

People who regularly consume foods rich in high quality protein may live longer. A life prolongation of two to six years, especially in people with illness, appears to be possible by increasing the consumption of proteins.
People with low blood levels of (total) protein and albumin, which reflect protein intake, have a 10 to 30% higher risk of dying, especially if they are suffering from a disease[26-27].
The mortality rate of women sufferers of breast cancer who are in the higher tertile of protein intake are half of that of breast cancer patients in the lower tertile of protein intake[28].
For this reason vegan diets deprived from animal foods should not be advised to women who have suffered from breast cancer. The consumption of meat, fish, poultry and other animal foods cooked at a high temperature should also not be recommended as we have seen elsewhere in the chapter on Macronutrients, subchapter on 'Unhealthy Fats'.

Concerns about consuming red meat?

The consumption of red meat may significantly increase the risk of dying by coronary heart disease. A 44 % higher risk of dying has been reported when protein was given to replace carbohydrate foods per 1,000 kcal (4.2 MJ) servings. It is likely that the high temperature at which red meat is usually cooked and consumed and that makes the meat toxic with burned fat and protein is responsible for most if not all of this adverse effect on longevity. Read the chapter on Macronutrients, subchapter on 'Unhealthy Fats' for more information on the adverse health effects of red meat. Very old people with chronic disease in particular do better when they avoid eating red meat. In a study with elderly people who suffer from a chronic disease had a 10-fold lower risk of dying if their diet was low in meat! The explanation that red meat is toxic because of its modified fats and proteins by the high temperature cooking may be valid here too[24].

Avoid Milk Products

Avoid milk and other dairy products to prevent and survive cardiovascular disease

If we do not want to die from cardiovascular disease, we should not consume milk and other dairy products.
Scientific research has shown that people who regularly eat dairy products may die easier from coronary heart disease and other types of cardiovascular disease. A significantly 41% higher risk of dying from cardiovascular disease was reported when protein was replaced by carbohydrate foods per 1,000 kcal (4.2 MJ) servings. Consequently, long-term adherence to high protein diets consisting of milk-derived products such as cheese or yogurt eating or milk powder consumption by body-builders may have potentially adverse health consequences[28]. Read the chapter on Macronutrients, subchapter on 'Unhealthy Proteins for more information on the adverse health effects of milk products.

The risk of dying by ischemic heart disease[29-30] in particular in postmenopausal women[28], increases at higher intakes of milk and related products[29].

Avoid milk and other dairy products to prevent and survive cancer

Avoid milk and other dairy products to avoid dying from cancer. People who regularly consume dairy products are at a statistically significant higher risk of dying from colon cancer[31] and prostate cancer[32]. The risk of fatal prostate cancer is more than twofold higher in men who drink three glasses of milk or more per day[33-34]. In one cohort study, there was no significant increase associated with the consumption of one glass of whole milk or more[35], but the discordance may be due to the fact that the frequency of overall prostate cancer was measured and not that of the dangerous and fatal form of prostate cancer. Further, the researchers did not check for a mortality differences between lower and higher intakes of milk products.

An exception: Malnourished and elderly persons may live longer by consuming milk products

The consumption of dairy products may be healthy for very old people as it may partially correct the insufficient protein intake that is often observed in these people.
Very old persons often have too low protein intake. This may

explain why in some regions the belief is high that consumption of milk and in particular yogurt is associated with longevity[24].

Consume Fruits and Vegetables

Consume fruits and in particular citrus fruits to extend life

The intake of **fruit** in general[36] and **citrus fruits**[37] such as lemon and grapefruit in particular has been shown to lowers the overall mortality by -22% and-48% respectively.

Citrus fruits such as lemon and grapefruits appear are good fruits to help us live longer. A five-year cohort study among 162 self-sufficient residents in a public home for elderly showed that the seniors who ate citrus fruits twice or more per week had twice a lower risk of dying than those with a citrus food intake of less than once a week (**figure 1**)[24].

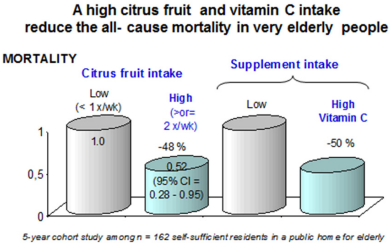

Figure 1: Frequent consumption of citrus fruit and a high intake of vitamin C, are associated with longevity

Fortes C, Forastiere F, Farchi S, Rapiti E, Pastori G, Perucci CA. Diet and overall survival in a cohort of very elderly people. Epidemiology. 2000 Jul;11(4):440-5. Department of Epidemiology, Lazio Regional Health Authority, Rome, Italy

Consume vegetables and in particular cruciferous vegetables and carrots in particular to extend life

For vegetables, it seems that **cruciferous vegetables** have more potent life-extension effects than other vegetables. A -26% lower mortality rate was found in people with regularly consume cruciferous vegetables (highest quintile versus lowest quintile of intake)[38].

Elderly men who regularly eat carrots, a primary source of alpha- and beta-carotene, have -17% less risk of dying from cardiovascular disease[39].

Consume fruit and vegetables to prevent and survive cardiovascular disease

The Mediterranean diet rich in **fruit** and **vegetables** has consistently been shown to reduce coronary heart disease mortality. The reduction in coronary disease mortality with a Mediterranean varies from 27% to 33%[40-41]. For sudden cardiac death, it is approximately -45%[42].

A high fruit and vegetable intake may reduce the cardiovascular mortality.

The overall cardiovascular mortality is apparently more influenced by fruit intake than by vegetable intake.
Fruits, and in particular **berries** and **citrus fruits**, seem to provide an excellent coronary artery protection. A Finnish study on a large population, Middle-aged men regularly eating berries and fruits in general showed a 41% less risk of dying by cardiovascular disease. Men who at more vegetables had 34% less risk of dying by cardiovascular disease than men with a low dietary intake of these foods (when the highest quintile of intake was compared with the lower quintile)[43].

Consume fruit and vegetables to prevent and survive cancer

A high fruit and vegetable intake may reduce the cancer mortality. In several studies a high vegetable intake seems to be more efficient way to reduce the risk of dying from cancer mortality than fruit intake. Nevertheless, one study suggested the opposite. The almost daily intake of fruits modestly but significantly reduced with -12% the overall cancer mortality in 38,540 men and women survivors of the atomic bomb in Hiroshima and Nagasaki, while the almost daily intake of yellow vegetables did it by a near significant -8%[44].

How much of these good carbs should we eat to reduce the risk of dying by cancer of any kind? At least **more than 400 grams** of fruits and vegetables per day, a minimal amount that decreases the cancer mortality by 10%[45].

Consuming high amounts of fruits has been reported to reduce the risk of dying by prostate cancer by half (-54%) in Brazilian men, while it significantly reduced the mortality from stomach cancer by -62% in high fruit consumers[46]. In the same group of men a high vegetable intake reduced the risk of dying from prostate cancer by -33% and the death rate from stomach cancer by -28% in a near significant manner (p = 0.06) [47].

Avoid Sugar, Sweet Foods and Soft Drinks

Rodents that receive sugar die earlier

Mice that receive drinking water containing sugar die sooner. Their life span is reduced with 8 to 10%[48].
Another experiment with copper deficiency in rats confirmed sugar an important life-threatening food.
Severe copper deficiency is not very life-threatening in rats when a normal diet is consumed. When next to the copper deficiency fructose- or sucrose- containing carbohydrates are supplemented about six to seven times more rats die, mainly by rupture of the apex region of the heart. Copper supplementation neutralizes the adverse effects of fructose and sucrose on lifespan.
Physicians should check the copper level in the blood of patients who consume high amounts of sugar or sugar rich foods[49-50].

Humans who consume sugar may too die earlier

Humans die easier from cardiovascular disease and cancer if they often consume sugar or sugar-rich foods[51-53]. This observation suggests that the overall life expectancy of frequent consumers of sugar-rich products is lower too.

Consume Foods Rich in Healthy Fats: Omega-3 Polyunsaturated Fatty Acids

Consume foods rich in polyunsaturated fats to prevent and survive longer cardiovascular disease

People who take foods rich in polyunsaturated fats have less risk of dying from cardiovascular disease. Several studies have linked the consumption of fish that is naturally rich in polyunsaturated fatty acids, in particular of the omega-3 type, to a lower incidence of cardiovascular disease mortality (**figure 2**).

Men, heavy smokers, with high fish consumption have a reduced excess mortality fromcoronary heart disease

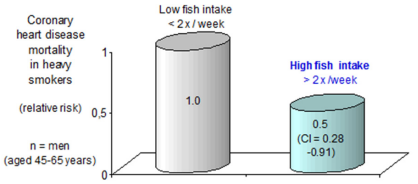

Figure 2: Coronary heart disease mortality over 23 years of follow-up in men who smoked more than 30 cigarettes/day in function of fish consumption.

Rodriguez BL, Sharp DS, et al. Fish intake may limit the increase in risk of coronary heart disease morbidity and mortality among heavy smokers. Circulation 1996; 94 (5°: 952-56

A lower risk of coronary heart disease is found in the Nurses' Health study, for instance, when the amount of polyunsaturated fats is above average in comparison to the amount of saturated fats in the diet[54].
People with high serum levels of omega-3 polyunsaturated fatty acids, levels that are within the higher tertile of polyunsaturated fat to saturated fat ratios, have three times more chances of not dying from cardiovascular disease than persons in the lowest tertile.
Chances are even better (5.6 times!) for patients with chest pain and a high ratio. The serum level of lipoprotein A, a level that is associated with more cardiovascular disease is also less than the half (2.5 times less) in these individuals[55].

It is particularly the consumption of high levels of polyunsaturated fatty acids of the omega-3 type in the diet that reduces the risk of dying from fatal and nonfatal myocardial infarction[222].

Consume sufficient amounts of (healthy) fat to live longer, also valid advice if you are a cancer patient

Consuming foods rich in fat may help us to live longer. In a Dutch cohort of 12,866 men aged 35-57 years, the overall cancer mortality was surprisingly higher in those who followed a disease risk reduction program that included a reduced fat consumption next to other strategies such as stopping smoking and taking drugs for high blood pressure when the blood pressure was higher.[340].
A low fat diet may - as much as a high fat diet - cause a breast cancer patient to die prematurely. In breast cancer patients, the mortality rate is approximately 30% lower in women who have an average consumption of fat in comparison with women in the upper and lower tertiles of fat intake[341].

Micronutrient Interventions to Prolong Life

Micronutrients play an interesting and possibly crucial role for longevity.

Multivitamin Preparations

Multivitamin preparations may help men more than women to live longer

The regular intake of vitamin associations may help us to live longer. In a large prospective French study, middleaged men (initially aged 45 to 60 years), not women, had a significant -37% lower overall death rate at the end of the study thanks to the intake of a preparation containing 100 mg of vitamin C, 30 mg of vitamin E and 100 µg of beta-carotene/day (**figure 3**)[59]. The reason why women may not have had any life span benefits from taking the same vitamin association is possibly due to their diet that often contains more fruits and vegetables - foods richer in the nutrients of the vitamin association than the diet of men. The nutritional richer diet may explain why the preparation that contains a relatively low dose in these nutrients did not make the difference, while in contrast French men may have benefited much more of the multivitamin preparation because their diet made of more meat and less fruits and vegetables is poorer in these nutrients.

A multinutritional supplement intake reduces mortality in men

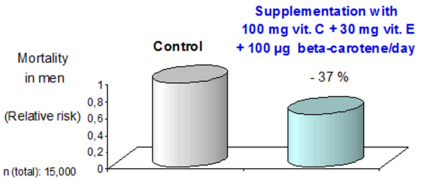

Figure 3: French men in SUVIMAX cohort (SUpplementation en VItamines et Mineraux AntioXydants) aged 45 to 60 years.

60. Hercberg S, Galan P, et al. The SUVI.MAX Study: a randomized, placebo-controlled trial of the health effects of antioxidant vitamins and minerals.Arch Intern Med. 2004 Nov 22;164(21):2335-42

What type of disease may benefit the most from the use of multivitamin preparations? Apparently, cardiovascular and cerebrovascular diseases benefit from regular multivitamin supplementation. Indeed, in another large prospective study, users of multivitamins containing vitamin A, vitamin C or vitamin E had a significantly -15% lower risk of dying from heart and blood vessel disease and stroke[60].

Greater survival in lung cancer patients who take multivitamin preparations

People with aggressive cancer may survive their cancer far longer by regular intake of a multivitamin preparation.
Patients with non-small cell lung cancer were reported to live almost four times longer after surgery if they took a multivitamin preparation. The median survival rate was 41 months in multivitamin users, while that of those who did not take any multivitamin preparation was only 11 months[61].

Minerals

Sodium

High sodium diets may prolong life, especially in the case of cardiovascular disease

We should revise our opinion on the health benefits of low sodium diets as well as we have to do it for low fat diets. Neither of the two seems to help us live longer, on the contrary! Alderman and his team at the Einstein College in New-York demonstrated the protective effects of sodium in general and for the heart in particular. They showed that in a large group of 11,346 US adults aged 25 to 75 years the 25% highest sodium consumers had not only an -18% lower all-cause mortality rate, but benefited from also a -20 % lower cardiovascular mortality.[62]

Sodium intake, but not too concentrated, may protect against death

In fact, in the study by the Einstein College, dietary sodium intake was found to be significantly inversely associated with cardiovascular and all-cause mortalities.
Thus, mortality was higher in people with the lowest sodium intake. However, in the same study, it was shown that in case people had a low calorie intake, salt became mildly toxic and mortalities slightly increased with a + 7% trend towards significance (p = 0.14)[17]. So, highly concentrated salted food should probably be avoided (**figure 4**).[62] Salt should be found diluted in the food, not concentrated.

A high sodium content of the diet reduces the cardiovascular disease and all-cause mortality

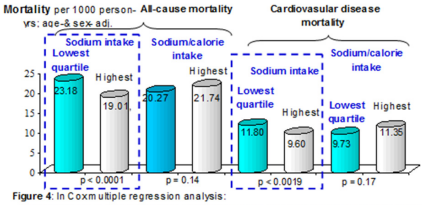

Figure 4: In Cox multiple regression analysis:
- sodium intake => inversely assoc. with all-cause (p=0.0069) & CVD mortality (p=0.086)
- sodium/calorie ratio => directly assoc. + all-cause (p=0.0004) & CVD mortality (p=0.0056)

n = 11,346 US adults (aged 25-75)

Alderman MH, Cohen H, Madhavan S. Dietary sodium intake and mortality: the National Health and Nutrition Examination Survey (NHANES I). Lancet. 1998 Mar 14;351(9105):781-5

Animal studies where high sodium diet prolongs life, while sodium-deficient diets shorten life

Animal experiences further confirm the importance of sodium for longevity. In chicks without disease, for example, a diet fourfold lower in sodium clearly made many chicks die earlier. Sodium is the main mineral in the blood to help animals as humans keep their blood pressure at an adequate level, assuring in this way the supply of enough blood, oxygen and nutrients, to the tissues. A deficiency in sodium may markedly reduce the blood and thus nutrient and oxygen supply to the tissues.[63]

Mice may live longer if they are put on a high sodium diet. Researchers observed that mice on a high sodium diet (24. 60 mEq Na: 1.45% NaCl) had a longer life span than mice with a medium or low sodium diet, again an indication that humans might need to introduce a sufficient amount of salt (sodium) into their diet to live longer.[64]

Avoid taking too high amounts of dietary sodium

However, the information on sodium is controversial and provides mixed feelings. The intake of very low as well as high amounts of salt in the diet should apparently not be recommended. In Finland, for example, each hundred millimoles increase in the 24 hour urinary sodium excretion, a reflection of dietary sodium intake, was found to be associated with a 26% increase in allcause mortality[16]. In fact, in Finland most of the salt in the diet comes for the consumption of preserved, salted foods. The salt is used as a preservative. If the concentrations of salt are high enough in the salted meat or cheese, bacterial proliferation is halted. It is known that preserved foods are not as good for our health as fresh food. For example men who consume high amounts of preserved foods, including salted meat, have been found to have a seven-fold higher rate of prostate cancer. It would not be surprising that the Finnish study had one important bias that was disregarded: the intake of preserved foods, which might be the factor that is associated with an increase in mortality, and not the salt itself used as a preservative.
Nevertheless, excessive amounts of salt in foods itself might be still harmful. Therefore, people should avoid consuming foods highly concentrated in salt.

Higher serum sodium levels may prolong life in patients with liver insufficiency or heart failure

A low serum sodium level is associated with a higher risk of dying in patients with liver insufficiency. Adding some kitchen salt (sodium) to foods may keep these patients alive, Biggins and colleagues found that patients with **cirrhosis** who had a low sodium level in the blood during three months of follow-up, a level below the 126 milli-Equivalents per liter, had a six to eight-fold higher risk of dying (**figure 5**)!

A very low serum sodium level increases mortality in cirrhotic patients.

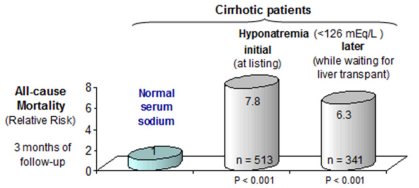

Figure 5: A serum sodium level in cirrhotic patients below the 126 mEq/L at listing or waiting for a liver transplantation is a strong independent predictor of mortality.

Biggins SW, Rodriguez HJ, Bacchetti P, Bass NM, Roberts JP, Terrault NA. Serum sodium predicts mortality in patients listed for liver transplantation. Hepatology. 2005;41(1):32-9
University of California - San Francisco

The risk of dying was at its highest when the serum sodium level was low at the moment they were listed for a liver transplant.[66]

Serum sodium	Mortality
135-145 mEq/L	Normal risk of 95% of the population
< or = 130 mEq/L	3x higher risk in cirrhotic patients
< 125 mEq/L	6 to 8x higher risk in cirrhotic patients

Another investigation showed that cirrhotic patients with a blood sodium level of 130 mEq per liter or below had a 3 times greater mortality than patients with normal serum sodium levels. Each increase of one mEq per liter of the sodium level decreased the odds of dying by -5%. These findings suggest that patients with disease, in particular liver disease, must avoid salt-restricted diets.[67]

For **heart failure** patients higher serum sodium levels may be life-saving contrary to the common belief that salt is bad for the heart. An investigation showed just the opposite: Heart failure patients benefit from higher serum sodium levels. They should avoid restricting (excessively) salt in their diet. Klein and colleagues showed that patients hospitalized for heart failure who had low serum sodium levels, which may reflect a low sodium intake, died twice as easy, suffering of a twofold higher mortality rate at the hospital and at 60 days after the begin of the hospitalization. In this study, the quartile of patients with the lowest serum sodium was compared to the quartile of highest levels.[68]

Potassium

Higher potassium levels prolongs life in humans and rats

Potassium depletion increases the risk of dying in **humans**. People with predisposition to heart disease should in particular be careful to have enough potassium in the diet as potassium depletion is associated with an increase in sudden death[69]. Most cases of sudden death are due to cardiac arrest, the heart stopping to beat efficiently.

Potassium depletion increases the risk of dying in **rats**. In one study, growing rats fed a diet that was severely impoverished in potassium during one month exhibited a two-fold (33 versus 17%) higher mortality rate than control rats with sufficient potassium.[70]

The consumption of potassium-rich foods prolongs life in patients with stroke

A 12 year follow-up study of 859 men and women aged 50 to 79 years, showed a gender discrepancy. While men in the lowest tertile of potassium intake had 2.6 times higher mortality from stroke, women in the lowest tertile of potassium intake had a fivefold higher strokemortality than women in the highest or middle tertiles.
Each 10 millimoles increase in daily potassium intake was associated with a 40% lower risk of dying from stroke (**figure 6**).[71]

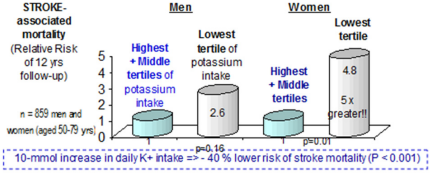

Figure 6: A high intake of potassium from food sources may protect against stroke => Effect independent of other dietary variables, including the intake of calories, fat, protein, fiber, calcium, magnesium and alcohol,cardiovascular risk factors, incl. age, sex, blood pressure, serum cholesterol, obesity, fasting glycaemia and smoking

Khaw KT, Barrett-Connor E. Dietary potassium and stroke-associated mortality. A 12-year prospective population study. N Engl J Med. 1987 Jan 29;316(5):235-40

Another investigation confirmed these findings for men, but paradoxically not in women in contrast with the previous study. Men in the lower tertile of potassium intake died easier. A racial difference in mortality rates was observed: White men had a 66% increase in strokemortality with the intake of moderately low potassium diet, while a low potassium intake by black men increased fourfold the risk of dying by stroke![72]

A high potassium diet may help rats survive stroke

High potassium (2.1%) diets strongly reduce rises in blood pressure and the risk of dying from stroke in hypertensive rats that are prone to develop stroke.
Similarly, medium-high (1.3%) levels of potassium in the diet significantly reduced blood pressure and stroke mortality but not nearly as much as the 2.1% potassium high diet. On the opposite side, high magnesium (0.26%) diets, unexpectedly, appeared in this experiment to increase stroke mortality and accelerate the rise of blood pressure in spontaneous hypertensive stroke prone rats.[74] Possibly, the deleterious effect of magnesium is due to the increased excretion of potassium in the urine at high magnesium conditions.

Potassium supplements may help survive myocardial infarction and cardiac failure in humans

Singh and colleagues showed that potassium supplementation reduces in patients with acute myocardial infarction the risk of dying with a more than half (-56%) thanks to a drastic reduction of the number of adverse cardiac events and ventricular ectopias (**figure 7**)[75].

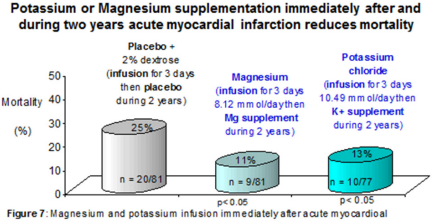

Figure 7: Magnesium and potassium infusion immediately after acute myocardial infarction (AMI) and addition of Mg and K salts to the AMI regimen leads to a significant reduction in mortality after two years.

N = 355 patients with suspected acute myocardial infarction

Singh RB, Singh NK, Niaz MA, Sharma JP. Effect of treatment with magnesium and potassium on mortality and reinfarction rate of patients with suspected acute myocardial infarction. Int J Clin Pharmacol Ther. 1996 May;34(5):219-25

Dangers of high levels of potassium in smokers and patients with antihypertensive drugs

Excessive serum levels of potassium in smokers and men taking antihypertensive drugs are associated with a greater risk of dying, in particular from death by causes other than cardiovascular disease.

In a large sample of 7.636 middle-aged British men, men with high serum potassium levels equal to 5.2 moles per liter or more were found to die easier, with a 70% increase in risk of dying from all causes, and an 80% increase in risk of dying from cancer, including a 2.5-fold higher risk of dying from lung cancer. The higher mortality rate from cardiovascular and non-cardiovascular diseases at elevated serum potassium was seen only among current smokers and men taking regular antihypertensive medication, not in others.[76]

Magnesium

Drinking magnesium-rich water may prolong life in general and help survive cardiovascular and stroke

Drinking magnesium-rich water may delay overall, cardiovascular and cerebrovascular death.
Several studies confirm that drinking water rich in magnesium may lower the risk of dying from cardiovascular diseases[77]. Only one study does not show any relationship between the two[78]. Men and women who live in cities where tap water is rich in magnesium (more than or equal to 8.3 mg of magnesium per liter), for example, liver longer, having a significantly -7.6% lower risk of dying whatever the cause of death may be (**figure 8**)[79].

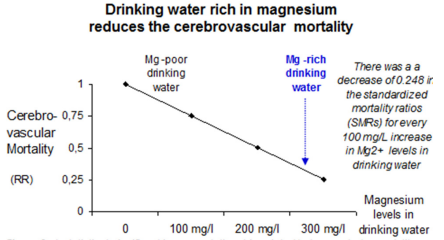

Figure 8: A statistical significant inverse relationship existed between stroke mortality and levels of both magnesium andcaldum after adjusting for urbanization index.
n = 227 municipalities in Taiwan

Yang CY, Chiu HF, Chiu JF, Wang TN, Cheng MF. Magnesium and calcium in drinking water and cerebrovascular mortality in Taiwan. Magnes Res. 1997 Mar;10(1):51-7 Kaohsiung Medical College,

Similarly, people drinking magnesium-rich or magnesium-poor drinking water, live longer. Their risk of dying from cerebrovascular diseases is -23% lower and from cardiovascular disease -8% lower (**figure 9**)[77].

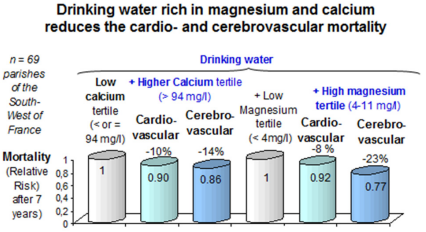

Figure 9: Potential protective dose-effect relation between calcium in drinking water and cardiovascular causes of mortality. For magnesium, a U-shape effect is possible, especially for cerebrovascular mortality.

Marque S, Jacqmin- Gadda H, Dartigues JF, Commenges D. Cardiovascular mortality and calcium and magnesium in drinking water: an ecological study in elderly people. Eur J Epidemiol. 2003;18(4):305-9 , Université de Bordeaux

Drinking magnesium-rich water may help reduce the risk of dying from stroke. For stroke, there is a similar protective relationship of magnesium. A statistical significant inverse relationship has thus been reported in Taiwan between levels of both magnesium and calcium and cerebrovascular mortality. For every one hundred milligrams per liter increase in magnesium levels in drinking water the standardized mortality ratio from stroke dropped by - 25%.[80]

Low magnesium levels increase mortality from septic shock in rats, while magnesium therapy helps rats survive the infectious shock

The longevity effects of magnesium extend also to infectious diseases. Magnesium replacement therapy provides a significant protection against endotoxin shock: three times more magnesium-supplemented rats survived an experimentally induced toxic shock than magnesium-deficient rats. The lower magnesium levels were, the greater the risk of dying was. A strong association was discovered.[81]

Magnesium therapy prolongs life in patients with coronary artery disease

Magnesium supplements help patients survive a myocardial infarction. Acute magnesium supplementation during the first 10 minutes or hours after a myocardial infarction lowers the mortality rate by approximately 40% (**figure 10**).[82]

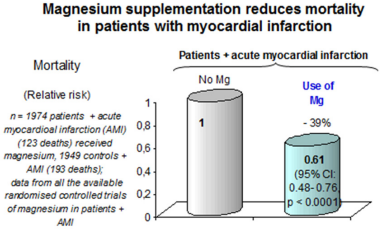

Figure 10: Magnesium supplemetation reduced the risk of dying in patients with acute myocardial infarction review of the evidence

Teo KK, Yusuf S. Role of magnesium in reducing mortality in acute myocardial infarction. A review of the evidence. Drugs. 1993 Sep;46(3):347-59 Division of Cardiology, University of Alberta, Edmonton,

Magnesium supplements also help in preventing myocardial infarction by minimizing the adverse consequences of coronary disease. Supplementation with 365 mg of elemental magnesium administered daily in two divided doses for six months to patients with coronary artery disease, for instance, increased exercise tolerance and reduces by more than twofold (-62%) the occurrence of exercise-induced chest pain[83]. Providing magnesium to patients who just had suffered a myocardial infarction decreases cardiac adverse events by half (-49%, ventricular tachycardia and fibrillation, -58% cardiac arrest). It also reduces the number of supraventricular tachycardia episodes. The risk of dying in this investigation that showed these benefits of magnesium, showed that magnesium therapy substantially reduced mortality by -54%.[84]

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Another investigation confirmed the helpful effect of magnesium in myocardial infarction. Patients with recent acute myocardial infarction who received intravenous magnesium infusion at small doses (20 mg or 8.1 mmol/day) immediately afterwards, had not only a marked reduction in mortality (more than twofold less: -56%), but also about half the complications, in particular less adverse cardiac events (-47%) and less ventricular ectopics (-62%). In the following two years, the beneficial effects of magnesium supplementation reduced to half the expected mortality (figure 3). [85]
Woods and colleagues obtained a -24% reduction in 28 day-mortality with intravenous magnesium supplementation, as

well as a -25% reduction in incidence of left ventricular failure in a randomized, double blind, placebo controlled study of 2316 patients with suspected acute myocardial infarction who received either intravenous magnesium sulphate (8 mmol or 2 grams of magnesium sulfate [= 197.2 mg of elemental magnesium] over 5 min followed by 65 mmol or 16,25 grams of magnesium sulphate [= 1.6 grams of elemental magnesium] or over 24 h) or physiological saline.[86]

Magnesium therapy saves pregnant women with preeclampsia from dying

Magnesium supplementation reduces also mortality in pregnant women, in particular eclampsia low doses of magnesium sulfate has reduced the mortality rate from 16 to 8 % (**figure 11**). The beneficial effects of magnesium are probably to the blood pressure-reducing and vasodilatatory effects of magnesium, which lowers the high blood pressure of preeclampsia and minimize its consequences.[87]

The intake of a low dosed magnesium supplement reduces mortality in women with ecclampsia

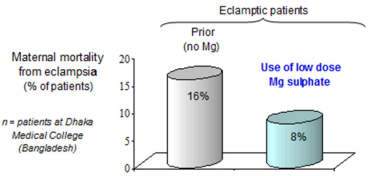


Figure 11: Since the introduction of low dose magnesium sulphate to treat eclamptic patients at Dhaka Medical College, mortality rates have fallen from 16% to 8%. Personal communications from other centres in Bangladesh show similar findings.

Begum R, Begum A, Bullough CH, Johanson RB. Reducing maternal mortality from eclampsia, using magnesium sulphate. Eur J Obstet Gynecol Reprod Biol. 2000 Oct;92(2):223-4 Dhaka Medical College, Dhaka, Bangladesh

Calcium

A high calcium intake prolongs life

The calcium intake can be measured by measuring the calcium excretion in the 24 hour urines. The more food people eat, the more calcium is excreted into the urine, because most foods contain calcium. Accordingly, the urinary calcium is a good parameter of the amount of foods people eat. A low calcium intake, reflected by a lower calcium excretion in the urine, is associated with a higher risk of dying. In areas of the Jinzu River basin in Japan, mortality rates tended to be greater in people who excrete poor quantities of calcium in the urine compared to high calcium excreting inhabitants.[88]

Drinking water rich in calcium may help to live longer

Drinking water rich in calcium may prevent patients from developing deadly (fatal) cardiovascular and cerebrovascular diseases and help heart patients survive cardiovascular disease longer. People living in cities where the drinking water is rich in calcium (above 94 mg per liter) have been reported to have a 10% lower risk of dying from cardiovascular diseases and a 14% reduction in cerebrovascular mortality than individuals living in cities with water low in calcium (figure 5).[77]

Dietary calcium and calcium supplements reduce coronary heart disease mortality

Both calcium-rich foods and calcium supplements independently decrease the mortality rate from ischemic heart disease in postmenopausal women by 27 and 33 %; as shown in a prospective cohort study of 34,486 postmenopausal women aged 55-69 years in Iowa - USA. The relative risk was 37% lower (0.63, 95% CI 0.40-0.98) for a diet rich in calcium but with no intake of calcium supplements and 34% lower (0.66, 95% CI 0.36-1.23) for a regular intake of calcium supplements in the presence of diet poor in calcium.[89]

Higher ionized calcium in the serum prolong life in critically ill patients

A low ionized calcium in the serum increase the risk of dying in critically ill patients. Calcium supplements may be helpful in patients with cardiovascular disease in a way similar to magnesium. A low serum level of ionized calcium is even an early predictor of imminent mortality in critically-ill surgical patients. Surviving patients have a significantly higher serum level of ionized calcium than the level checked before death in patients who are going to die.[90]

Water-Soluble Vitamins

Folic Acid

Higher serum folate levels may help cancer patients live longer

Folic acid may help cancer patients, not healthy persons[91], to live longer. In an oncological unit, a trend (that approached statistical significance) toward longterm survival was seen among **patients with non-small cell lung cancer** who had a higher serum level of folic acid.[92]

High serum folate levels may help survive prostate cancers too. The death risk by prostate cancer is higher in men with decreased serum folate levels. Each 2 micrograms per liter decrease in folic acid, increases the risk of dying from prostate cancer by + 56%. Men whose folic acid levels are in the lowest quartile are 5 times more likely to die from prostate cancer than men with folic acid levels in the upper quartile.[93] Nevertheless what is true for some cancer patients, does not seem to be true for healthy people (without disease). There is no difference in dying was noted in two large scale studies between people with a high folic acid level: and people with low levels.[91]

The intake of foods rich in folic acid and folic acid supplements may modestly help patients with disease to live longer

A slight -3 to -7%.reduction in mortality rate is observed among patients with coronary heart disease (who underwent coronary angiography) when foods fortified in folic acid are taken.[94]
This finding is also confirmed by another study where the intake of foods high in folic acid were was to reduce the risk of dying from coronary heart dsiease by -5% in women and even more strongly in men by -17%.[95]

Both foods rich in folic acid and supplements also improve the survival of women with breast cancer.
Women with breast cancer and total folic acid intake (food + supplements) in the highest tertile have 12% less risk of dying than women in the lowest tertile of folate intake.[96]

Infants with gross neurological abnormalities such as spina bifida or encephalocele are at high risk of dying during the first year of their life. The administration of folic acid supplements during the first year of their life seems to help, but very little. Once study found a very small, statistically nonsignificant, 2 to 4% increase in survival rate.[97]

Studies with no effect of folic acid on lifespan in patients

Folic acid treatments may, but do not always improve lifespan. A high dose of folic acid (15 mg per day) administered during more than three years did not reduce the cardiovascular mortality in patients with chronic renal failure for example.[98] Neither did a combination of folic acid with vitamin B6 and B 12 during more than seven years reduce the risk of dying by cardiovascular disease among US health professionals aged 42 years or older.[99] So neither did the use of a combination of 12.5 mg of iron and 50 mcg of folic acid daily reduce the risk of death in very young children up to age 36 months.[100]

Folic acid treatment may prolong lifespan of mice

Methylenetetrahydrofolate, the active form of folic acid seems to be more efficient than folic acid to improve lifespan. Pregnant mice with a severe deficiency in methylenetetrahydrofolate delivered many dead pups. Interestingly, the survival rate of the pups was found to be greatly enhanced by the supplementation with methylenetetrahydrofolate (64%), but not with folic acid.[101]

Vitamin B6

Vitamin B6 intake may prevent and help to survive stroke

Vitamin B6 intake may reduce the risk of dying from stroke. A study on the dietary intake of vitamin B6 in more than 21,000 US households showed that the higher the intake of vitamin B6 the more people were (significantly) protected against dying from cerebrovascular disease.[95]

Vitamin B12

Vitamin B12 may decrease the risk of dying in general

The same above-mentioned study on the dietary intake of vitamin B6 in more than 21,000 US households showed that taking vitamin B12 significantly protected against death from all causes (-14% in women and -26% in men), but not from cerebrovascular disease.[95]

Higher B12 levels in alcoholics associated with higher mortality

Patients with alcoholic liver disease with high plasma vitamin B12 levels above the 800 picograms per milliliter die easier. The high vitamin B12 level are not a cause, but a consequence and indicator of severe liver damage. As the vitamin B12 cannot accumulate in the very sick liver of these patients - its normal place - it accumulates in the blood.[102]

Vitamin C

High serum vitamin C levels prolong life in elderly persons

Low serum vitamin C levels in elderly persons increase the risk of dying. Prospective studies showed that people with a serum vitamin C level above the 66 µmol per liter, a level in the highest quintile of the population levels, had approximately twice less risk of dying than people with serum vitamin C below the 17 µmol per liter, levels found in the lowest population quintile. This indicates that vitamin C may help living longer (**figure 12**).[103]

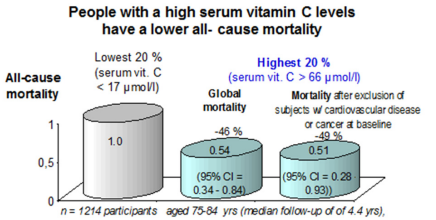


Figure 12: Strong inverse trends for serum vit. C with all-cause and cardiovascular disease mortality, only marginally reduced after adjustment for confounders or supplement use. In fully adjusted models, there was no evidence for an influence of vitamin E, beta-carotene or retinol on total mortality.
Fletcher AE, Breeze E, Shetty PS. Antioxidant vitamins & mortality in older persons: findings from the nutrition add-on study to the Medical Research Council Trial of Assessment & Management of Older Community People. Am J Clin Nutr. 2003; 78(5):999-1010.

Not all studies show a significant beneficial effect of vitamin C levels on the global risk of dying (all-cause mortality)[104], but some did[105] in fact, most, but not all studies, show significant protective effects of high vitamin C levels against the risk of dying from diseases such as cardiovascular disease[104] and cancer[105].

Longevity and mortality threshold levels for vitamin C

Khaw and colleagues found that the plasma ascorbic acid concentration was inversely related to the mortality rate from all-causes, and from cardiovascular disease and in particular from ischaemic heart disease in men and women. The risk of dying in the top ascorbic acid quintile was about half the risk in the lowest quintile ($p<0.0001$).
The relation with mortality was continuous through the whole distribution of ascorbic acid concentrations. A 20 micromoles per liter rise in plasma ascorbic acid concentration, equivalent to about 50 g per day increase in fruit and vegetable intake, was associated with about a -20% reduction in risk of all-cause mortality ($p<0.0001$), independent of age, systolic blood pressure, blood cholesterol, cigarette smoking habit, diabetes, and supplement use. Ascorbic acid was inversely related to cancer mortality in men but not in women.[106]
To avoid dying young, vitamin C levels in adults should **exceed the 73.8 micromoles** per liter (about 1**.33 milligrams per 100 milliliter**), a level well within the reference range of 23 to 85 micromoles per liter (or 0.4 to 1.5 milligrams per 100 milliliter) for serum vitamin C.
Levels of vitamin C below the 28.4 micromoles per liter, a level that may be found in 25% of the US population (lowest quartile), have 57% more risk of dying from all causes and 62% more risk of dying from cancer than individuals above the 73.8 micromoles per liter.).[105]
Levels of vitamin C below the 22.7 µmol/l have also been reported to be related to a higher risk of dying from ischemic heart disease and stroke.[107] This observation confirms the findings of another study that people with serum vitamin C levels below the 23 µmol/l or 0.4 mg/dl face significantly

increased risks of dying from ischemic heart disease, even after adjustment with classical risk factors and vitamin E.[108]
In order to avoid dying from cardiovascular disease, vitamin C levels in hemodialysis patients should be above the 60 µmol per liter (about 1.1 mg per 100ml).
Levels of vitamin C between 32 and 60 µmol/l (0.58 - 1.08 mg/dl) are associated with a threefold l(2.89) greater likelihood of dying from cardiovascular disease, while the risk of cardiovascular death is at levels below the 32 µmol/l nearly 4 times (3.79) greater.[104]

The intake of vitamin C-rich foods may lower the mortality rate by coronary heart disease

People with high dietary intake of vitamin C-rich foods on the other hand have less risk of dying from coronary disease (-30% and all causes of dying (-31%).[109]
A lower risk of dying from breast cancer was found in people in the highest quartiles of intake vitamin C-rich foods (hazard ratio = 0.43; 95% CI: 0.21-0.86). Vitamin C showed a significant dose-response relationship (P for trend, < or = .05).[110]

The consumption of foods rich in vitamin C may not reduce influence longevity

The consumption of foods rich in vitamin C that provide of 250 mg per day or more of vitamin C, which is a higher amount than the FDA recommended daily allowance, did not appear to significantly reduce the risk of dying in a group of 3119 'healthy' adults in California.[111]

Vitamin C supplementation may prolong life in men more than in women

Vitamin C supplementation seems to be more efficient in men than in women. A study of 11,348 noninstitutionalized U.S. adults aged 25 to 74 years followed up during 14 to 18 years showed that the mortality ratio (SMR) for all causes of death strongly declined in men with increasing vitamin C intake was, while it did this only weakly in women. Mortality rate decreased for men with highest vitamin C intake with -35% on the average, while in women 'only' 10%.[112]

Regular intake of vitamin C supplements may lower the mortality in middle-aged and elderly persons and terminal cancer patients

Taking a vitamin C supplement may reduce the risk of dying among **middle-aged men.** In a group of 763 **middleaged men** constituting 16 cohorts in 7 countries followed up during 25 years vitamin C intake was inversely associated with all-cause mortality.[113] The longevity effects of vitmin C were further confirmed in another study, where residents of a public home for elderly with a high vitamin C intake were twice less likely to die than people with a low intake.[24]
Also terminal cancer patients may live longer when they take large doses of vitamin C. In two Japanese studies on terminal cancer patients, survival times were respectively two and six times longer with the use of high doses of vitamin C compared to patients not taking any vitamin C supplement (**figure 13**).[114]

Terminal cancer patients taking large doses of vitamin C had a longer survival and better quality of life

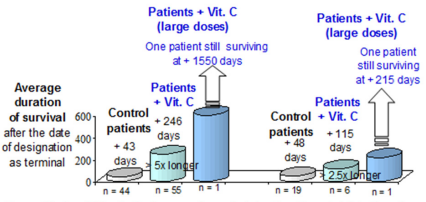


Figure 13: In addition to the increase in survival duration, the administration of large doses of ascorbate seemed to improve the quality of life.

Murata A, Morishige F, Yamaguchi H. Prolongation of survival times of terminal cancer patients by administration of large doses of ascorbate. Int J Vitam Nutr Res Suppl. 1982;23:103-13

High doses of vitamin C prolong the survival of cancer patients

The administration of very high doses of vitamin C to terminal cancer patients may considerably improve their prognosis and delay death. When in a trial **10 grams per day** of vitamin C supplements were administered to 100 terminal cancer patients as ascorbate as an adjuvant to their treatment, the number of patients survived the mean survival time was considerably greater, about 4.2 times longer (approximately 210 days of survival) than for the controls (1000 similar patients who survived only 50 days on the average). Death occurred in 90% of the ascorbate-treated patients at three times a slower rate than for the controls, while the other 10% of patients who took ascorbate became exceptional survivors with much greater survival times, averaging more than 20 times that of the controls. 22% of the ascorbate-treated patients survived more **than one year** after the date of untreatability (with a mean survival of 2.4 years for this group), while this was only possible for 0.4% of the patients not taking vitamin C supplements.[115]

Several studies have confirmed the efficacy of regular use of vitamin C to reduce the risk of dying of specific cancers such as:

- stomach cancer (-32%), but only for vitamin C use of less than ten years duration, not for longer periods)[116]
- bladder cancer (-40%), but only with vitamin C use for more than ten years, not for shorter periods)[117]
- colorectal cancer before the age of 65, rectal cancer at any age (-52%) and with more than ten years of regular use (-60 %)[117]

However, it is important to stress that the irregular intake of vitamin C or E supplements, even when used for long periods of time, has no beneficial effect on colorectal cancer mortality.[117]

Amount of vitamin C necessary to make a difference in longevity

In the fore-mentioned group of middle-aged men from 7 countries, each 20 milligrams per day increase in vitamin C intake decreased by -12.4% the all-cause population mortality rate over a period of 25 years.[113]

A study where vitamin C did not seem to bet helpful to improve lifespan

A Japanese study on hemodialysis patients did not show any beneficial effects of vitamin C on morbidity or mortality. On the contrary, a twofold higher level of oxalate - hyperoxalemia, an adverse effect - was noted in the vitamin C supplemented group compared to the non-supplemented group.[118]

Vitamin C supplementation may prolong life in animals

Mice that receive ascorbic acid (1,4 mg/kg body weight) in their drinking water, live longer. Their average life span increases by +8.6% ($p < 0.05$) to +20.4% compared to the average lifespan of control mice. The ascorbic acid-supplemented mice weighed 6 to7% less than the controls. However, ascorbic acid supplementation had less of an impact on the maximum life span of mice: a modest +2.9% increase.[119]

Vitamin C treatment may reduce the mortality rate caused by vitamin E and selenium deficiencies in ducks. A study showed that adding ascorbic acid to a diet deficient in vitamin E and selenium substantially lowered the associated mortality in growing ducks.[120]

Vitamin C supplementation is not very helpful in emergency conditions in animals

There are limits to vitamin C's beneficial effects on lifespan. In emergency situations such as hemorrhagic[121] and septic shock[122], vitamin C treatment does not make rats live longer. Nor does vitamin C influence the outcome of infectious shock in animals. On the other hand, vitamin E administration does efficiently help rats survive hemorrhagic and septic shock[121-122] as we will see a later in this chapter.

The simultaneous use of vitamin E and C supplements, not the single use of one of the two supplements, prolongs life in general, and in particular prevents and helps survive cardiovascular disease

The simultaneous use of vitamins E and C during 9 years by more than 11,000 elderly persons lowered the mortality for all-causes with 42%, and in particular the coronary heart mortality with 53%. In this study, the use of either of the vitamin supplements alone was not efficient for longevity.[123]

Vitamin A

Supplements: *Vitamin A supplementation may reduce mortality in children*

Vitamin A supplementation is crucial for many children in third world countries who suffer from malnutrition and do not get adequate amounts of vitamin A in the diet. For example among young children, aged 6 months to 5 years from Tanzania, the regular administration of a vitamin A supplement was reported to substantially reduce their risk of dying by approximately 50%. A vitamin A treatment is a particularly efficient way of reducing childhood mortality from diarrhea: -95%!

The impact of retinol treatment is even more important in children with AIDS. The mortality for all causes and from AIDS drops down to approximately one third of the mortality of children not receiving a vitamin A supplement. It is worth mentioning that the study only examined children who had no clinical signs of vitamin A deficiency and that were not severely malnourished (**figure 14**).[124]

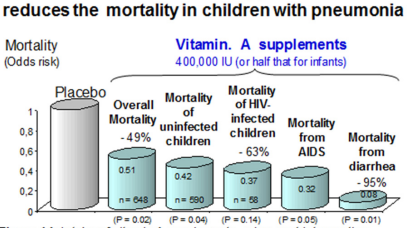


Figure 14: Intake of vitamin A supplements, a low cost intervention, reduces
(687 children (age: 6 months- 5 yrs) w/ pneumonia, children who were severely malnourished or had clinical signs of vitamin A deficiency were excluded; mean follow-up = 24.4 months)
Fawzi WW, Mbise RL, Hertzmark E, et al. A randomized trial of vitamin A supplements in relation to mortality among human immunodeficiency virus-infected & uninfected children in Tanzania. Pediatr Infect Dis J. 1999 Feb;18(2):127-33

Potential harm of vitamin A supplements associated to beta-carotene supplements for lung cancer mortality

A potential harm of vitamin A supplements combined with beta-carotene supplements with statistical increases in lung cancer incidence (+42%) and mortality (+75%) in people with risk factors for lung cancer (smoking and/or occupational exposure to asbestos) who took both supplements compared to placebo takers has been reported by Caraballoso and colleagues in a metaanalysis study. There was no effect on total cancer incidence, mortality or all-cause mortality. Neither was there any significant effect of any of the two supplements taken alone. Possibly, vitamin A supplements combined to beta-carotene supplements may become pro-oxidant rather than anti-oxidant in smokers and asbestos workers. The pro-oxidant action in these people with higher levels of free radicals may explain the increase in cancer mortality.[125]

Carotenoids

Beta-Carotene

Elderly persons and cancer, cardiac or stroke patients with high serum carotenoid levels live longer

Elderly people aged 65 or over with low serum levels of carotenoid of the 'oxygenated' type such as **betacrypto-xanthin, lutein, zeaxanthin**, or with a low levels of the sum of these oxygenated carotenoid levels (levels in the lower tertile) are at an increased risk of dying from all causes (overall mortality) as observed in a large scale prospective study with a follow-up period of seven years compared to people with high levels of these carotenoids - levels in the highest tertile. The strongest increase in all-cause mortality risk was seen for betacryptoxanthin (+ 52 %, 95% CI: 1.00, 2.32), lutein (+56%, 95% CI : 1.05, 2.31) and zeaxanthin (+32%, 95% CI: 0.89, 1.97) and their sum (oxygenated carotenoids: +73%, 95% CI: 1.12, 2.67). Tests for trend were significant ($P < 0.05$) for all-cause mortality risk and serum levels of total carotenoids, oxygenated carotenoids and beta-cryptoxanthin (**figure 15**).[125]

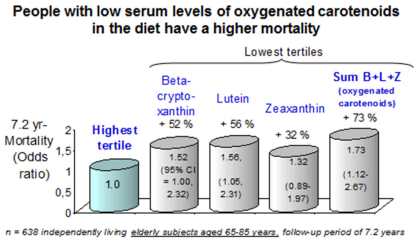


Figure 15: The serum levels of individual carotenoids, particularly the oxygenated species are inversely associated with the all-cause mortality.

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

Findings of another study further confirm how important carotenoids are to stay alive. People with low plasma carotene levels (below the 0.23 micromoles per liter or 13 micrograms per deciliter) face a significantly increased risk of dying by **ischemic heart disease** and **stroke** within the next 12 years, even after adjustment with classical risk factors and vitamin E.[107]

The importance of carotenoids is apparently more important for sick people. **Lung cancer** patients with high levels of various carotenoids such as alpha- and beta carotene, lycopene, beta-cryptoxanthin, and canthaxanthin have a two to five-fold lower risk of dying than subjects with low levels[125], even after adjustment for smoking (upper quartile was compared to the lower quartile). Major cancer risk reductions for men were seen for high serum alpha-carotene levels with -59% fewer cases of lung cancer to -72% less lung cancer for men with high serum beta-carotene concentrations.[127]

High serum levels of carotenoids such as alphacarotene, beta- carotene and lycopene were found to marginally significantly and significantly reduce the risk for mortality for cancer of all sites and in particular for colorectal cancers, respectively.[128]
High serum values of carotenoids including xanthophylls were associated with low odds for dying by cancer of all sites or from cardiovascular disease. High serum values of beta-carotene, total carotene, provitamin A and total carotenoid for colorectal cancer or stroke also appeared to be related to low risks of dying.[129]
In a randomized, double-blind, placebo-controlled primary prevention trial a higher serum alpha-tocopherol at baseline was associated with improved prostate cancer survival (HR, 0.67; 95% CI, 0.45-1.00), especially among cases who had received the alphatocopherol intervention of the trial and who were in the highest quintile of alpha-tocopherol at baseline (HR, 0.51; 95% CI, 0.20-0.90) or at the 3-year follow-up measurement (HR, 0.26; 95% CI, 0.09-0.71). Serum beta-carotene, serum retinol, and supplemental betacarotene had no apparent effects on survival.[130]

The consumption of foods rich in carotenoids reduces the risk of dying from cancer, especially from colorectal cancer and breast cancer

A high intake of green-yellow vegetables, which contribute to increasing the serum levels of alphacarotene, beta-carotene, as well as lycopene, may reduce the global risk of dying from **cancer mortality**, and specifically of dying from **colorectal cancer**, in Japanese rural areas.[128]

In two investigations, a prospective study and a retrospective study, a high intake of foods rich in carotenoids was observed to reduce the risk of dying from **breast cancer**. In the prospective study, a high intake of b -carotene from foods (in the highest quartiles of intake) before the diagnosis of breast cancer reduced the risk of dying from breast cancer by half (RR = 0.48).
Beta carotene showed a significant dose-response relationship (P for trend, < or = .05).[110] In the retrospective study, breast cancer patients with a positive estrogen receptor status and a high intake of foods rich in b -carotene survived longer.[131]

The consumption of foods rich in beta-carotene reduces the risk of dying from cardiovascular, while only the consumption of foods rich in beta-carotene appears to reduce the global risk of dying

The intake of beta-carotene-rich foods may lower the mortality in general, and specifically from coronary heart disease. People with high dietary intake of betacarotene-rich foods have less risk of dying from all causes of dying in general and in particular from coronary disease (-30% and (-31%).[109] of the other carotenoids, only alpha-carotene next to beta-carotene was found by Buijsse and colleagues of the Wageningen University in the Netherlands to reduce the risk of dying from cardiovascular disease.[39]

The intake of alpha- and beta-carotene may help to survive cardiovascular disease and pregnancy

The intake of alpha- and beta-carotene reduces the risk of dying from cardiovascular disease in humans. The intake of alpha- and beta-carotene-rich foods may lower the mortality rate by cardiovascular disease in general.
Elderly men who take alpha- and beta-carotene supplements, for example, reduce by -19% and -20% respectively their likelihood of dying from cardiovascular disease. This beneficial effect was not observed in the same study with the intake of other carotenoids, nor with vitamin C or alpha- and gamma-tocopherol (vitamins E).[39] In a cross-cultural epidemiological stydy, beta-, carotene supplementation reduced pregnancy-related mortality both among smokers and nonsmokers (**figure 16**: *Christian P, West KP Jr, Katz J, Kimbrough-Pradhan E, LeClerq SC, Khatry SK, Shrestha SR. Cigarette smoking during pregnancy in rural Nepal. Risk factors and effects of beta-carotene and vitamin A supplementation. Eur J Clin Nutr. 2004 Feb;58(2):204-11).*

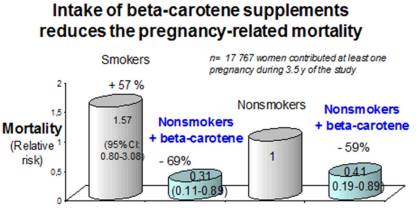


Figure 16: Mother mortality per 100,000 pregnancies appeared to be higher among smokers than nonsmokers in the placebo group (915 vs 584)- Nepal. Beta-Carotene supplementation reduced pregnancy-related mortality both among smokers & nonsmokers. Similar results obtained with vitamin A were not statistically significant.

Christian P, West KP Jr, Katz J, Kimbrough-Pradhan E, LeClerq SC, Khatry SK, Shrestha SR. Cigarette smoking during pregnancy in rural Nepal. Risk factors and effects of beta-carotene and vitamin A supplementation. Eur J Clin Nutr. 2004

Potential harm of beta-carotene supplements

A potential harm of beta-carotene supplements combined to vitamin A supplements has been reported by Caraballoso and colleagues in a meta-analysis of nutrient supplementation trials with 109,394 subjects out of 4 studies with follow-up of two to five years The findings took everybody by surprise. The researchers announced that nutrient supplementation increased with+ 70% the risk of dying from lung cancer in individuals who took supplement of vitamin A and betacarotene.
This association was significant for people with risk factors for lung cancer (smoking and/or occupational exposure to asbestos) who took both supplements compared to placebo takers. There was no effect on total cancer incidence, mortality or all-cause mortality. Neither was there any significant effect of any of the two supplements taken alone. Nor did betacarotene supplements combined with vitamin E supplements cause any harm.[125] Furthermore, Virtamo and colleagues showed that the subgroup of male smokers, not drinking alcohol - only about 10% of the population, who took beta-carotene supplements had a significant lower rate of prostate cancer. In the absence of alcohol consumption, beta-carotene supplements were protective.[134]

Possibly, beta-carotene supplements combined with vitamin A supplements may become pro-oxidant rather than anti-oxidant in alcohol-drinking smokers and asbestos workers. The pro-oxidant action in these people with higher levels of free radicals may explain the increase in cancer mortality.

Another potential harm of 20 milligrams per day of betacarotene supplements was reported by *Heinonen and colleagues* for male smokers. A + 15% increases in prostate cancer mortality and +23% increase in prostate cancer incidence was found among the 14560 smokers who took beta-carotene supplements compared to 14573 placebo takers.[133] This association disappeared after stopping the intake of beta-carotene supplements.[134] Le Marchand and colleagues, restudied the data and found that the intake of papaya, rich in beta-carotene, rather than beta-carotene itself produces a higher rate of prostate mortality. With the exception of papaya, which was positively associated with risk among men aged 70 years and older, the consumption of other yellow-orange fruits and vegetables, tomatoes, dark green vegetables, and cruciferous vegetables rich in beta-carotene is not associated with prostate cancer risk. Perhaps some adverse compounds in the papaya other than betacarotene may cause the problem.[135]

Vitamin D

People with risk factors for vitamin D deficiency are less likely to live long and more likely to die from cancer

In the USA Afro-Americans have a high risk of vitamin D deficiency because their dark skin needs intensive sun exposure to produce vitamin D. Most Afro-Americans do not receive the sun exposure they need to obtain optimal levels. This fact may explain why Afro-Americans have a +57% higher risk of dying from cancer.[136]
Thus, a major risk factor for poor vitamin D status is the lack of sun exposure. As most of the exposure of the human skin to sun occurs in the summer, the levels of vitamin D are, in general, the highest in summer and autumn. In Norway a study on 14,000 individuals showed that the survival from cancers such as colon, breast, prostate cancers and Hodgkin's lymphoma, is best when the cancers are detected in the summer and in autumn[137], seasons that correspond to the highest calcidiol levels in the human blood.

As sun exposure decreases in higher latitudes of the earth, vitamin D levels are generally lower in people living in countries situated in higher latitude countries such as Sweden and Norway compared to Italy and Spain. The lower vitamin D status in people living in Northern countries may explain why people die easier from cancer mortality in these countries. The fiveyear survival rates after appearance of cancers of the stomach, pancreas, colon, breast, ovary, prostate, and kidney, and non-Hodgkin's lymphoma, are 20 to 50% higher in people living near or above 55 degrees in the northern hemisphere in comparison to people living in lower latitudes, below the 50 degrees of the Northern hemisphere.[138]

In the United States as well, people who benefit from a greater exposure to ultraviolet B radiation from the sun, the trigger responsible for vitamin D production in the skin, have a lower risk of dying from cancers of the breast, esophagus, stomach, colon, and rectum. The associations are stronger for white Americans than for black Americans.[139]

Furthermore, the risk for women of dying from ovarian cancer is inversely proportional to the mean annual intensity of local sunlight.[140]

All these studies confirm the crucial importance of sun exposure and vitamin D production to live long and survive cancer longer.

Higher serum levels of vitamin D may prolong the survival rate of cancer patients

Noteworthy is that men and women followed up for 18 months after diagnosis of colon cancer survived longer if they were diagnosed in the summer or in autumn, periods of higher vitamin D concentrations. A high serum concentration of calcidiol at the time of diagnosis provides greater chances of survival. Here too a relationship between the season of diagnosis and the vitamin D status and cancer was demonstrated.[141-142]

A great body of evidence is now emerging and now shows that the mortality rate from more than 17 different types of cancer is likely to be influenced by the vitamin D status. A poor vitamin D status may increase the risk of dying from those cancers.[143]

Optimal level of vitamin D for survival and a longer life

In a 15 year long prospective study with 1095 men, each increment of 25 nmol per liter of vitamin D 3 in blood reduced the total cancer incidence by -17% and the total cancer mortality by -29%, especially reducing with -45% the mortality from digestive system cancer.[144]
Interestingly, patients who had surgery in the summer for non-small cell lung cancer had a better chance of surviving than those with surgery in the winter with, in particular, a longer survival period free of any cancer recurrence. This finding was especially evident in the patients whit a high nutritional intake of vitamin D.[145]

Patients with kidney failure who undergo hemodialysis are prone to develop vitamin D deficiency. They also die easier if they have low vitamin D levels.

Early death is more common in hemodialysis patients with vitamin D deficiency and who are not treated with vitamin D.[142]

Optimal levels of vitamin D3 to avoid dying from cancer

The critical level of vitamin D3 that helps to avoid dying from colorectal cancer is a level of 80 nanomoles per liter. Levels of 80 nanomoles per liter or higher are associated with a -72% reduction in death risk compared to people with vitamin D levels below the 50 nanomoles per liter. If not all studies concluded that high vitamin D levels are related to a lower cancer mortality in general, almost all studies conclude that higher serum vitamin D3 levels lower the specifically colon and rectal cancer mortality.[146]
Patients infected by the HIV virus die also easier with an abnormally low 1,25-vitamin D level in the serum, a level below 25 picograms per milliliter.[147]

Efficacy of vitamin D supplements to prolong life in patients with chronic disease

In a meta-analysis of 18 independent randomized controlled trials including 57,311 participants, a daily intake of 528 international units (= 13.5 micrograms) vitamin D during a mean of 5.7 years significantly lowered the global risk of dying with -7% compared to the untreated group. Taking the vitamin D supplement produced a +40 to +400% increase in serum 25-hydroxy-vitamin D level.[148]

Several other studies that investigate the influence of vitamin D on mortality and lifespan concern patients with kidney failure treated with hemodialysis. In a large group of 38,066 patients under hemodialysis from 12 countries, vitamin D therapy lowered the mortality rate with a significant -8%. But the significant character of the finding disappeared after adjustment for several factors.[149]

In another study on 51,037 chronic hemodialysis patients, the two-year mortality rate was nearly 50% lower in the patients who received injectable vitamin D than in the untreated patients. The patients who received injectable vitamin D were less likely to die from cardiovascular disease than the patients who did not take any vitamin D.[150]

Other studies among hemodialysis patients have confirmed the beneficial effect of vitamin D supplements in prolonging survival as well by reducing the overall mortality as lowering the risk of death by cardiovascular diseases, cancer or infections.[142,151]

Optimal vitamin D doses that prolong life

What dose of vitamin D may help in prolonging life in patients on chronic hemodialysis? Efficient doses of one of its activated forms, calcitriol, are between the 0.25 to 0.5 micrograms per day for a treatment of about two years.[152] At this dose vitamin D is safe.

Synthetic forms of vitamin D (vitamin D analogues) such as paricalciferol[153] and doxecalciferol[153-154] may be more efficient than the natural calcitriol, offering to hemodialysis patients a -20 to -21% lower risk of dying.[154]

A recent meta-analysis concluded that the intake of 1,000 international units of oral vitamin D per day reduces by -50% the incidence of colorectal cancer. It reduced the colorectal cancer mortality rate too, but to a lesser degree with -7% in men and -9% in women in the United States and -14 to -20% for men and women in Western European countries below 59 degrees of latitude.[143]

Vitamin E

High serum levels of vitamin E reduce the risk of dying from heart disease

A low serum level of vitamin E increases the risk of dying from heart disease. Patients with a low serum vitamin E level have a 62% higher risk of dying from ischemic heart disease. The death risk further increases (+ 79%) in patients with a high cholesterol level. People with both low vitamin D and E levels, beneath the lower reference limits, and a high cholesterol level, have an even higher risk of ischemic heart disease, almost double that of normal (+83%), which is on its turn further aggravated in the presence of arterial hypertension (+ 87%) (**figure 17**).[155]

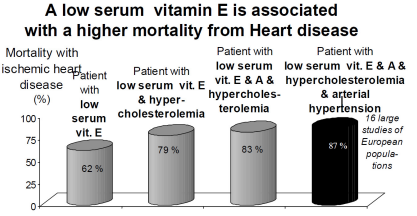


Figure 17: Serum vit. E has a strong inverse association with mortality from ischemic heart & the only sign. risk factor found in 12 populations + normal cholesterol. Only serum cholesterol & blood pressure were moderately associated when all populations were evaluated, but their correlation was inferior to that of serum vit. E.

Grey KF, Puska P, et al. Inverse correlation between plasma vitamin E and mortality from ischemic heart disease in cross-cultural epidemiology. Am J Clin Nutr. 1991; 53 (1): Suppl: 326S-334S

In a large epidemiological study of apparently healthy individuals from 12 European study populations, the lipid standardized levels of vitamin E showed a strong inverse correlation to the age-specific coronary mortality, thus showing that people with low vitamin E levels die easier from coronary heart disease.[156]

Vitamin E: potent survival nutrient

That vitamin E supplements may help prolong life becomes gradually a certainty for elderly or ill persons.
The simultaneous use of vitamin E alone during 9 years by more than 11,000 elderly persons, for example, lowered the mortality by all causes with -34%, and in particular the coronary heart mortality rate with -47%.[123]

In the fore-mentioned Finnish study on 29133 male smokers aged 50-69 years from southwestern Finland those who randomly assigned to receive 50 mg per day alpha-tocopherol had a -41% lower prostate cancer fatality (95% confidence interval [CI] = -65% to -1%) and a -32% decrease (95% CI = -47% to -12%) in the incidence of prostate cancer, in particular clinical, and not latent, prostate cancer.[133]
However, for stomach mortality, vitamin E does not seem to have a life-prolonging effect. In a cohort study, no association was found between the regular use of vitamin E and stomach mortality.[116]

Vitamin E supplements may prolong the life of patients with moderate Alzheimer's disease

Patients with Alzheimer's disease of moderate severity may benefit from high doses of vitamin E supplements.
In a study on 341 patients with Alzheimer's disease, 2,000 international units of vitamin E supplements per day during two years significantly delayed the time to death or severe dementia in these patients with +52 % longer survival (**figure 18**).[157]

High-dosed vitamin E suppplementation delayed the death of patients with Alzheimer's dementia

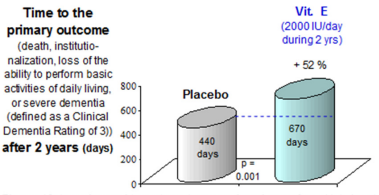


Figure 18: In patients with moderately severe impairment from Alzheimer's disease, alpha-tocopherol treatment significantly slowed the disease progression
n = 341 patients + Alzheimer's disease of moderate severity
Sano M, ... Thal LJ. A controlled trial of selegiline, alpha-tocopherol, or both as treatment for Alzheimer's disease. The Alzheimer's Disease Cooperative Study. N Engl J Med. 1997 Apr 24;336(17):1216-22.Columbia University

Vitamin E treatment helps rats survive medical emergencies

Vitamin E treatment helps rats survive medical emergencies such hemorrhagic and endotoxin shock. In an experimental **hemorrhagic shock**, a vitamin E analogue treatment in an infusion nearly doubled the number of rats that survive: After 72 hours, 75 % of the rats survived the hemorrhagic shock compared to 40% in the control group. [121]

Vitamin E administration efficiently helps rats survive **septic shock** too.[122] This characteristic of permitting survival in shock conditions of vitamin E seems to be typical to vitamin E and is not found with vitamin C for example.[121-122]

Caution is recommended with the association of vitamin E and vitamin C in postmenopausal women with coronary heart disease

A potential harm has been suggested from the use of vitamin E in cardiac patients. In a randomized doubleblind trial of 800 IU of vitamin E and 1000 mg of vitamin C per day during nearly three years, the combined use of vitamin E and vitamin C supplements significantly increased almost threefold the mortality rate in postmenopausal women who suffered from 15 to 75% stenosis of the coronary arteries at the baseline coronary angiography compared to placebo.[158]
Explanations have been sought for these discrepancies with other existing data. Some experts say that the cause is that the human body needs other vitamin E forms such as gamma-tocopherol and not exclusively alpha-tocopherol, which is generally the only one supplied in vitamin E supplements. Using a wellbalanced 'mixed tocopherol' preparation, which contains all the different forms of vitamin E, would prevent in the blood any vitamin E imbalance that results from supplementation with alpha-tocopherol alone.

Coenzyme Q 10

High serum levels of coenzyme Q 10 may prolong life in patients with disease

In patients over age 50 with disease, the presence of a low coenzyme Q10 level in the serum, below the 0.55 mcg per milliliter, has been found to be associated with a 13-fold higher mortality rate compared to patients with a high Co Q10 level, above the 0.55 mcg per milliliter. A low coenzyme Q10 level was found in patients with chemotherapy, on cholesterol lowering agents or suffering from heart failure or severe myalgias (**figure 19**).[159]

Elderly sick patients with reduced serum coenzyme Q 10 have a higher mortality

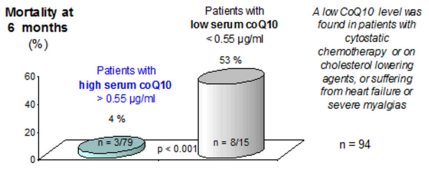


Figure 19: Severe increase in mortality at 6 months in patients with serum coenzyme Q10 under one standard deviation of the mean of a population of patients over age 50 (mean age = 72 years).
Jamieson. Statistical data support prediction for death within six months on low levels of coenzymeQ10 and other entities. Clin Investig. 1993; 71: S137-9

Coenzyme Q10 supplementation may reduce the risk of dying in cardiac patients

Patients who have had a myocardial infarction should take coenzyme Q10 supplements to live longer.
Researchers have observed that the daily intake of coenzyme Q10 by patients with myocardial infarction reduced the mortality from myocardial infarction by -45% (**figure 20**).[160]

One year of Co Q10 supplementation reduces the cardiac mortality after acute myocardial infarct

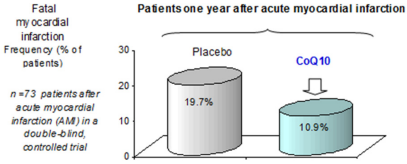


Figure 20: Co Q10 intake reduced approximately by half the risk of dying from myocardial infarction.
Singh RB, Neki NS, Kartikey K, Pella D, Kumar A, Niaz MA, Thakur AS. Effect of coenzyme Q10 on risk of atherosclerosis in patients with recent myocardial infarction. Mol Cell Biochem. 2003;246(1-2):75-82

Polyunsaturated Fatty Acids

A high intake of polyunsaturated fatty acids reduces the risk of dying by cardiovascular disease

The cardiovascular protective action of polyunsaturated fatty acids has been known for many years. A deficiency in polyunsaturated fatty acids may facilitate the development of cardiovascular diseases and increase the risk of dying by cardiovascular disease.

When the amount of polyunsaturated fatty acids in the diet is low compared to the amount of saturated fatty acids, for example, the risk of dying by coronary artery disease increases.[161]

Omega Six Polyunsaturated Fatty Acids Such As Linoleic Acid

A high intake of linoleic acid prolong life in elderly persons

Residents in a public home for elderly whose intake of linoleic acid was above average had better chance of living longer. Their risk of dying dropped down by 60% compared to people with a lower than average intake
(**figure 21**).

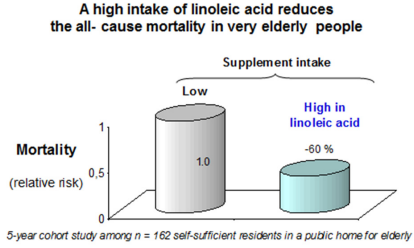


Figure 21: A high intake of linoleic acid is associated with longevity.

Fortes C, Forastiere F, Farchi S, Rapiti E, Pastori G, Perucci CA. Diet and overall survival in a cohort of very elderly people. Epidemiology. 2000 Jul;11(4):440-5.
Department of Epidemiology, Lazio Regional Health Authority, Rome, Italy

Omega-3 Polyunsaturated Fatty Acids

Vegetable oils such as flaxseed, rapeseed, hemp and walnut oils are rich in omega-3 polyunsaturated fatty acids. Fish too, such as mackerel, herring, tuna and anchovy, has roughly double the amount of eicosapentaenoic (EPA) and docosahexaenoic (DHA) acids - the major omega-3 polyunsaturated fatty acids in fish - compared to salmon and sardines.[163] People who consume plenty of fish and vegetable oils rich in omega-3 fatty acids are less prone to develop cardiovascular disease.

The intake of omega-3 polyunsaturated fatty acids may lower the risk of dying by coronary heart disease or the all-cause mortallity

Men who are heavy smokers will particularly benefit from eating fish, which is rich in omega-3 polyunsaturated fatty acids. The risk of dying by coronary heart disease during a 23 year follow-up study in men who were heavy smokers and consumed above average amounts of fish was half of that of heavy smoking men with low fish intake.[164] Scientific research showed that people with high levels of omega-3 polyunsaturated fatty acids in their blood have a considerable lower myocardial infarction rate and lower myocardial infarction mortality rate.[165]
The ingestion of these long chain omega-3 polyunsaturated fatty acids also lowers the risk of dying by all types of heart disease (overall cardiac mortality), in particular it decreases the risk of primary cardiac arrest and dying by sudden cardiac death.[166]

In a study on 7951 coronary heart disease patients, the subjects who took supplements of omega-3 polyunsaturated fatty acids had -20 to -30% reductions in overall mortality rate, sudden-death rate and mortality by myocardial infarction, respectively (**figure 22**).[167]

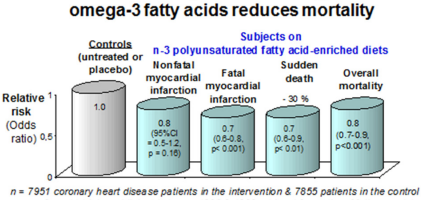


Figure 22: Dietary and non-dietary intake of omega-3 polyunsaturated fatty acids reduces the overall mortality, the mortality due to myocardial infarction, and sudden death rate in patients with coronary heart disease in randomized controlled trials.

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

Trans Fatty Acids

High dietary intake of trans fatty acids increases the coronary artery mortality in men

People should avoid consuming trans fatty acids. These rigid fatty acids are produced by cooking foods at high temperature. Margarine, white bread, cookies, rice waffles are rich in trans fatty acids and their consumption is not recommended. These dangerous fatty acids penetrate after ingestion and absorption in the intestinal tract into cell membranes, the outer membrane that protects the cell and the membranes of organelles inside of the cells. Their rigidity weakens the membranes and favors damage and cell death. The cell damage may explain the development in high trans fatty acid consumers of cancer and cardiovascular disease.
Men with a high intake of foods rich in trans fatty acids, for instance, have approximately 40% higher risk of dying by coronary heart disease (when the highest quintile of trans fatty acid consumers is compared with the lowest consumers).[168]

Trace Elements

Copper

Too low or too high copper levels may shorten lifespan.

Life-threatening danger of copper deficiency in rats, when sugar is supplemented to the diet

Severe copper deficiency is not very life-threatening in rats in the presence of a normal diet. When next to the copper deficiency fructose- or sucrose- containing carbohydrates are supplemented approximately seven times more rats die, mainly by heart rupture in the region of the apex. Copper supplementation neutralizes the adverse effects on lifespan of fructose dose and sucrose.[169-170]

Higher copper levels

People who have a higher copper level in their blood may easier die, in particular when their zinc level is low.

High copper levels may facilitate the loss of zinc in the urine and thus cause a zinc deficiency. Excessive levels of copper may increase the formation of free radicals and thus increase the level of oxidative stress, leading to cell damage and cell death. These mechanisms may explain the adverse effects on longevity of high copper levels.

In a group of 64 chronic heart failure patients, baseline serum copper concentrations were checked and found to be significantly higher, also correlating with higher one-year mortality and morbidity.[171]

In another study, individuals with an above average copper level (forth quartile) were found to have a 50% higher risk of dying by all types of deaths, including

- a 30 % increase in the risk of dying by cardiovascular disease: for every increase of one hundred micrograms per deciliter of copper in the serum, the risk of dying by cardiovascular disease doubles.
- a 40% increase in cancer mortalitycompared to individuals with copper levels in the lowest quartile.

Additionally, the risk of dying increases in subjects with both low zinc and high copper levels in their blood:

- 2.6 higher all-cause mortality
- 2.7 times higher cancer mortality.[172]

Iron

High iron levels may increase the risk of dying in humans

For every 100 micrograms per liter of iron increase the risk of dying increases with 10%. However, only people with iron levels in the upper quartile have a significant increase in the risk of dying, namely +86%.[173]

Molybdenum

Higher molybdenum levels may protect against the risk of dying from cancer

Women with high molybdenum levels in blood have been shown to easier die from esophagus, pancreas or rectum cancer. For these cancers, molybdenum had stronger adverse effects than selenium.[174]

Selenium

High blood levels of selenium keeps the risk of dying from coronary heart disease or cancer low

In men who belong to a population group among which the risk of dying from coronary heart disease is low, selenium levels were found to be slightly higher (8%) than in populations with normal or high mortality.[175] This finding suggests a protective role of selenium against dying from coronary heart disease.

In cancers and precancerous states such as aggressive B-cell non-Hodgkin's lymphoma, higher selenium levels predict higher chances of overall survival: the risk of dying is -24 %: less for each 0.2 µmol per liter increase in serum selenium concentration.[176]

Higher toenail selenium levels are also linked with a lower risk of dying from liver cancer (hepatocellular carcinoma).

The survival rate is double for people whose selenium levels are in the highest quartile of serum selenium levels compared to people from the lower quartile The protective effect of selenium against dying from liver cancer is stronger among women and individuals who do not consume alcohol.[177]

In various investigations, higher serum selenium levels have been reported to significantly protect individuals against dying from colon, rectum, prostate, breast, ovary and lung cancers, and from leukaemia. Weaker protective effects of whole blood selenium concentrations were found for dying from cancers of the pancreas, skin and bladder.[178-179]

Inefficacy of selenium supplementation on cardiovascular mortality, but efficient reducer of cancer mortality

A randomized placebo-controlled trial on 1004 persons taking 200 µg per day of selenium or placebo did not show any significant beneficial effect of selenium on the risk of dying from heart disease.[180]

On the other hand, treatment with 200 micrograms of (yeast enriched) selenium per day or placebo in 13,112 patients with a history of basal squamous cell carcinomas of the skin, showed significant reductions in total cancer mortality and in the incidence of long, colorectal, prostate and total cancers in the selenium treated group.[181]

Zinc

People with a lower zinc level die easier from all causes, and specifically from cardiovascular disease and cancer

Among 3316patients referred for coronary angiography, followed up for nearly 8 years, the subjects with initially lower zinc levels had a 44% higher risk of dying than subjects with higher zinc levels (upper versus lower quartiles of zinc levels). In particular the risk of dying from cardiovascular diseases was considerably higher in patients with low zinc levels: three to four-fold higher!
Furthermore, these patients had more than double the risk of dying from illnesses other than cardiovascular disease. On the average, each quartile of decrease in serum zinc level increased the overall risk of dying with +15%, more than doubled the cardiovascular death rate (+120%) and increased by one third (+32%) the noncardiovascular mortality. Furthermore, higher serum zinc concentrations were associated with lower levels of inflammation markers, higher levels of other antioxidants and with a younger age,[182]

People with higher serum zinc levels but still within the reference range have a lower risk of dying from cancer

In a large study of 3000 men and 3244 women free from cancer at baseline, individuals with zinc levels in the lower half of the reference range (between the 10th and 50th percentile) had a significantly higher risk of dying.
However these individuals between the 50th and 19th percentile of zinc levels had a -36% lower risk of dying than individuals with a zinc level below the 10th percentile. These findings clearly suggest that zinc can make people live longer.[173]

Eating foods rich in zinc may protect alcohol drinkers against dying from cardiovascular disease

Meat, seafood, dairy products, nuts, legumes and whole grains contain relatively high concentrations of zinc[69].
Eating foods rich in zinc may protect against dying from heart disease, at least among consumers of alcohol. A study in postmenopausal women who regularly drank alcohol; for example, progressively higher zinc intakes were reported to be associated with increasingly lower cardiovascular disease mortality. Compared to the lowest quintile, reductions in mortality rank from -39% for the second lowest quintile to -63% for the highest quintile of zinc intake. Women who consumed 30 g or more of alcohol per day had further increases of the risk of dying (**figure 23**).[183]

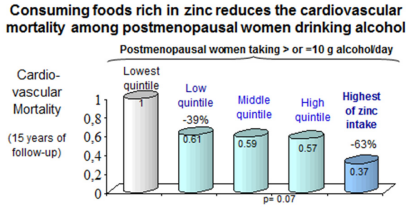


Figure 23: A high dietary intake of zinc might reduce the cardiovascular mortality in postmenopausal women drinking > or =10 g alcohol/day. In an analysis restricted to those who consumed >/=30 g alcohol/d, the risk gradients strengthened n = 34'492 postmenopausal women aged 55-69 years

Lee DH, Folsom AR, Jacobs DR Jr. Iron, zinc, and alcohol consumption and mortality from cardiovascular diseases: the Iowa Women's Health Study. Am J Clin Nutr. 2005 Apr;81(4):787-91 University of Minnesota, Minneapolis

Zinc therapy prolongs life in humans.

Zinc therapy decreases the global risk of dying in humans. In one large prospective study, participants who during more than six years took zinc supplements had -27% less risk of dying (**figure 24**).[184]

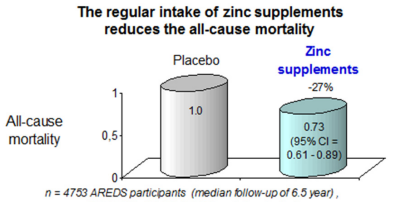
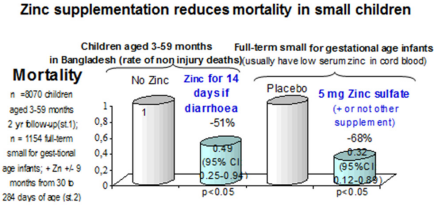


Figure 24: A significantly reduced mortality was found in participants who were randomly assigned to receive zinc supplements in the Age-Related Eye Disease Study (AREDS).

Clemons TE, Kurinij N, Sperduto RD. Associations of mortality with ocular disorders and an intervention of high-dose antioxidants and zinc in the Age-Related Eye Disease Study: AREDS Report No. 13. Arch Ophthalmol. 2004 May; 122(5): 716-26

In Bangladesh, a third world country, zinc supplementation at low dose of 5 mg per day is recommended in small children as it decreases in them the fatality from diarrhea by -51% (**figure 25**).[185]



Some small (about 7-8% more), often non-significant increases in survival have been reported with 10 mg per day of zinc supplementation in children (5 mg per day in children younger than 12 months).[186-187]

Zinc supplementation may prolong life in animals

Zinc therapy may save the life of mice and rats that have been irradiated by gamma-rays or are infected with salmonella typhimurium. Zinc helps in the salmonella typhimurium infections only when administered before the onset of infection.[188-189]

In pregnancy, zinc and protein deficiencies lead to a +57 and +67% higher fetal fatality, respectively, and a +72 to +74% higher incidence of foetal malformations. Zinc supplementation on the other hand drastically reduces the foetal mortality and malformations.[190]

Zinc therapy may prolong survival in mice with cancer

In zinc-deficient mice with cancer, zinc therapy has been shown to increase survival, but not when initiated at tumor inoculation. Zinc therapy only works when supplemented at the time the implanted tumor starts growing.[191]

The danger of administering high doses of zinc in children with protein calorie malnutrition

If zinc is life-saving in many conditions, high doses however may not help. In one trial, high-dose supplements at 6 mg of zinc per kilo body weight made 4.5 times more children between the ages of six months and three year die during a protein calorie malnutrition compared to lower doses of 1.5 mg per kilo.[192]

Aggravation of the adverse effects of low zinc levels on mortality by higher copper levels

In another study, lower zinc levels tended to be associated with a higher mortality rate. Each 100 µg per deciliter increase in zinc level zinc level reduces mortality by -43%. In the presence of high copper levels, zinc mortality substantially increase. The global risk of dying (overall mortality) is more than twofold higher (2.6 times) in people with both a low zinc level and a high copper level. Also the risk of dying from cancer is 2.7 times higher in these patients with low zinc/high copper levels.[172]

In patients with AIDS too, it is safer to have a high zinc and relatively low copper level. In one study for example, a copper plasma level greater than the plasma zinc level, resulting in a copper to zinc ratio above one is associated with a five to eight times higher risk of dying![193]

No effects of zinc supplementation on mortality

No studies have shown any significant beneficial effects on overall mortality in young children (1), nor on cancer mortality in adults (2).[173,194]

Carnitine

Carnitine supplementation helps patients with heart disease to live longer

Carnitine supplements may help to live longer. In patients with recent myocardial infarction and who take the usual pharmacological treatment, four grams a day of L-carnitine reduced by tenfold the death rate, dropping it from 12.5% to 1.2% during the year after having a myocardial infarction (**figure 26**).

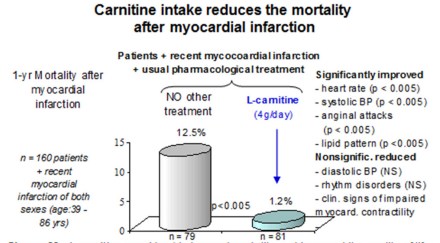


Figure 26 : L-carnitine considerably lowered mortality and improved the quality of life in patients with recent myocardial infarction. In controls deaths caused by reinfarction and sudden death were clearly prevalent, contrary to the carnitine group.
Davini P, Bigalli A, Lamarma F, Boem A. Controlled study on L-carnitine therapeutic efficacy in post-infarction. Drugs Exp Clin Res. 1992;18(8):555-65 Santa Chiara Hospital, Pisa, Italy

Carnitine essential role for energy productions as a component of the oxidative phosphorylation chain in the mitochondria may explain its strong protective effects on cardiac cells.[195]

In heart failure too, L-carnitine supplementation can be near miraculous. During a three-year follow-up of patients with chronic heart failure, the patients who took two grams per day of L-carnitine in addition to the regular medication had a six-fold lower mortality rate than the placebo group.[196]

Life-saving effects of L-carnitine in animal studies

The administration of very large doses of L-carnitine of at least 150 milligrams per kilo body weight may help chickens survive severe cold exposure. The protective effect shows up at slightly lower doses (100 mg per kilo body weight or less).[197].
L-carnitine supplementation may also convincingly neutralize the adverse cardiac effects of drugs such as adriamycin, drastically decreasing more than threefold the death rate due to adriamycin in rats.[198]
L-carnitine treatment has also been shown to drastically lower the mortality of rats submitted to an endotoxin shock.[99]

REFERENCES: on life-prolonging effects of nutrients

Dietary improvement

Eat less to live longer

Low calorie diet

1. Heilbronn LK, de Jonge L, Frisard MI, DeLany JP, Larson-Meyer DE, Rood J, Nguyen T, Martin CK, Volaufova J, Most MM, Greenway FL, Smith SR, Deutsch WA, Williamson DA, Ravussin E; Pennington CALERIE Team. Effect of 6-month calorie restriction on biomarkers of longevity, metabolic adaptation, and oxidative stress in overweight individuals: a randomized controlled trial. JAMA. 2006 Apr 5;295(13):1539-48.
2. Ingram DK, Roth GS, Lane MA, Ottinger MA, Zou S, de Cabo R, Mattison JA. The potential for dietary restriction to increase longevity in humans: extrapolation from monkey studies. Biogerontology. 2006 Jun;7(3):143-8.
3. Le Bourg E, Rattan SI. Can dietary restriction increase longevity in all species, particularly in human beings? Introduction to a debate among experts. Biogerontology. 2006 Jun;7(3):123-5.

Periodic fasting

4. Kozubik A, Pospisil M. Protective effect of intermittent fasting on the mortality of gamma-irradiated mice. Strahlentherapie. 1982 Dec;158(12):734-8
5. Sogawa H, Kubo C. Influence of short-term repeated fasting on the longevity of female (NZB x NZW)F1 mice. Mech Ageing Dev. 2000 May 18;115(1-2):61-71.
6. Siegel I, Liu TL, Nepomuceno N, Gleicher N. Effects of short-term dietary restriction on survival of mammary ascites tumor-bearing rats. Cancer Invest. 1988;6(6):677-80

Low calorie diet as common feature of the diets of centenarians

7. Sullivan, Walter. Scientists seek key to longevity. New York Times. 1973. pg 1.
8. Sullivan, Walter. Very old people in the Andes are found to be merely old. New York Times, 1978. pg. A8.
9. Gueresi P, Troiano L, Minicuci N, Bonafé M, Pini G, Salvioli G, Carani C, Ferrucci L, Spazzafumo L, Olivieri F, Cavrini G, Valentini D, Franceschi C. The MALVA (MAntova LongeVA) study: an investigation on people 98 years of age and over in a province of Northern Italy. Exp Gerontol. 2003 Oct;38(10):1189-97.
10. Lane MA, Ingram DK, Roth GS. Nutritional modulation of aging in nonhuman primates. J Nutr Health Aging. 1999;3(2):69-76.
11. Meyer TE, Kovacs SJ, Ehsani AA, Klein S, Holloszy JO, Fontana L. Long-term caloric restriction ameliorates the decline in diastolic function in humans. J Am Coll Cardiol. 2006 Jan 17;47(2):398-402.
12. Fontana L, Meyer TE, Klein S, Holloszy JO. Longterm calorie restriction is highly effective in reducing the risk for atherosclerosis in humans. Proc Natl Acad Sci U S A. 2004 Apr 27;101(17):6659-63.
13. Heilbronn LK, de Jonge L, Frisard MI, DeLany JP, Larson-Meyer DE, Rood J, Nguyen T, Martin CK, Volaufova J, Most MM, Greenway FL, Smith SR, Deutsch WA, Williamson DA, Ravussin E; Pennington CALERIE Team. Effect of 6-month calorie restriction on biomarkers of longevity, metabolic adaptation, and oxidative stress in overweight individuals: a randomized controlled trial. JAMA. 2006 Apr 5;295(13):1539-48.

The greater the food variation, the longer the life

14. Wllcox BJ, Willcox DC, Todoriki H, Fujiyoshi A, Yano K, He Q, Curb JD, Suzuki M. Caloric restriction, the traditional Okinawan diet, and healthy aging: the diet of the world's longest-lived people and its potential impact on morbidity and life span. Ann N Y Acad Sci. 2007 Oct;1114:434-55.
15. Willcox BJ, Willcox DC, Suzuki M. The Okinawa program. River Press, 2001, New York (18 different foods a day)
16. Michels KB, Wolk A. A prospective study of variety of healthy foods and mortality in women. Int J Epidemiol 2002 Aug;31(4):847-54.

Drink more water

Dehydration causes premature death

17. Sansevero AC. Dehydration in the elderly: strategies for prevention and management. Nurse Pract 1997 Apr;22(4):41-2, 51-7, 63-66.
18. Warren JL, Bacon WE, Harris T, McBean AM, Foley DJ, Phillips C. The burden and outcomes associated with dehydration among US elderly, 1991. Am J Public Health 1994 Aug;84(8): 1265-9.

Drinking more water may prolong life in mice

19. Mittal A, Muthukumar A, Jolly CA, Zaman K, Fernandes G. Reduced food consumption increases water intake and modulates renal aquaporin-1 and -2 expression in autoimmune prone mice. Life Sci 2000;66(16):1471-9.

Alcohol drinking can shorten life increase the risk of dying - increasing the overall risk as well as the risk by cardiovascular and respiratory diseases

20. ackson VA, Sesso HD, Buring JE, Gaziano JM. Alcohol consumption and mortality in men with preexisting cerebrovasculardisease. Arch Intern Med. 2003 May 26;163(10):1189-93.
21. Doll R, Peto R, Boreham J, Sutherland I. Mortality in relation to alcohol consumption: a prospective study among male British doctors. Int J Epidemiol. 2005 Feb;34(1):199-204.
22. Wannamethee SG, Shaper AG. Taking up regular drinking in middle age: effect on major coronary heart disease events and mortality. Heart. 2002 Jan;87(1):32-6.**:**
23. ello LM, Saavedra P, Serra L. Trends in mortality and years of life lost related to alcohol in the Canary Islands, Spain [1980-1998]). Gac Sanit. 2003 Nov-Dec;17(6):466-

Coffee: good for the longevity of very old people?

24. Fortes C, Forastiere F, Farchi S, Rapiti E, Pastori G, Perucci CA. Diet and overall survival in a cohort of very elderly people. Epidemiology. 2000 Jul;11(4):440-5. Department of Epidemiology, Lazio Regional Health Authority, Rome, Italy

Eat high protein foods

Eat animal foods to become a centenarian

25. Personal communication from Professor Vladimir Khavinson, president of the Insiture of Gerontliogy of St Petersbourg

Longer lifespan in patients eating more protein

26. Sullivan DH, Walls RC. Protein-energy undernutrition and the risk of mortality within six years of hospital discharge. J Am Coll Nutr. 1998 Dec;17(6):571-8.
27. Borugian MJ, Sheps SB, Kim-Sing C, Van Patten C, Potter JD, Dunn B, Gallagher RP, Hislop TG. Insulin, macronutrient intake, and physical activity: are potential indicators of insulin resistance associated with mortality from breast cancer? Cancer Epidemiol Biomarkers Prev. 2004 Jul;13(7):1163-72.

Avoid milk and other dairy products to prevent and survive cardiovascular disease

28. 190. Kelemen LE, Kushi LH, Jacobs DR Jr, Cerhan JR. Associations of dietary protein with disease and mortality in a prospective study of postmenopausal women. Am J Epidemiol. 2005 Feb 1;161(3):239-49.
29. 237. Laugesen M, Elliott R. Ischaemic heart disease, Type 1 diabetes, & cow milk A1 beta-casein. N Z Med J. 2003; 116(1168): U295
30. 248. Menotti A, Kromhout D, Blackburn H, Fidanza F, Buzina R, Nissinen A. Food intake patterns and 25-year mortality from coronary heart disease: crosscultural correlations in the Seven Countries Study. The Seven CountriesStudy Research Group. Eur J Epidemiol. 1999 Jul; 15(6): 507-1
31. Kelemen LE, Kushi LH, Jacobs DR Jr, Cerhan JR. Associations of dietary protein with disease and mortality in a prospective study of postmenopausal women. Am J Epidemiol. 2005 Feb 1;161(3):239-49.

Avoid milk and other dairy products to prevent and survive cancer

32. Hara N, Sakata K, Nagai M, Fujita Y, Hashimoto T, Yanagawa H. Geographical difference of mortality of digestive cancers and food consumption. Gan No Rinsho. 1984 Oct; 30(13): 1665-74.
33. Mills PK, Beeson WL, Phillips RL, Fraser GE. Cohort study of diet, lifestyle, and prostate cancer in Adventist men. Cancer. 1989 Aug 1;64(3):598-604.
34. Snowdon DA, Phillips RL, Choi W. Diet, obesity, and risk of fatal prostate cancer. Am J Epidemiol 1984;120: 244-50.
35. Snowdon DA. Animal product consumption and mortality because of all causes combined, coronary heart disease, stroke, diabetes, and cancer in Seventh-day Adventists. Am J Clin Nutr. 1988 Sep;48(3 Suppl):739-48.
36. Pryor M, Slattery ML, Robison LM, Egger M. Adolescent diet and breast cancer in Utah. Cancer Res. 1989 Apr 15;49(8):2161-7

Eat more fruits and vegetables

Consume fruits and in particular citrus fruits to extend life

37. Steffen LM, Jacobs DR Jr, Stevens J, Shahar E, Carithers T, Folsom AR. - Associations of wholegrain, refined-grain, and fruit and vegetable consumption with risks of all-cause mortality and incident coronary artery disease and ischemic stroke: the Atherosclerosis Risk in Communities (ARIC) Study.Am J Clin Nutr. 2003 Sep;78(3):383-90.
38. Fortes C, Forastiere F, Farchi S, Rapiti E, Pastori G, Perucci CA. Diet and overall survival in a cohort of very elderly people. Epidemiology. 2000 Jul;11(4):440-5.

Consume vegetables and in particular cruciferous vegetables and carrots to extend life

39. Genkinger JM, Platz EA, Hoffman SC, Comstock GW, Helzlsouer KJ. Fruit, vegetable, and antioxidant intake and all-cause, cancer, and cardiovascular disease mortality in a community-dwelling population in Washington County, Maryland. Am J Epidemiol. 2004 Dec 15;160(12):1223-33.
40. Buijsse B, Feskens EJ, Kwape L, Kok FJ, Kromhout D. Both alpha- and beta-carotene, but not tocopherols and vitamin C, are inversely related to 15-year cardiovascular mortality in Dutch elderly men. J Nutr. 2008 Feb;138(2):344-50. Division of Human Nutrition, Wageningen University, Wageningen, 6700 EV The Netherlands. **DOUBLE with carotenoids**
41. Takeuchi T, Kawana T. Oral glucose challenge effects on growth and sex steroid hormones in normal women and women with hypothalamic amenorrhea. Int J Gynaecol Obstet. 1998 May;61(2):171-8.
42. Hubert GD, Schriock ED, Givens JR, Buster JE. Department of Obstetrics and Gynecology Suppression of circulating delta 4-androstenedione and dehydroepiandrosterone sulfate during oral glucose tolerance test in normal females. J Clin Endocrinol Metab. 1991 Oct;73(4):781-4.
43. Vasarhelyi B, Bencsik P, Treszl A, Bardoczy Z, Tulassay T, Szathmari M. The Effect of Physiologic Hyperinsulinemia during an Oral Glucose Tolerance Test on the Levels of Dehydroepiandrosterone (DHEA) and Its Sulfate (DHEAS) in Healthy Young Adults Born with Low and with Normal Birth Weight. Endocr J. 2003 Dec;50(6):689-95.
44. Goodman-Gruen D, Barrett-Connor E. Sex differences in the association of endogenous sex hormone levels and glucose tolerance status in older men and women. Diabetes Care. 2000 Jul;23(7):912-8.
45. Sauvaget C, Nagano J, Hayashi M, Spencer E, Shimizu Y, Allen N. Vegetables and fruit intake and cancer mortality in the Hiroshima/Nagasaki Life Span Study. Br J Cancer. 2003; 88(5): 689-94.
46. Bazzano LA, He J, Ogden LG, Loria C, Vupputuri S, Myers L, Whelton PK. Legume consumption and risk of coronary heart disease in US men and women : NHANES I Epidemiologic Follow-up Study. Arch Intern Med. 2001 Nov 26;161(21):2573-8.
47. Vasarhelyi B, Bencsik P, Treszl A, Bardoczy Z, Tulassay T, Szathmari M. The Effect of Physiologic Hyperinsulinemia during an Oral Glucose Tolerance Test on the Levels of Dehydroepiandrosterone (DHEA) and Its Sulfate (DHEAS) in Healthy Young Adults Born with Low and with Normal Birth Weight. Endocr J. 2003 Dec;50(6):689-95.
48. Sichieri R, Everhart JE, Mendonca GA. Diet and mortality from common cancers in Brazil: an ecological study. Cad Saude Publica. 1996 Jan; 12(1): 53-59.
49. Mlekusch W, Lamprecht M, Ottl K, Tillian M, Reibnegger G. A. glucose-rich diet shortens longevity of mice. Mech Ageing Dev 1996 Nov 29;92(1):43-51.
50. Reiser S, Ferretti RJ, Fields M, Smith JC Jr. Role of dietary fructose in the enhancement of mortality and biochemical changes associated with copper deficiency in rats. Am J Clin Nutr. 1983 Aug;38(2):214-22
51. Fields M, Ferretti RJ, Smith JC Jr, Reiser S. Effect of copper deficiency on metabolism and mortality in rats fed sucrose or starch diets. J Nutr. 1983 Jul;113(7):1335-45
52. Menotti A, Kromhout D, Blackburn H, Fidanza F, Buzina R, Nissinen A. Food intake patterns and 25-year mortality from coronary heart disease: crosscultural correlations in the Seven Countries Study. The Seven Countries Study Research Group. Eur J Epidemiol. 1999 Jul; 15(6): 507-15
53. Carroll KK. Dietary factors in hormone - dependent cancers, in M Winick, Ed. Current concepts in Nutrition, Volume 6: Nutrition & Cancer. New-York, John Wiley & Sons, 1977: 25-40.
54. Hara N, Sakata K, Nagai M, Fujita Y, Hashimoto T, Yanagawa H. Geographical difference of mortality of digestive cancers and food consumption. Gan No Rinsho. 1984 Oct; 30(13): 1665-74).
55. Haglund O, Wallin R, Luostarinen R, Saldeen T.. Effects of a new fluid fish oil concentrate, ESKIMO-3, on triglycerides, cholesterol, fibrinogen and blood pressure. J Intern Med 1990; 227 (5): 347-53
56. Roth-Walter F, Berin MC, Arnaboldi P, Escalante CR, Dahan S, Rauch J, Jensen-Jarolim E, Mayer L. Pasteurization of milk proteins promotes allergic sensitization by enhancing uptake through Peyer's patches. Allergy. 2008 Jul;63(7):882-90.
57. Schulmeister U, Swoboda I, Quirce S, de la Hoz B, Ollert M, Pauli G, Valenta R, Spitzauer S. Sensitization to human milk. Clin Exp Allergy. 2008 Jan;38(1):60-8.

Longer life in people, including cancer patients, who consume sufficient amounts of (healthy) fat

58. Meijler FL. The failing of the MRFIT (multiple risk intervetntion trial). Ned Tijdschr Geneesk. 1982; 126 (52):2390-1.
59. Rohan TE, Hiller JE, McMichael AJ.Dietary factors and survival from breast cancer. Nutr Cancer. 1993;20(2):167-77.

Micronutrient interventions to prolong life

Multivitamin preparations

Multivitamin preparations may help men more than women to live longer

60. Hercberg S, Galan P, Preziosi P, Bertrais S, Mennen L, Malvy D, Roussel AM, Favier A, Briançon S. The SU.VI.MAX Study: a randomized, placebo-controlled trial of the health effects of antioxidant vitamins and minerals. Arch Intern Med. 2004 Nov 22;164(21):2335-42. Erratum in: Arch Intern Med. 2005 Feb 14;165(3):286
61. Watkins ML, Erickson JD, Thun MJ, Mulinare J, Heath CW Jr. Multivitamin use and mortality in a large prospective study. : Am J Epidemiol. 2000 Jul 15;152(2):149-62

Greater survival in lung cancer patients who take multivitamin preparations

62. Jatoi A, Daly BD, Kramer G, Mason JB. A crosssectional study of vitamin intake in postoperative nonsmall cell lung cancer patients. J Surg Oncol. 1998 Aug;68(4):231-6

Sodium

High sodium diets may prolong life, especially in the case of cardiovascular disease

63. Alderman MH, Cohen H, Madhavan S. Dietary sodium intake and mortality: the National Health and Nutrition Examination Survey (NHANES I). Lancet. 1998 Mar 14;351(9105):781-5

Animal studies where high sodium diet prolongs life, while sodium-deficient diets shorten life

64. Brady RC, Trock SC, Jones CJ, Ross PF. Stunted growth and mortality associated with sodium deficiency. Avian Dis. 2002 Jul-Sep;46(3):740-4.
65. Ki Yull Lee. Some Effects of High and Low Sodium Intake on a Vegetarian Diet in Rats Yonsei Med J 1963 December;4(1):6-16.

Avoid taking too high amounts of dietary sodium

66. Tuomilehto J, Jousilahti P, Rastenyte D, Moltchanov V, Tanskanen A, Pietinen P, Nissinen A. Urinary sodium excretion and cardiovascular mortality in Finland: a prospective study. Lancet. 2001 Mar 17;357(9259):848-51

Higher serum sodium levels may prolong life in patients with liver insufficiency or heart failure

67. Biggins SW, Rodriguez HJ, Bacchetti P, Bass NM, Roberts JP, Terrault NA. Serum sodium predicts mortality in patients listed for liver transplantation. Hepatology. 2005 Jan;41(1):32-9
68. Ruf AE, Kremers WK, Chavez LL, Descalzi VI, Podesta LG, Villamil FG. Addition of serum sodium into the MELD score predicts waiting list mortality better than MELD alone. Liver Transpl. 2005 Mar;11(3):336-43
69. Klein L, O'Connor CM, Leimberger JD, Gattis-Stough W, Pina IL, Felker GM, Adams KF Jr, Califf RM, Gheorghiade M; OPTIME-CHF Investigators. Lower serum sodium is associated with increased shortterm mortality in hospitalized patients with worsening heart failure: results from the Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure (OPTIMECHF) study. Circulation. 2005 May 17;111(19):2454-60.

Potassium

Potassium depletion increases the risk of dying in humans and rats

70. Packer M. Potential role of potassium as a determinant of morbidity and mortality in patients with systemic hypertension and congestive heart failure. Am J Cardiol. 1990 Mar 6;65(10):45E-51E
71. Hubbard RW, Mager M, Bowers WD, Leav I, Angoff G, Matthew WT, Sils IV. Effect of low-potassium diet on rat exercise hyperthermia and heat stroke mortality. J Appl Physiol. 1981 Jul;51(1):8-13.
72. The consumption of potassium-rich foods prolongs life in patients with stroke
73. Khaw KT, Barrett-Connor E. Dietary potassium and stroke-associated mortality. A 12-year prospective population study. N Engl J Med. 1987 Jan 29;316(5):235-40
74. Fang J, Madhavan S, Alderman MH. Dietary potassium intake and stroke mortality. Stroke. 2000 Jul;31(7):1532-7

A high potassium diet may help rats survive stroke

75. Ganguli M, Tobian L, Sugimoto T. High magnesium diets increase blood pressure and enhance stroke mortality in hypertensive SHRsp rats. Am J Hypertens. 1989 Oct;2(10):780-3

Potassium supplements may help survive myocardial infarction and cardiac failure in humans

76. Singh RB, Singh NK, Niaz MA, Sharma JP. Effect of treatment with magnesium and potassium on mortality and reinfarction rate of patients with suspected acute myocardial infarction. Int J Clin Pharmacol Ther. 1996 May;34(5):219-25

Dangers of high levels of potassium in smokers and patients with antihypertensive drugs

77. Wannamethee SG, Lever AF, Shaper AG, Whincup PH. Serum potassium, cigarette smoking, and mortality in middle-aged men. Am J Epidemiol. 1997 Apr 1;145(7):598-606

Magnesium

Drinking magnesium-rich water may prolong life in general and help survive cardiovascular and stroke

78. Marque S, Jacqmin-Gadda H, Dartigues JF, Commenges D. Cardiovascular mortality and calcium and magnesium in drinking water: an ecological study in elderly people. Eur J Epidemiol. 2003;18(4):305-9
79. Rosenlund M, Berglind N, Hallqvist J, Bellander T, Bluhm G. Daily intake of magnesium and calcium from drinking water in relation to myocardial infarction. Epidemiology. 2005 Jul;16(4):570-576
80. Rubenowitz E, Molin I, Axelsson G, Rylander R. Magnesium in drinking water in relation to morbidity and mortality from acute myocardial infarction. Epidemiology. 2000 Jul;11(4):416-21.
81. Yang CY, Chiu HF, Chiu JF, Wang TN, Cheng MF. Magnesium and calcium in drinking water and cerebrovascular mortality in Taiwan. Magnes Res. 1997 Mar;10(1):51-7.

Low magnesium levels increase mortality from septic shock in rats, while magnesium therapy helps rats survive the infectious shock

82. Salem M, Kasinski N, Munoz R, Chernow B. Progressive magnesium deficiency increases mortality from endotoxin challenge: protective effects of acute magnesium replacement therapy. Crit Care Med. 1995 Jan;23(1):108-18

Magnesium therapy prolongs life in patients with coronary artery disease

83. Teo KK, Yusuf S. Role of magnesium in reducing mortality in acute myocardial infarction. A review of the evidence.

Drugs. 1993 Sep;46(3):347-59
84. Shechter M, Bairey Merz CN, Stuehlinger HG, Slany J, Pachinger O, Rabinowitz B. Effects of oral magnesium therapy on exercise tolerance, exerciseinduced chest pain, and quality of life in patients with coronary artery disease. Am J Cardiol. 2003 Mar 1;91(5):517-21 The Heart Institute, Sheba Medical Center, Tel Hashomer, Israel. shechtes@netvision.net.il
85. Horner SM. Efficacy of intravenous magnesium in acute myocardial infarction in reducing arrhythmias and mortality. Meta-analysis of magnesium in acute myocardial infarction. Circulation. 1992 Sep;86(3):774-9 Department of Cardiology, Middlesex Hospital, London, UK.
86. Singh RB, Singh NK, Niaz MA, Sharma JP. Effect of treatment with magnesium and potassium on mortality and reinfarction rate of patients with suspected acute myocardial infarction. Int J Clin Pharmacol Ther. 1996 May;34(5):219-25 Source: Department of Food Science, Rutgers University, USA
87. Woods KL, Fletcher S, Roffe C, Haider Y. Intravenous magnesium sulphate in suspected acute myocardial infarction: results of the second Leicester Intravenous Magnesium Intervention Trial (LIMIT-2). Lancet. 1992;339(8809):1553-1558. Magnesium therapy saves pregnant women with preeclampsia from dying
88. Begum R, Begum A, Bullough CH, Johanson RB. Reducing maternal mortality from eclampsia, using magnesium sulphate. Eur J Obstet Gynecol Reprod Biol. 2000 Oct;92(2):223-4. Obstetrics & Gynaecology, Dhaka Medical College, Dhaka, Bangladesh.

Calcium

Low calcium in the diet increases the risk of dying

89. Kobayashi E, Okubo Y, Suwazono Y, Kido T, Nishijo M, Nakagawa H, Nogawa K. Association between urinary calcium excretion level and mortality in inhabitants of the Jinzu River basin area of Japan. Biol Trace Elem Res. 2002 Nov;89(2):145-53.

Dietary calcium and calcium supplements reduce coronary heart disease mortality

90. Bostick RM, Kushi LH, Wu Y, Meyer KA, Sellers TA, Folsom AR. Relation of calcium, vitamin D, and dairy food intake to ischemic heart disease mortality among postmenopausal women. Am J Epidemiol. 1999 Jan 15;149(2):151-61.Department of Family and Preventive Medicine, School of Medicine, University of South Carolina, Columbia, USA.

A low ionized calcium in the serum shortens life in critically ill patients

91. Burchard KW, Gann DS, Colliton J, Forster J. Ionized calcium, parathormone, and mortality in critically ill surgical patients. Ann Surg. 1990 Oct;212(4):543-9; discussion 549-50

Water-soluble vitamins

Folic acid

Higher serum folate levels may help cancer patients live longer

92. Dangour AD, Breeze E, Clarke R, Shetty PS, Uauy R, Fletcher AE. Plasma homocysteine, but not folate or vitamin B-12, predicts mortality in older people in the United Kingdom. J Nutr. 2008 Jun;138(6):1121-8.
93. Jatoi A, Daly BD, Kramer G, Mason JB. A crosssectional study of vitamin intake in postoperative nonsmall cell lung cancer patients. J Surg Oncol. 1998 Aug;68(4):231-6
94. Rossi E, Hung J, Beilby JP, Knuiman MW, Divitini ML, Bartholomew H. Folate levels and cancer morbidity and mortality: prospective cohort study from Busselton, Western Australia. Ann Epidemiol. 2006 Mar;16(3):206-12.

The intake of foods rich in folic acid and folic acid supplements may modestly help patients with disease to live longer

95. Anderson JL, Jensen KR, Carlquist JF, Bair TL, Horne BD, Muhlestein JB. Effect of folic acid fortification of food on homocysteine-related mortality. Am J Med. 2004 Feb 1;116(3):158-64.
96. Medrano MJ, Sierra MJ, Almazán J, Olalla MT, López-Abente G. The association of dietary folate, B6, and B12 with cardiovascular mortality in Spain: an ecological analysis. Am J Public Health. 2000 Oct;90(10):1636-8.
97. Sellers TA, Alberts SR, Vierkant RA, Grabrick DM, Cerhan JR, Vachon CM, Olson JE, Kushi LH, Potter JD. High-folate diets and breast cancer survival in a prospective cohort study. Nutr Cancer. 2002;44(2):139-44.
98. Bol KA, Collins JS, Kirby RS; National Birth Defects Prevention Network. Survival of infants with neural tube defects in the presence of folic acid fortification. Pediatrics. 2006 Mar;117(3):803-13. *Studies with no effect of folic acid on lifespan in patients*
99. Zoungas S, McGrath BP, Branley P, Kerr PG, Muske C, Wolfe R, Atkins RC, Nicholls K, Fraenkel M, Hutchison BG, Walker R, McNeil JJ. Cardiovascular morbidity and mortality in the Atherosclerosis and Folic Acid Supplementation Trial (ASFAST) in chronic renal failure: a multicenter, randomized, controlled trial. J Am Coll Cardiol. 2006 Mar 21;47(6):1108-16.
100. Albert CM, Cook NR, Gaziano JM, Zaharris E, MacFadyen J, Danielson E, Buring JE, Manson JE. Effect of folic acid and B vitamins on risk of cardiovascular events and total mortality among women at high risk for cardiovascular disease: a randomized trial. JAMA. 2008 May 7;299(17):2027-36.
101. Black RE. Effect of routine prophylactic supplementation with iron and folic acid on preschool child mortality in southern Nepal: community-based, cluster-randomised, placebo-controlled trial. Lancet. 2006 Jan 14;367(9505):144-52.μ

Folic acid treatment may prolong lifespan of mice

102. Li D, Karp N, Wu Q, Wang XL, Melnyk S, James SJ, Rozen R. Mefolinate (5-methyltetrahydrofolate), but not folic acid, decreases mortality in an animal model of severe methylenetetrahydrofolate reductase deficiency. J Inherit Metab Dis. 2008 Jun;31(3):403-11.

Vitamin B12

Higher B12 levels in alcoholics associated with higher mortality

103. Baker H, Frank O, DeAngelis B. Plasma vitamin B12 titres as indicators of disease severity and mortality of patients with alcoholic hepatitis. Alcohol

Vitamin C

Low serum vitamin C levels in elderly persons increases the risk of dying

104. Fletcher AE, Breeze E, Shetty PS. Antioxidant vitamins & mortality in older persons: findings from the nutrition add-on study to the Medical Research Council Trial of Assessment & Management of OlderCommunityPeople Am J Clin Nutr. 2003;78(5):999-1010.
105. Deicher R, Ziai F, Bieglmayer C, Schillinger M, Hörl WH. Low total vitamin C plasma level is a risk factor for cardiovascular morbidity and mortality in hemodialysis patients. Am Soc Nephrol. 2005 Jun;16(6):1811-8.
106. Loria CM, Klag MJ, Caulfield LE, Whelton PK. Vitamin C status and mortality in US adults. Am J Clin Nutr. 2000 Jul;72(1):139-45. Division of Epidemiology and Clinical Applications, National Heart, Lung, and Blood Institute, Bethesda, MD 20892-7934, USA. loriac@nih.gov

Longevity and mortality threshold levels for vitamin C

107. Khaw KT, Bingham S, Welch A, Luben R, Wareham N, Oakes S, Day N. Relation between plasma ascorbic acid and mortality in men and women in EPIC-Norfolk prospective study: a prospective population study. European Prospective Investigation into Cancer and Nutrition. Lancet. 2001 Mar 3;357(9257):657-63
108. Gey KF, Stähelin HB, Eichholzer M. Poor plasma status of carotene and vitamin C is associated with higher mortality from ischemic heart disease and stroke: Basel Prospective Study. Clin Investig. 1993 Jan;71(1):3-6. Vitamin-Forschungseinheit and Reference Centre for Vitamins, WHO/MONICA Project, Universität Bern.
109. Gey KF, Stähelin HB, Puska P, Evans A. Relationship of plasma level of vitamin C to mortality from ischemic heart disease. Ann N Y Acad Sci. 1987;498:110-23. The Intake of vitamin C-rich foods may lower the mortality by coronary heart disease and breast cancer
110. Pandey DK, Shekelle R, Selwyn BJ, Tangney C, Stamler J. Dietary vitamin C and beta-carotene and risk of death in middle-aged men. The Western Electric Study. Am J Epidemiol. 1995 Dec 15;142(12):1269-78.
111. Jain M, Miller AB, To T. Premorbid diet and the prognosis of women with breast cancer. J Natl Cancer Inst. 1994 Sep 21;86(18):1390-7.

The consumption of foods rich in vitamin C may not reduce influence longevity

112. Enstrom JE, Kanim LE, Breslow L. The relationship between vitamin C intake, general health practices, and mortality in Alameda County, California. Am J Public Health. 1986 Sep;76(9):1124-30.

Supplements: *Vitamin C supplementation may prolong life in men more than in women*

113. Enstrom JE, Kanim LE, Klein MA. Vitamin C intake and mortality among a sample of the United States population. Epidemiology. 1992 May;3(3):194-202. School of Public Health, University of California, Los Angeles 90024.

Regular intake of vitamin C supplements may lower the mortality in middle-aged and elderly persons and terminal cancer patients

114. Kromhout D, Bloemberg B, Feskens E, Menotti A, Nissinen A. Saturated fat, vitamin C and smoking predict long-term population all-cause mortality rates in the Seven Countries Study. Int J Epidemiol. 2000 Apr;29(2):260-5
115. Murata A, Morishige F, Yamaguchi H. Prolongation of survival times of terminal cancer patients by administration of large doses of ascorbate. Int J Vitam Nutr Res Suppl. 1982;23:103-13 High doses of vitamin C help cancer patients prolong their survival
116. Cameron E, Pauling L. Supplemental ascorbate in the supportive treatment of cancer: reevaluation of prolongation of survival times in terminal human cancer. Proc Natl Acad Sci U S A. 1978 Sep;75(9):4538-42.
117. Jacobs EJ, Connell CJ, McCullough ML, Chao A, Jonas CR, Rodriguez C, Calle EE, Thun MJ. Vitamin C, vitamin E, and multivitamin supplement use and stomach cancer mortality in the Cancer Prevention Study II cohort. Cancer Epidemiol Biomarkers Prev. 2002 Jan;11(1):35-41. Department of Epidemiology and Surveillance Research, American Cancer Society, 1599 Clifton Road NE, Atlanta, GA 30329-4251, USA.
118. Jacobs EJ, Connell CJ, Patel AV, Chao A, Rodriguez C, Seymour J, McCullough ML, Calle EE, Thun MJ. Vitamin C and vitamin E supplement use and colorectal cancer mortality in a large American Cancer Society cohort. Cancer Epidemiol Biomarkers Prev. 2001 Jan;10(1):17-23. Department of Epidemiology and Surveillance Research, American Cancer Society, Atlanta, Georgia 30329-4251, USA.

A study where vitamin C did not seem to bet helpful to improve lifespan

119. Ono K. The effect of vitamin C supplementation and withdrawal on the mortality and morbidity of regular hemodialysis patients. Clin Nephrol. 1989 Jan;31(1):31-4. Ono Geka Clinic, Fukuoka, Japan. Vitamin C supplementation may prolong life in animals
120. Massie HR, Aiello VR, Doherty TJ. Dietary vitamin C improves the survival of mice. Gerontology. 1984;30(6):371-5.
121. Moran ET Jr, Carlson HC, Brown RG, Sweeny PR, George JC, Stanley DW. Alleviating mortality associated with a vitamin E-selenium deficiency by dietary ascorbic acid. Poult Sci. 1975 Jan;54(1):266-9.

Vitamin C supplementation is not very helpful in emergency conditions in animals

122. DOUBLE Daughters K, Waxman K, Gassel A, Zommer S. Anti-oxidant treatment for shock: vitamin E but not vitamin C improves survival. Am Surg. 1996 Oct;62(10):789-92. Department of Surgery, University of California Irvine Medical Center, Orange, USA.
123. Peck MD, Alexander JW. Survival in septic guinea pigs is influenced by vitamin E, but not by vitamin C in enteral diets. JPEN J Parenter Enteral Nutr. 1991 Jul-Aug;15(4):433-6. Department of Surgery, University of Miami School of Medicine, Florida.

The simultaneous use of vitamin E and C supplements, not the single use of one of the two supplements, prolongs life in general, and in particular prevents and helps survive cardiovascular disease

124. Losonczy KG, Harris TB, Havlik RJ. Vitamin E and vitamin C supplement use and risk of all-cause and coronary heart disease mortality in older persons: the Established Populations for Epidemiologic Studies of the Elderly. Am J Clin Nutr. 1996 Aug;64(2):190-6.

Vitamin A

Vitamin A supplementation may reduce mortality in children

125. Fawzi WW, Mbise RL, Hertzmark E, et al. A randomized trial of vitamin A supplements in relation to mortality among human immunodeficiency virusinfected & uninfected children in Tanzania. Pediatr Infect Dis J. 1999 Feb;18(2):127-33
126. Caraballoso M, Sacristan M, Serra C, Bonfill X. Drugs for preventing lung cancer in healthy people. Cochrane Database Syst Rev. 2003;(2):CD002141. Escuela Nacional de Salud Publica de Cub, Habana, Cuba

Carotenoids

Elderly persons and cancer, cardiac or stroke patients with high serum carotenoid levels live longer

127. De Waart FG, Schouten EG, Stalenhoef AF, Kok FJ. Serum carotenoids, alpha-tocopherol and mortality risk in a prospective study among Dutch elderly. Int J Epidemiol. 2001 Feb;30(1):136-43
128. Ito Y, Wakai K, Suzuki K, Tamakoshi A, Seki N, Ando M, Nishino Y, Kondo T, Watanabe Y, Ozasa K, Ohno Y; JACC Study Group. Serum carotenoids and mortality from lung cancer: a case-control study nested in the Japan Collaborative Cohort (JACC) study. Cancer Sci. 2003 Jan;94(1):57-63
129. Ito Y, Wakai K, Suzuki K, Ozasa K, Watanabe Y, Seki N, Ando M, Nishino Y, Kondo T, Ohno Y, Tamakoshi A; JACC Study Group. Lung cancer mortality and serum levels of carotenoids, retinol, tocopherols, and folic acid in men and women: a case-control study nested in the JACC Study. J Epidemiol. 2005 Jun;15 Suppl 2:S140-9. Department of Public Health, Fujita Health University School of Health Sciences, Japan. yoshito@fujita-hu.ac.jp

130. Ito Y, Kurata M, Hioki R, Suzuki K, Ochiai J, Aoki K. Cancer mortality and serum levels of carotenoids, retinol, and tocopherol: a population-based follow-up study of inhabitants of a rural area of Japan. Asian Pac J Cancer Prev. 2005 Jan-Mar;6(1):10-5.
131. Watters JL, Gail MH, Weinstein SJ, Virtamo J, Albanes D. Associations between alpha-tocopherol, beta-carotene, and retinol and prostate cancer survival. Cancer Res. 2009 May 1;69(9):3833-41
132. Ito Y, Suzuki K, Ishii J, Hishida H, Tamakoshi A, Hamajima N, Aoki K. A population-based follow-up study on mortality from cancer or cardiovascular disease and serum carotenoids, retinol and tocopherols in Japanese inhabitants. Asian Pac J Cancer Prev. 2006 Oct-Dec;7(4):533-46. The consumption of foods rich in carotenoids reduces the risk of dying from cancer, especially from colorectal cancer and breast cancer
133. Rock CL, Saxe GA, Ruffin MT 4th, August DA, Schottenfeld D. Carotenoids, vitamin A, and estrogen receptor status in breast cancer. Nutr Cancer. 1996;25(3):281-96.

The consumption of foods rich in beta-carotene reduces the risk of dying from cardiovascular disease, while only the consumption of foods rich in beta-carotene appears to reduce the global risk of dying

134. Heinonen OP, Albanes D, Virtamo J, Taylor PR, Huttunen JK, Hartman AM, Haapakoski J, Malila N, Rautalahti M, Ripatti S, Mäenpää H, Teerenhovi L, Koss L, Virolainen M, Edwards BK. Prostate cancer and supplementation with alpha-tocopherol and betacarotene: incidence and mortality in a controlled trial. J Natl Cancer Inst. 1998 Mar 18;90(6):440-6.
135. Virtamo J, Pietinen P, Albert P. ATBC Study Group. Incidence of cancer and mortality following alphatocopherol and beta-carotene supplementation: a postintervention follow-up. JAMA. 2003 Jul 23;290(4):476-85
136. Le Marchand L, Hankin JH, Kolonel LN, Wilkens LR. Vegetable and fruit consumption in relation to prostate cancer risk in Hawaii: a reevaluation of the effect of dietary beta-carotene. Am J Epidemiol. 1991;133(3):215-9. Cancer Research Center of Hawaii, University of Hawaii

Vitamin D

People with risk factors for vitamin D deficiency are less likely to live long and more likely to die from cancer

137. Giovannucci E, Liu Y, Willett WC. Cancer incidence and mortality and vitamin D in black and white male health professionals. Cancer Epidemiol Biomarkers Prev. 2006 Dec;15(12):2467-72. Channing Laboratory, Department of Medicine, Harvard School of Public Health, 665 Huntington Avenue, Boston, MA 02115, USA. edward.giovannucci@channing.harvard.edu
138. Porojnicu A, Robsahm TE, Berg JP, Moan J. Season of diagnosis is a predictor of cancer survival. Suninduced vitamin D may be involved: a possible role of sun-induced Vitamin D. J Steroid Biochem Mol Biol. 2007 Mar;103(3-5):675-8.
139. Grant WB. The likely role of vitamin D from solar ultraviolet-B irradiance in increasing cancer survival. Anticancer Res. 2006 Jul-Aug;26(4A):2605-14. Sunlight, Nutrition and Health Research Center (SUNARC), San Francisco, CA 94109-2529, USA. wgrant@sunarc.org

140. Grant WB. Lower vitamin-D production from solar ultraviolet-B irradiance may explain some differences in cancer survival rates. J Natl Med Assoc. 2006 Mar;98(3):357-64. Sunlight, Nutrition and Health Research Center, San Francisco, CA 94109-2529, USA. wgrant@sunarc.org
141. Lefkowitz ES, Garland CF. Sunlight, vitamin D, and ovarian cancer mortality rates in US women. Int J Epidemiol. 1994 Dec;23(6):1133-6. Department of Family and Preventive Medicine, University of California, San Diego, La Jolla 92093-0620, USA

Higher serum levels of vitamin D may prolong the survival of cancer patients

142. Moan J, Porojnicu AC, Robsahm TE, Dahlback A, Juzeniene A, Tretli S, Grant W. Solar radiation, vitamin D and survival rate of colon cancer in Norway. J Photochem Photobiol B. 2005 Mar 1;78(3):189-93. Avdeling for strålingsbiologi, Institutt for kreftforskning, Montebello, N-0310 Oslo, Norway. johan.moan@labmed.uio.no
143. Wolf M, Shah A, Gutierrez O, Ankers E, Monroy M, Tamez H, Steele D, Chang Y, Camargo CA Jr, Tonelli M, Thadhani R. Vitamin D levels and early mortality among incident hemodialysis patients. Kidney Int. 2007 Oct;72(8):1004-13.
144. Grant WB, Garland CF, Gorham ED. An estimate of cancer mortality rate reductions in Europe and the US with 1,000 IU of oral vitamin D per day. Recent Results Cancer Res. 2007;174:225-34. Sunlight, Nutrition and Health Research Center, San Francisco, CA 94109-2510, USA.

Optimal level of vitamin D for survival and a longer life

145. Giovannucci E, Liu Y, Rimm EB, Hollis BW, Fuchs CS, Stampfer MJ, Willett WC. Prospective study of predictors of vitamin D status and cancer incidence and mortality in men. J Natl Cancer Inst. 2006 Apr 5;98(7):451-9. Department of Medicine, Harvard Medical School, Brigham and Women's Hospital, Boston, MA, USA. edward.giovannucci@channing.harvard.edu
146. Zhou W, Suk R, Liu G, Park S, Neuberg DS, Wain JC, Lynch TJ, Giovannucci E, Christiani DC. Vitamin D is associated with improved survival in early-stage non-small cell lung cancer patients. Cancer Epidemiol Biomarkers Prev. 2005 Oct;14(10):2303-9. Occupational Health Program, Department of Environmental Health, Harvard School of Public Health, 665 Huntington Avenue, Boston, MA 02115, USA.

Protective levels of vitamin D3

147. Freedman DM, Looker AC, Chang SC, Graubard BI. Prospective study of serum vitamin D and cancer mortality in the United States. J Natl Cancer Inst. 2007 Nov 7;99(21):1594-602.
148. Haug C, Müller F, Aukrust P, Frøland SS. Subnormal serum concentration of 1,25-vitamin D in human immunodeficiency virus infection: correlation with degree of immune deficiency and survival. J Infect Dis. 1994 Apr;169(4):889-93. Kaptein Wilhelmsen og Frues Institute of Bacteriology, Medical Department A, University of Oslo, National Hospital, Norway.

Efficacy of vitamin D supplements to prolong life in patients with chronic disease

149. Autier P, Gandini S. Vitamin D supplementation and total mortality: a meta-analysis of randomized controlled trials. Arch Intern Med. 2007 Sep 10;167(16):1730-7.
150. Tentori F, Albert JM, Young EW, Blayney MJ, Robinson BM, Pisoni RL, Akiba T, Greenwood RN, Kimata N, Levin NW, Piera LM, Saran R, Wolfe RA, Port FK. The survival advantage for haemodialysis patients taking vitamin D is questioned: findings from the Dialysis Outcomes and Practice Patterns Study. Nephrol Dial Transplant. 2009 Mar;24(3):963-72.
151. Teng M, Wolf M, Ofsthun MN, Lazarus JM, Hernán MA, Camargo CA Jr, Thadhani R. Activated injectable vitamin D and hemodialysis survival: a historical cohort study. J Am Soc Nephrol. 2005 Apr;16(4):1115-25.
152. Naves-Díaz M, Alvarez-Hernández D, Passlick-Deetjen J, Guinsburg A, Marelli C, Rodriguez-Puyol D, Cannata-

Andía JB. Oral active vitamin D is associated with improved survival in hemodialysis patients. Kidney Int. 2008 Oct;74(8):1070-8.

Optimal vitamin D doses that prolong life

153. Kovesdy CP, Ahmadzadeh S, Anderson JE, Kalantar-Zadeh K. Association of activated vitamin D treatment and mortality in chronic kidney disease. Arch Intern Med. 2008 Feb 25;168(4):397-403. Division of Nephrology, Salem Veterans Affairs Medical Center, Salem, VA 24153, USA. csaba.kovesdy@va.gov
154. Wolf M, Thadhani R. Vitamin D in patients with renal failure: a summary of observational mortality studies and steps moving forward. J Steroid Biochem Mol Biol. 2007 Mar;103(3-5):487-90.
155. Tentori F, Hunt WC, Stidley CA, Rohrscheib MR, Bedrick EJ, Meyer KB, Johnson HK, Zager PG; Medical Directors of Dialysis Clinic Inc. Mortality risk among hemodialysis patients receiving different vitamin D analogs. Kidney Int. 2006 Nov;70(10):1858-65.

Vitamin E

A low serum level of vitamin E increases the risk of dying from heart disease

156. Grey KF, Puska P, et al. Inverse correlation between plasma vitamin E and mortality from ischemic heart disease in cross-cultural epidemiology. Am J Clin Nutr. 1991; 53 (1): Suppl: 326S-334S
157. Grey KF. Plasma vitamin A and E correlate inversely with coronary mortality. Soz Praventiv med. 1989;34(2):78-80

Vitamin E, potent survival nutrient

Vitamin E supplements may lower mortality of patients with moderate Alzheimer's disease

158. 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. The Alzheimer's Disease Cooperative Study. N Engl J Med. 1997 Apr 24;336(17):1216-22.

Caution is recommended with the association of vitamin E and vitamin C in postmenopausal women with coronary heart disease

159. 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. JAMA. 2002 Nov 20;288(19):2432-40

Coenzyme Q 10

High serum levels of coenzyme Q 10 may prolong life in patients with disease

160. Jameson. Statistical data support prediction for death within six months on low levels of coenzymeQ10 and other entities. Clin Investig. 1993; 71: S137-9

Coenzyme Q10 supplementation may reduce the risk of dying in cardiac patients

161. Singh RB, Neki NS, Kartikey K, Pella D, Kumar A, Niaz MA, Thakur AS. Effect of coenzyme Q10 on risk of atherosclerosis in patients with recent myocardial infarction. Mol Cell Biochem. 2003 Apr;246(1-2):75-82

Polyunsaturated fatty acids

A high intake of polyunsaturated fatty acids reduces the risk of dying by cardiovascular disease

162. Salonen JT, Salonen R, Penttila I, Herranen J, Jauhiainen M, Kantola M, Lappetelainen R, Maenpaa PH, Alfthan G, Puska P. Serum fatty acids, apolipoproteins, selenium and vitamin antioxidants and the risk of death from coronary artery disease. Am J Cardiol. 1985 Aug 1;56(4):226-31

Omega six polyunsaturated fatty acids such as linoleic acid

A high intake of linoleic acid prolong life in elderly persons

163. Double Fortes C, Forastiere F, Farchi S, Rapiti E, Pastori G, Perucci CA. Diet and overall survival in a cohort of very elderly people. Epidemiology. 2000 Jul;11(4):440

Omega-3 polyunsaturated fatty acids

164. **Simopoulos AP, Robinson J: The Omega Diet. The** Lifesaving Nutritional Program Based on the Diet of the Island of Crete. New York, HarperCollins, 1999.

The intake of omega-3 polyunsaturated fatty acids may lower the risk of dying by coronary heart disease

165. Rodriguez BL, Sharp DS, Abbott RD, Burchfiel CM, Masaki K, Chyou PH, Huang B, Yano K, Curb JD. Fish intake may limit the increase in risk of coronary heart disease morbidity and mortality among heavy smokers. The Honolulu Heart Program.Circulation. 1996 Sep 1;94(5):952-6.
166. Bucher HC, Hengstler P, Schindler C, Meier G. N-3 polyunsaturated fatty acids in coronary heart disease: a meta-analysis of randomized controlled trials.Am J Med. 2002 Mar;112(4):298-304.Comment in: ACP J Club. 2002 Sep-Oct; 137(2):49. Am J Med. 2002 Mar;112(4):316-9.
167. Nettleton JA, Katz R. n-3 long-chain polyunsaturated fatty acids in type 2 diabetes: a review. J Am Diet Assoc. 2005 Mar;105(3):428-40
168. Bucher HC, Hengstler P, Schindler C, Meier G. N-3 polyunsaturated fatty acids in coronary heart disease: a meta-analysis of randomized controlled trials. Am J Med. 2002 Mar;112(4):298-304

Trans fatty acids

High dietary intake of trans fatty acids increases the coronary artery mortality in men

169. Pasini E, Cargnoni A, Condorelli E, Marzo A, Lisciani R, Ferrari R. Effect of prolonged treatment with propionyl-L-carnitine on erucic acid-induced myocardial dysfunction in rats. Mol Cell Biochem. 1992 Jun 26;112(2):117-23 Cattedra di Cardiologia, Universita degli Studi di Brescia, Italy.

Trace elements

Copper

Life-threatening danger of copper deficiency in rats, when sugar is supplemented to the diet

170. Reiser S, Ferretti RJ, Fields M, Smith JC Jr. Role of dietary fructose in the enhancement of mortality and biochemical changes associated with copper deficiency in rats. Am J Clin Nutr. 1983 Aug;38(2):214-22
171. Fields M, Ferretti RJ, Smith JC Jr, Reiser S. Effect of copper deficiency on metabolism and mortality in rats fed sucrose or starch diets. J Nutr. 1983 Jul;113(7):1335-45

Higher copper levels

172. Málek F, Dvorák J, Jiresová E, Spacek R. Difference of baseline serum copper levels between groups of patients with different one year mortality and morbidity and chronic

heart failure. Cent Eur J Public Health. 2003 Dec;11(4):198-201
173. Leone N, Courbon D, Ducimetiere P, Zureik M. Zinc, copper, and magnesium and risks for all-cause, cancer, and cardiovascular mortality. Epidemiology. 2006 May;17(3):308-14. Unit 744 National Institute of Health and Medical Research (INSERM), Lille Pasteur Institute, Lille, France

Iron

High iron levels may increase the risk of dying in humans

174. Wu T, Sempos CT, Freudenheim JL, Muti P, Smit E. Serum iron, copper and zinc concentrations and risk of cancer mortality in US adults. Ann Epidemiol. 2004 Mar;14(3):195

Molybdenum

Higher molybdenum levels may protect against the risk of dying from cancer

175. Nakadaira H, Endoh K, Yamamoto M, Katoh K. Distribution of selenium and molybdenum and cancer mortality in Niigata, Japan. Arch Environ Health. 1995 Sep-Oct;50(5):374-80 Department of Hygiene and Preventive Medicine, Niigata University School Medicine, Japan

Selenium

High blood levels of selenium keeps the risk of dying from coronary heart disease or cancer low

176. Luoma PV, Nayha S, Sikkila K, Hassi J. High serum alpha-tocopherol, albumin, selenium and cholesterol, and low mortality from coronary heart disease in northern Finland. J Intern Med. 1995 Jan;237(1):49-54
177. Last KW, Cornelius V, Delves T, Sieniawska C, Fitzgibbon J, Norton A, Amess J, Wilson A, Rohatiner AZ, Lister TA. Presentation serum selenium predicts for overall survival, dose delivery, and first treatment response in aggressive non-Hodgkin's lymphoma. J Clin Oncol. 2003 Jun 15;21(12):2335-41. Cancer Research UK Medical Oncology Unit, Department of Medical Oncology, St Bartholomew's Hospital, London EC1M 6BQ, United Kingdom. kim.last@cancer.org.uk
178. Sakoda LC, Graubard BI, Evans AA, London WT, Lin WY, Shen FM, McGlynn KA. Toenail selenium and risk of hepatocellular carcinoma mortality in Haimen City, China. Int J Cancer. 2005 Jul 1;115(4):618-24. Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institute of Health, Department of Health and Human Services, Rockville, MD 20852, USA. sakodal@mail.nih.gov
179. Schrauzer GN, White DA, Schneider CJ. Cancer mortality correlation studies--III: statistical associations with dietary selenium intakes. Bioinorg Chem. 1977;7(1):23-31.
180. Vinceti M, Nacci G, Rocchi E, Cassinadri T, Vivoli R, Marchesi C, Bergomi M. Mortality in a population with long-term exposure to inorganic selenium via drinking water. J Clin Epidemiol. 2000 Oct;53(10):1062-8. Department of Hygiene, Microbiology and Biostatistics, University of Modena and Reggio Emilia, Modena, Via Campi 287-41100, Modena, Italy. vinceti@unimo.it

Inefficacy of selenium supplementation on cardiovascular mortality, but efficient reducer of cancer mortality

181. Stranges S, Marshall JR, Trevisan M, Natarajan R, Donahue RP, Combs GF, Farinaro E, Clark LC, Reid ME. Effects of selenium supplementation on cardiovascular disease incidence and mortality: secondary analyses in a randomized clinical trial. Am J Epidemiol. 2006 Apr 15;163(8):694-9. Department of Social and Preventive Medicine, State University of New York at Buffalo, Buffalo, NY 14214, USA. stranges@buffalo.edu
182. Combs GF Jr, Clark LC, Turnbull BW. Reduction of cancer mortality and incidence by selenium supplementation. Med Klin (Munich). 1997 Sep 15;92 Suppl 3:42-5. Division of Nutritional Sciences, Cornell University, Ithaca, NY, USA. gfc2@cornell.edu

Zinc

People with a lower zinc level die easier from all causes, and specifically from cardiovascular disease and cancer

183. Pilz S, Dobnig H, Winklhofer-Roob BM, Renner W, Seelhorst U, Wellnitz B, Boehm BO, März W. Low serum zinc concentrations predict mortality in patients referred to coronary angiography. Br J Nutr. 2009 May;101(10):1534-40. Department of Public Health, Social and Preventive Medicine, Mannheim Medical Faculty, University of Heidelberg, Ludolf-Krehl-Strasse 7-11, D-68167 Mannheim, Germany

Eating foods rich in zinc may protect alcohol drinkers against dying from cardiovascular disease

184. Lee DH, Folsom AR, Jacobs DR Jr. Iron, zinc, and alcohol consumption and mortality from cardiovascular diseases: the Iowa Women's Health Study. Am J Clin Nutr. 2005 Apr;81(4):787-91. Division of Epidemiology, School of Public Health, University of Minnesota, Minneapolis, MN, USA.

Zinc therapy prolongs life in humans

185. Clemons TE, Kurinij N, Sperduto RD. Associations of mortality with ocular disorders and an intervention of high-dose antioxidants and zinc in the Age-Related Eye Disease Study: AREDS Report No. 13. Arch Ophthalmol.2004 May;122(5):716-26
186. Sazawal S, Black RE, Menon VP, Dinghra P, Caulfield LE, Dhingra U, Bagati A. Zinc supplementation in infants born small for gestational age reduces mortality: a prospective, randomized, controlled trial. : Pediatrics. 2001 Dec;108(6):1280-6
187. Tielsch JM, Khatry SK, Stoltzfus RJ, Katz J, LeClerq SC, Adhikari R, Mullany LC, Black R, Shresta S. Effect of daily zinc supplementation on child mortality in southern Nepal: a community-based, cluster randomised, placebo-controlled trial. Lancet. 2007 Oct 6;370(9594):1230-9. Department of International Health, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD 21205-2013, USA. jtielsch@jhsp.edu
188. Sazawal S, Black RE, Ramsan M, Chwaya HM, Dutta A, Dhingra U, Stoltzfus RJ, Othman MK, Kabole FM. Effect of zinc supplementation on mortality in children aged 1-48 months: a community-based randomised placebo-controlled trial. Lancet. 2007 Mar 17;369(9565):927-34. Department of International Health, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD 21205, USA.

Zinc supplementation may prolong life in animals

189. Ogata H, Izumo Y. [Mortality reduction in mice administered a single abundant dose of zinc, manganese or magnesium after irradiation by gamma-rays at sublethal doses] Radioisotopes. 1990 Dec;39(12):573-6. Institute of Public Health, Tokyo, Japan.
190. Tocco-Bradley R, Kluger MJ. Zinc concentration and survival in rats infected with Salmonella typhimurium. Infect Immun. 1984 Aug;45(2):332-8.
191. Neggers YH, Singh J. Zinc supplementation to protein-deficient diet in CO-exposed mice decreased fetal mortality and malformation. Biol Trace Elem Res. 2006 Winter;114(1-3):269-79. Department of Human Nutrition, University of Alabama, Tuscaloosa, AL, USA.

Zinc therapy may prolong survival in mice with cancer

192. Song MK, Adham NF, Costea NV. Effect of different levels of dietary zinc on longevity of BALB/c mice inoculated with plasmacytoma MOPC 104E. J Natl Cancer Inst. 1984 Mar;72(3):647-52

The danger of administering high doses of zinc in children with protein calorie malnutrition

193. Doherty CP, Sarkar MA, Shakur MS, Ling SC, Elton RA, Cutting WA. Zinc and rehabilitation from severe protein-energy malnutrition: higher-dose regimens are associated with increased mortality. Am J Clin Nutr. 1998 Sep;68(3):742-8. Department of Child Life and Health, University of Edinburgh, Scotland, United Kingdom. cd1c@clinmed.gla.ac.uk

Aggravation of the adverse effects of low zinc levels on mortality by higher copper levels

194. Lai H, Lai S, Shor-Posner G, Ma F, Trapido E, Baum MK. Plasma zinc, copper, copper:zinc ratio, and survival in a cohort of HIV-1-infected homosexual men. J Acquir Immune Defic Syndr. 2001 May 1;27(1):56-62.

No effects of zinc supplementation on mortality

195. Bhandari N, Taneja S, Mazumder S, Bahl R, Fontaine O, Bhan MK; Zinc Study Group. Adding zinc to supplemental iron and folic acid does not affect mortality and severe morbidity in young children. J Nutr. 2007 Jan;137(1):112-7

Carnitine

Carnitine supplementation helps patients with heart disease to live longer

196. Davini P, Bigalli A, Lamanna F, Boem A. Controlled study on L-carnitine therapeutic efficacy in postinfarction. Drugs Exp Clin Res. 1992;18(8):355-65
197. Rizos I. Three-year survival of patients with heart failure caused by dilated cardiomyopathy and Lcarnitine administration. Am Heart J. 2000 Feb;139(2 Pt 3):S120-3. University of Athens Medical School, Greece.

Life saving effects of L-carnitine in animal studies

198. Geng A, Guo Y, Yuan J. Effects of dietary L-carnitine and coenzyme Q10 supplementation on performance and ascites mortality of broilers. Arch Anim Nutr. 2004 Dec;58(6):473-82. Department of Animal Nutrition and Feed Science, College of Animal Science and Technology, China Agricultural University, Beijing, P R China. ailiangengcau@126.com
199. Kawasaki N, Lee JD, Shimizu H, Ueda T. Long-term 1-carnitine treatment prolongs the survival in rats with adriamycin-induced heart failure. J Card Fail. 1996 Dec;2(4):293-9.
200. Takeyama N, Takagi D, Matsuo N, Kitazawa Y, Tanaka T. Altered hepatic fatty acid metabolism in endotoxicosis: effect of L-carnitine on survival. Am J Physiol. 1989 Jan;256(1 Pt 1):E31-8. First Department of Internal Medicine, Fukui Medical School, Japan.

Nutrient Supplements to Prolong Life

Since millions of years humans have tried to find ways to live longer.
A good life style, positive psychological attitudes, regular physical exercise, an improved diet, corrective hormone treatments, living in non-polluted areas may all help us to live longer.

Which nutritional supplements may help us to live longer?
In his quest to find ways to lengthen life, while improving the quality of life and physical appearance of his patients, Dr Hertoghe has extensively reviewed the scientific publications that show associations between a longer life and nutritional tissue levels or nutritional supplementations.
This book contains his overview of the topic.

Author: **Dr. Thierry Hertoghe**, born in 1957.
Dr. Thierry Hertoghe is a leading expert in anti-aging hormone therapies, focusing more and more on techniques that may reverse aging.
Starting as a general practitioner, Dr. Hertoghe focused on the use of hormones, extensively researching and developing hormone therapies for his patients.
In his family he is a forth generation doctor specializing in hormone and nutritional treatments.

Dr. Hertoghe is president of theWorld Society of Anti-Aging Medicine (WOSAAM) with over 7000 physicians and president of the International Hormone Society (IHS) with over 3000 physicians.
He supervises the international Anti-Aging Medicine Specialization and the Hormone Therapy Specialty programs, the post-graduate fellowships for physicians of the WOSAAM and HIS respectively.

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