Garland, C. F.; Comstock, G. W.; Garland, F. C.; Helsing, K. J.; Shaw, E. K.; Gorham, E. D. (1989): Serum 25-hydroxyvitamin D and colon cancer: eight-year prospective study. In: Lancet, Jg. 2, H. 8673, S. 1176–1178.

Abstract	Blood samples taken in 1974 in Washington County, Maryland, from 25 620 volunteers were used to investigate the relation of serum 25-hydroxyvitamin D (25-OHD) with subsequent risk of getting colon cancer. 34 cases of colon cancer diagnosed between August, 1975, and January, 1983, were matched to 67 controls by age, race, sex, and month blood was taken. Risk of colon cancer was reduced by 75% in the third quintile (27-32 ng/ml) and by 80% in the fourth quintile (33-41 ng/ml) of serum 25-OHD. Risk of getting colon cancer decreased three-fold in people with a serum 25-OHD concentration of 20 ng/ml or more. The results are consistent with a protective effect of serum 25-OHD on colon cancer.
Schlagwörter	25-Hydroxyvitamin D 2bloodmetabolism; Adult; Aged; Blood Specimen Collectionmethods; Carcinomabloodepidemiologymetabolismprevention & control; Colonic Neoplasmsbloodepidemiologymetabolismprevention & control; Female; Humans; Male; Maryland; Middle Aged; Prospective Studies; Risk Factors; Seasons; Time Factors

Garland, C. F.; Garland, F. C.; Gorham, E. D. (1991): Can colon cancer incidence and death rates be reduced with calcium and vitamin D. In: The American journal of clinical nutrition, Jg. 54, H. 1 Suppl, S. 193S-201S.

Abstract	It was proposed in 1980 that vitamin D and calcium could reduce the risk of colon cancer. This assertion was based on the decreasing gradient of mortality rates from north to south, suggesting a mechanism related to a favorable influence of ultraviolet-induced vitamin D metabolites on metabolism of calcium. A 19-y prospective study of 1954 Chicago men found that a dietary intake of greater than 3.75 micrograms vitamin D/d was associated with a 50% reduction in the incidence of colorectal cancer, whereas an intake of greater than or equal to 1200 mg Ca/d was associated with a 75% reduction. Clinical and laboratory studies further support these findings. A nested case-control study based on serum drawn from a cohort of 25,620 individuals reported that moderately elevated concentrations of 25-hydroxyvitamin D, in the range 65-100 nmol/L, were associated with large reductions (P less than 0.05) in the incidence of colorectal cancer.
Schlagwörter	Calcium, Dietarytherapeutic use; Colonic Neoplasmsepidemiologymortalityprevention & control; Female; Humans; Incidence; Male; Sex Factors; Sunlight; Vitamin Dtherapeutic use

Garland, C. F.; Garland, F. C.; Gorham, E. D. (1993): Rising trends in melanoma. An hypothesis concerning sunscreen effectiveness. In: Annals of epidemiology, Jg. 3, H. 1, S. 103–110.

Abstract	Incidence rates of melanoma have risen especially steeply since the mid-1970s. The two principal strategies for reduction of risk of melanoma and other skin cancers are sun avoidance and use of chemical sunscreens. Rising trends in the incidence of and mortality from melanoma have continued since the 1970s and 1980s, when sunscreens with high sun protection factors became widely used. Commonly used chemical sunscreens block ultraviolet B (UVB) but are virtually transparent to ultraviolet A (UVA), which makes up 90 to 95% of ultraviolet energy in the solar spectrum. Because sunscreens prevent erythema and sunburn, and inhibit accommodation of the skin to sunlight, their use may permit excessive exposure of the skin to portions of the solar spectrum other than UVB. If melanoma and basal cell carcinoma are initiated or promoted by solar radiation other than UVB, as laboratory data suggest, then UVB sunscreens might not be effective in preventing these cancers, and sunscreen use might increase the risk of their occurrence. Alternative explanations for the rapid rise in the incidence and mortality rates of melanoma, such as changes in patterns of recreational sun exposure, are discussed. Traditional means of limiting overexposure to the sun, such as wearing of hats and adequate clothing and avoidance of prolonged sunbathing, may be more prudent than reliance on chemical sunscreens.

Schlagwörter	Carcinoma, Basal Cellepidemiologyprevention & control; Female; Humans; Incidence; Male; Melanomaepidemiologyprevention & control; Neoplasms, Radiation-Inducedepidemiologyprevention & control; Risk Factors; Skinradiation effects; Skin Neoplasmsepidemiologyprevention & control; Sunscreening Agentsadministration & dosageadverse effects; Ultraviolet Raysadverse effects

Garland, C. F.; Garland, F. C.; Gorham, E. D. (1994): Melanoma incidence in Connecticut. In: Cancer causes & control : CCC, Jg. 5, H. 6, S. 581–582.

Schlagwörter	Connecticutepidemiology; Humans; Incidence; Melanomaepidemiology

Garland, C. F.; Garland, F. C.; Gorham, E. D. (1994): Re: Effect of sunscreens on UV radiation-induced enhancement of melanoma growth in mice. In: Journal of the National Cancer Institute, Jg. 86, H. 10, S. 798–800.

Schlagwörter	Animals; Humans; Melanomaprevention & control; Melanoma, Experimentaletiologyprevention & control; Mice; Skin Neoplasmsprevention & control; Sunscreening Agentspharmacology; Ultraviolet Raysadverse effects

Garland, C. F.; Garland, F. C.; Gorham, E. D. (1999): Calcium and vitamin D. Their potential roles in colon and breast cancer prevention. In: Annals of the New York Academy of Sciences, Jg. 889, S. 107–119.

Abstract	The geographic distribution of colon cancer is similar to the historical geographic distribution of rickets. The highest death rates from colon cancer occur in areas that had high prevalence rates of rickets--regions with winter ultraviolet radiation deficiency, generally due to a combination of high or moderately high latitude, high-sulfur content air pollution (acid haze), higher than average stratospheric ozone thickness, and persistently thick winter cloud cover. The geographic distribution of colon cancer mortality rates reveals significantly low death rates at low latitudes in the United States and significantly high rates in the industrialized Northeast. The Northeast has a combination of latitude, climate, and air pollution that prevents any synthesis of vitamin D during a five-month vitamin D winter. Breast cancer death rates in white women also rise with distance from the equator and are highest in areas with long vitamin D winters. Colon cancer incidence rates also have been shown to be inversely proportional to intake of calcium. These findings, which are consistent with laboratory results, indicate that most cases of colon cancer may be prevented with regular intake of calcium in the range of 1,800 mg per day, in a dietary context that includes 800 IU per day (20 micrograms) of vitamin D3. (In women, an intake of approximately 1,000 mg of calcium per 1,000 kcal of energy with 800 IU of vitamin D would be sufficient.) In observational studies, the source of approximately 90% of the calcium intake was vitamin D-fortified milk. Vitamin D may also be obtained from fatty fish. In addition to reduction of incidence and mortality rates from colon cancer, epidemiological data suggest that intake of 800 IU/day of vitamin D may be associated with enhanced survival rates among breast cancer cases.
Schlagwörter	Breast Neoplasmsmetabolismmortalityprevention & control; Calciumadministration & dosagemetabolism; Colonic Neoplasmsmetabolismmortalityprevention & control; Diet; Female; Humans; Survival Analysis; United States; Vitamin Dadministration & dosagemetabolism

Garland, Cedric F.; Garland, Frank C.; Gorham, Edward D. (2003): Epidemiologic evidence for different roles of ultraviolet A and B radiation in melanoma mortality rates. In: Annals of epidemiology, Jg. 13, H. 6, S. 395–404.

Abstract	PURPOSE: The action spectrum of ultraviolet radiation mainly responsible for melanoma induction is unknown, but evidence suggests it could be ultraviolet A (UVA), which has a different geographic distribution than ultraviolet B (UVB). This study assessed whether melanoma mortality rates are more closely related to the global distribution of UVA or UVB. METHODS: UVA and UVB radiation and age-adjusted melanoma mortality rates were obtained for all 45 countries reporting cancer data to the World Health Organization. Stratospheric ozone data were

	obtained from NASA satellites. Average population skin pigmentation was obtained from skin reflectometry measurements. RESULTS: Paradoxically, melanoma mortality rates decreased with increasing UVB in men (r = -0.48, p < 0.001), and women (r = -0.57, p < 0.001), and with increasing UVA in both sexes. By contrast, rates were positively associated with increasing UVA/UVB ratio in men (r = + 0.49, p < 0.001) and women (r = + 0.55, p < 0.001). After multiple adjustment that included controlling for skin pigmentation, only UVA was associated with melanoma mortality rates in men (p < 0.02) with a suggestive but non-significant trend present in women (p = 0.12). CONCLUSIONS: UVA radiation was associated with melanoma mortality rates after controlling for UVB and average pigmentation. The results require confirmation in observational studies.
Schlagwörter	Female; Geography; Humans; Incidence; Male; Melanomaetiologymortality; Neoplasms, Radiation-Inducedetiologymortality; Ozone; Radiation Monitoring; Skin Neoplasmsetiologymortality; Skin Pigmentation; Sunlightadverse effects; Ultraviolet Raysadverse effectsclassification; World Health

Garland, Cedric F.; Garland, Frank C.; Gorham, Edward D.; Lipkin, Martin; Newmark, Harold; Mohr, Sharif B.; Holick, Michael F. (2006): The role of vitamin D in cancer prevention. In: American journal of public health, Jg. 96, H. 2, S. 252–261. Online verfügbar unter doi:10.2105/AJPH.2004.045260.

Abstract	Vitamin D status differs by latitude and race, with residents of the northeastern United States and individuals with more skin pigmentation being at increased risk of deficiency. A PubMed database search yielded 63 observational studies of vitamin D status in relation to cancer risk, including 30 of colon, 13 of breast, 26 of prostate, and 7 of ovarian cancer, and several that assessed the association of vitamin D receptor genotype with cancer risk.The majority of studies found a protective relationship between sufficient vitamin D status and lower risk of cancer. The evidence suggests that efforts to improve vitamin D status, for example by vitamin D supplementation, could reduce cancer incidence and mortality at low cost, with few or no adverse effects.
Schlagwörter	Breast Neoplasmsepidemiology; Colorectal Neoplasmsepidemiology; Continental Population Groupsstatistics & numerical data; Female; Humans; Male; Neoplasmsepidemiologyprevention & control; Prostatic Neoplasmsepidemiology; United Statesepidemiology; Vitamin Dadministration & dosagebloodtherapeutic use; Vitamin D Deficiencybloodepidemiology

Garland, Cedric F.; Gorham, Edward D.; Baggerly, Carole A.; Garland, Frank C. (2008): Re: Prospective study of vitamin D and cancer mortality in the United States. In: Journal of the National Cancer Institute, Jg. 100, H. 11, S. 826–827. Online verfügbar unter doi:10.1093/jnci/djn041.

Schlagwörter	Anticarcinogenic Agentsblood; Breast Neoplasmsbloodmortality; Colorectal Neoplasmsbloodmortality; Female; Humans; Incidence; Male; Neoplasmsbloodepidemiologymortalityprevention & control; Prospective Studies; Sunlight; Ultraviolet Rays; United Statesepidemiology; Vitamin Danalogs & derivativesblood

Garland, Cedric F.; Gorham, Edward D.; Mohr, Sharif B.; Garland, Frank C. (2009): Vitamin D for cancer prevention: global perspective. In: Annals of epidemiology, Jg. 19, H. 7, S. 468–483. Online verfügbar unter doi:10.1016/j.annepidem.2009.03.021.

Abstract	PURPOSE: Higher serum levels of the main circulating form of vitamin D, 25-hydroxyvitamin D (25(OH)D), are associated with substantially lower incidence rates of colon, breast, ovarian, renal, pancreatic, aggressive prostate and other cancers. METHODS: Epidemiological findings combined with newly discovered mechanisms suggest a new model of cancer etiology that accounts for these actions of 25(OH)D and calcium. Its seven phases are disjunction, initiation, natural selection, overgrowth, metastasis, involution, and transition (abbreviated DINOMIT). Vitamin D metabolites prevent disjunction of cells and are beneficial in other phases. RESULTS/CONCLUSIONS: It is projected that raising the minimum year-

around serum 25(OH)D level to 40 to 60 ng/mL (100-150 nmol/L) would prevent approximately 58,000 new cases of breast cancer and 49,000 new cases of colorectal cancer each year, and three fourths of deaths from these diseases in the United States and Canada, based on observational studies combined with a randomized trial. Such intakes also are expected to reduce case-fatality rates of patients who have breast, colorectal, or prostate cancer by half. There are no unreasonable risks from intake of 2000 IU per day of vitamin D(3), or from a population serum 25(OH)D level of 40 to 60 ng/mL. The time has arrived for nationally coordinated action to substantially increase intake of vitamin D and calcium.

Garland, Cedric F.; Gorham, Edward D.; Mohr, Sharif B.; Grant, William B.; Giovannucci, Edward L.; Lipkin, Martin et al. (2007): Vitamin D and prevention of breast cancer: pooled analysis. In: The Journal of steroid biochemistry and molecular biology, Jg. 103, H. 3-5, S. 708–711. Online verfügbar unter doi:10.1016/j.jsbmb.2006.12.007.

Abstract: BACKGROUND: Inadequate photosynthesis or oral intake of Vitamin D are associated with high incidence and mortality rates of breast cancer in ecological and observational studies, but the dose-response relationship in individuals has not been adequately studied. METHODS: A literature search for all studies that reported risk by of breast cancer by quantiles of 25(OH)D identified two studies with 1760 individuals. Data were pooled to assess the dose-response association between serum 25(OH)D and risk of breast cancer. RESULTS: The medians of the pooled quintiles of serum 25(OH)D were 6, 18, 29, 37 and 48 ng/ml. Pooled odds ratios for breast cancer from lowest to highest quintile, were 1.00, 0.90, 0.70, 0.70 and 0.50 (p trend<0.001). According to the pooled analysis, individuals with serum 25(OH)D of approximately 52 ng/ml had 50% lower risk of breast cancer than those with serum <13 ng/ml. This serum level corresponds to intake of 4000 IU/day. This exceeds the National Academy of Sciences upper limit of 2000 IU/day. A 25(OH)D level of 52 ng/ml could be maintained by intake of 2000 IU/day and, when appropriate, about 12 min/day in the sun, equivalent to oral intake of 3000 IU of Vitamin D(3). CONCLUSIONS: Intake of 2000 IU/day of Vitamin D(3), and, when possible, very moderate exposure to sunlight, could raise serum 25(OH)D to 52 ng/ml, a level associated with reduction by 50% in incidence of breast cancer, according to observational studies.

Schlagwörter: Administration, Oral; Breast Neoplasmsepidemiologypathologyprevention & control; Humans; Risk Factors; Vitamin Dadministration & dosagebloodpharmacology

Garland, Cedric F.; Grant, William B.; Mohr, Sharif B.; Gorham, Edward D.; Garland, Frank C. (2007): What is the dose-response relationship between vitamin D and cancer risk. In: Nutrition reviews, Jg. 65, H. 8 Pt 2, S. S91-5.

Schlagwörter: Anticarcinogenic Agentsadministration & dosage; Dose-Response Relationship, Drug; Humans; Neoplasmsepidemiologyetiology; Risk Factors; Vitamin Dadministration & dosage

Garland, Cedric F.; Mohr, Sharif B.; Gorham, Edward D.; Grant, William B.; Garland, Frank C. (2006): Role of ultraviolet B irradiance and vitamin D in prevention of ovarian cancer. In: American journal of preventive medicine, Jg. 31, H. 6, S. 512–514. Online verfügbar unter doi:10.1016/j.amepre.2006.08.018.

Abstract: BACKGROUND: There is a north-south gradient in age-adjusted mortality rates of ovarian cancer in the United States, with the highest rates in the Northeast and the lowest in the South through Southwest. This suggests that lower levels of solar irradiance might be associated with higher risk of ovarian cancer. Laboratory findings also suggest that low levels of vitamin D metabolites could play a role in the etiology of ovarian cancer. METHODS: The association of solar ultraviolet B (UVB) irradiance, stratospheric column ozone, and fertility rates at ages 15 to 19 years with incidence rates of ovarian cancer in 175 countries in 2002 were examined using multiple linear regression in 2006. RESULTS: Age-adjusted ovarian cancer

	incidence rates generally were highest in countries located at higher latitudes (R(2)=0.45, p< or =0.01). According to multivariate analysis, UVB irradiance (p< or =0.002) and fertility rates at ages 15 to 19 (p=0.01) were inversely associated with incidence rates, while stratospheric ozone (p< or =0.0008), which reduces transmission of UVB, was positively associated with incidence (R(2)=0.49, p<0.0001). CONCLUSIONS: Solar UVB irradiance was inversely associated with incidence rates of ovarian cancer in this study, adding new evidence to the theory that vitamin D might play a role in the prevention of ovarian cancer. Cohort studies are needed to confirm this possible association.
Schlagwörter	Adolescent; Adult; Female; Geography; Humans; Incidence; Ovarian Neoplasmsepidemiologyphysiopathologyprevention & control; Ozone; Sunlight; Ultraviolet Rays; Vitamin Dphysiology

Garland, F. C.; Garland, C. F.; Gorham, E. D.; Young, J. F. (1990): Geographic variation in breast cancer mortality in the United States: a hypothesis involving exposure to solar radiation. In: Preventive medicine, Jg. 19, H. 6, S. 614–622.

Abstract	Epidemiologic and laboratory evidence suggests that vitamin D may play a role in reducing breast cancer risk. Lack of exposure to ultraviolet sunlight can increase the prevalence of vitamin D deficiency. This deficiency may place some populations at higher risk for breast cancer. The association between total average annual sunlight energy striking the ground and age-adjusted breast cancer mortality rates in 87 regions of the United States was evaluated. Annual age-adjusted mortality rates for breast cancer varied over a 1.8-fold range, from 17-19 per 100,000 in the South and Southwest United States to 33 per 100,000 in the Northeast; the overall U.S. rate was 27.3 per 100,000. Risk of fatal breast cancer in the major urban areas of the United States was inversely proportional to intensity of local sunlight (r = -0.80, P = 0.0001); multiple regression with stratospheric ozone measurements, r = -0.82, P = 0.0001). Vitamin D from sunlight exposure may be associated with low risk for fatal breast cancer, and differences in ultraviolet light reaching the United States population may account for the striking regional differences in breast cancer mortality. The ecological nature of this study is emphasized, and the possibility that an indirect association with dietary and socioeconomic factors could explain these findings is discussed.
Schlagwörter	Age Factors; Breast Neoplasmsepidemiologyetiologymortality; Female; Humans; Ozoneanalysis; Prevalence; Risk Factors; Socioeconomic Factors; Sunlight; United Statesepidemiology; Urbanization; Vitamin D Deficiencycomplicationsepidemiologyetiology

Garland, F. C.; Gorham, E. D.; Garland, C. F. (1994): Effect of occupational and recreational activity on the risk of colorectal cancer among males: a case-control study. In: International journal of epidemiology, Jg. 23, H. 3, S. 645.

Schlagwörter	Case-Control Studies; Colorectal Neoplasmsepidemiologyprevention & control; Humans; Male; Occupations; Recreation; Risk Factors

Garland, F. C.; Shaw, E.; Gorham, E. D.; Garland, C. F.; White, M. R.; Sinsheimer, P. J. (1990): Incidence of leukemia in occupations with potential electromagnetic field exposure in United States Navy personnel. In: American journal of epidemiology, Jg. 132, H. 2, S. 293–303.

Abstract	Leukemia is the fourth most commonly occurring cancer in the United States population between the ages of 17 and 34 years, an age group heavily represented in the US Navy. Historical computerized military career records maintained at the Naval Health Research Center, San Diego, California, were used to determine person-years at risk (total, 4,072,502 person-years) by demographic characteristics and occupation for active-duty naval personnel during 1974-1984. Computerized inpatient medical records were searched for first hospitalizations for leukemia. Cases of leukemia (n = 102) were verified by using pathology reports or Navy Medical Board or Physical Evaluation Board findings. For comparisons, age-

	adjusted incidence rates and standardized incidence ratios were calculated by using rates for the US population provided by the Surveillance, Epidemiology, and End Results program of the National Cancer Institute. The overall age-adjusted incidence rate of leukemia in active-duty naval personnel was found to be very close to that of the Surveillance, Epidemiology, and End Results program population (6.0 vs. 6.5 per 100,000 person-years). Only one occupation, electrician's mate, emerged with a borderline statistically significant excess risk of leukemia (standardized incidence ratio compared with the Surveillance, Epidemiology, and End Results program population = 2.4, 95% confidence interval 1.0-5.0). This finding is intriguing in the light of several studies showing an excess risk of leukemia associated with exposure to electromagnetic fields.
Schlagwörter	Adolescent; Adult; Aged; Calciumphysiology; Electromagnetic Fields; Electromagnetic Phenomena; Environmental Exposure; Humans; Incidence; Leukemiaepidemiologyetiologyphysiopathology; Male; Middle Aged; Military Personnel; Occupations; Prospective Studies; Risk Factors; Vitamin Dphysiology

Garland, F. C.; White, M. R.; Garland, C. F.; Shaw, E.; Gorham, E. D.: Occupational sunlight exposure and melanoma in the U.S. Navy. In: Archives of environmental health, Jg. 45, H. 5, S. 261–267.

Abstract	Melanoma is the second most common cancer, after testicular cancer, in males in the U.S. Navy. A wide range of occupations with varying exposures to sunlight and other possible etiologic agents are present in the Navy. Person-years at risk and cases of malignant melanoma were ascertained using computerized service history and inpatient hospitalization files maintained at the Naval Health Research Center. A total of 176 confirmed cases of melanoma were identified in active-duty white male enlisted Navy personnel during 1974-1984. Risk of melanoma was determined for individual occupations and for occupations grouped by review of job descriptions into three categories of sunlight exposure: (1) indoor, (2) outdoor, or (3) indoor and outdoor. Compared with the U.S. civilian population, personnel in indoor occupations had a higher age-adjusted incidence rate of melanoma, i.e., 10.6 per 100,000 (p = .06). Persons who worked in occupations that required spending time both indoors and outdoors had the lowest rate, i.e., 7.0 per 100,000 (p = .06). Incidence rates of melanoma were higher on the trunk than on the more commonly sunlight-exposed head and arms. Two single occupations were found to have elevated rates of melanoma: (1) aircrew survival equipmentman, SIR = 6.8 (p less than .05); and (2) engineman, SIR = 2.8 (p less than .05). However, there were no cases of melanoma or no excess risk in occupations with similar job descriptions. Findings on the anatomical site of melanoma from this study suggest a protective role for brief, regular exposure to sunlight and fit with recent laboratory studies that have shown vitamin D to suppress growth of malignant melanoma cells in tissue culture. A mechanism is proposed in which vitamin D inhibits previously initiated melanomas from becoming clinically apparent.
Schlagwörter	Adolescent; Adult; Environmental Exposure; Humans; Male; Melanomaepidemiologyetiology; Middle Aged; Military Personnel; Occupations; Skin Neoplasmsepidemiologyetiology; Sunlightadverse effects; United States

Gorham, E. D.; Garland, F. C.; Garland, C. F. (1990): Sunlight and breast cancer incidence in the USSR. In: International journal of epidemiology, Jg. 19, H. 4, S. 820–824.

Abstract	Epidemiological and laboratory evidence suggest that vitamin D may play a role in reducing risk of breast cancer. Lack of exposure to ultraviolet sunlight can increase the prevalence of vitamin D deficiency, and may place some populations at higher risk of breast cancer. The association between total average annual sunlight energy striking the ground and age-adjusted breast cancer incidence rates in the USSR was evaluated. Breast cancer had a threefold range of incidence. Sunlight levels varied from 210 to 400 calories per cm2 per day. A statistically significant negative association was found between breast cancer incidence rates and total sunlight levels (R = -0.75, p = 0.001). The slope of the regression line corresponded to two

	additional cases per 100,000 per year for each reduction of 35 calories per cm2 of sunlight. The pattern of increased breast cancer incidence in regions of low solar radiation in the USSR is consistent with the geographical pattern seen for breast cancer mortality in the US and worldwide. A positive relationship between socioeconomic status and breast cancer incidence was also present in the Soviet Union, based on an approximate socioeconomic measure, the number of doctors per 1000 population (R = +0.89, p = 0.0001). The possibility that correlates of socioeconomic status, such as dietary, ethnic, or behavioural factors, could account for the association is discussed.
Schlagwörter	Breast Neoplasmsepidemiology; Environmental Exposure; Female; Humans; Incidence; Socioeconomic Factors; Sunlight; USSRepidemiology; Vitamin D

Gorham, Edward D.; Garland, Cedric F.; Garland, Frank C.; Grant, William B.; Mohr, Sharif B.; Lipkin, Martin et al. (2005): Vitamin D and prevention of colorectal cancer. In: The Journal of steroid biochemistry and molecular biology, Jg. 97, H. 1-2, S. 179–194. Online verfügbar unter doi:10.1016/j.jsbmb.2005.06.018.

Abstract	BACKGROUND: Inadequate photosynthesis or oral intake of Vitamin D are associated with high incidence rates of colorectal cancer, but the dose-response relationship has not been adequately studied. METHODS: Dose-response gradients from observational studies of Vitamin D intake and serum 25-hydroxyvitamin D were plotted as trend lines. The point on each linear trend line corresponding to an odds ratio of 0.50 provided the prediagnostic Vitamin D intake or 25-hydroxyvitamin D concentration associated with 50% lower risk compared to <100IU/day Vitamin D or <13ng/ml serum 25-hydroxyvitamin D. Medians of these values were determined. RESULTS: Overall, individuals with >or=1000IU/day oral Vitamin D (p<0.0001) or >or=33ng/ml (82nmol/l) serum 25-hydroxyvitamin D (p<0.01) had 50% lower incidence of colorectal cancer compared to reference values. CONCLUSIONS: Intake of 1000IU/day of Vitamin D, half the safe upper intake established by the National Academy of Sciences, was associated with 50% lower risk. Serum 25-hydroxyvitamin D of 33ng/ml, which is known to be safe, also was associated with 50% lower risk. Prompt public health action is needed to increase intake of Vitamin D(3) to 1000IU/day, and to raise 25-hydroxyvitamin D by encouraging a modest duration of sunlight exposure.
Schlagwörter	Calciummetabolism; Case-Control Studies; Clinical Trials as Topic; Colorectal Neoplasmsepidemiologymetabolismprevention & control; Female; Humans; Incidence; MEDLINE; Male; Vitamin Dadministration & dosagebloodpharmacology

Gorham, Edward D.; Garland, Cedric F.; Garland, Frank C.; Grant, William B.; Mohr, Sharif B.; Lipkin, Martin et al. (2007): Optimal vitamin D status for colorectal cancer prevention: a quantitative meta analysis. In: American journal of preventive medicine, Jg. 32, H. 3, S. 210–216. Online verfügbar unter doi:10.1016/j.amepre.2006.11.004.

Abstract	BACKGROUND: Previous studies, such as the Women's Health Initiative, have shown that a low dose of vitamin D did not protect against colorectal cancer, yet a meta-analysis indicates that a higher dose may reduce its incidence. METHODS: Five studies of serum 25(OH)D in association with colorectal cancer risk were identified using PubMed. The results of all five serum studies were combined using standard methods for pooled analysis. The pooled results were divided into quintiles with median 25(OH)D values of 6, 16, 22, 27, and 37 ng/mL. Odds ratios were calculated by quintile of the pooled data using Peto's Assumption-Free Method, with the lowest quintile of 25(OH)D as the reference group. A dose-response curve was plotted based on the odds for each quintile of the pooled data. Data were abstracted and analyzed in 2006. RESULTS: Odds ratios for the combined serum 25(OH)D studies, from lowest to highest quintile, were 1.00, 0.82, 0.66, 0.59, and 0.46 (p(trend)<0.0001) for colorectal cancer. According to the DerSimonian-Laird test for homogeneity of pooled data, the studies were homogeneous (chi(2)=1.09, df=4, p=0.90. The pooled odds ratio for the highest quintile versus the lowest was 0.49 (p<0.0001, 95% confidence interval, 0.35-0.68). A 50% lower risk of colorectal

	cancer was associated with a serum 25(OH)D level > or =33 ng/mL, compared to < or =12 ng/mL. CONCLUSIONS: The evidence to date suggests that daily intake of 1000-2000 IU/day of vitamin D(3) could reduce the incidence of colorectal with minimal risk.
Schlagwörter	Californiaepidemiology; Colorectal Neoplasmsepidemiologyprevention & control; Dose-Response Relationship, Drug; Humans; Incidence; Nutritional Status; Odds Ratio; Preventive Medicine; Risk Factors; Vitamin Dadministration & dosageadverse effectsblood

Gorham, Edward D.; Mohr, Sharif B.; Garland, Cedric F.; Chaplin, George; Garland, Frank C. (2007): Do sunscreens increase risk of melanoma in populations residing at higher latitudes. In: Annals of epidemiology, Jg. 17, H. 12, S. 956–963. Online verfügbar unter doi:10.1016/j.annepidem.2007.06.008.

Abstract	BACKGROUND: Sunscreens may allow overexposure to ultraviolet A (UVA) in fair-skinned persons and prevent symptoms of sunburn, but their benefits for the prevention of melanoma are uncertain. METHODS: A PubMed search was performed that identified all known studies of the association of sunscreen use with melanoma risk during 1966-2007. A total of 18 studies were identified, of which 17 met criteria for inclusion in the analysis. Of these, 10 were conducted at latitudes >40 degrees from the equator and 7 at <or=40 degrees . Data were pooled for all latitudes combined and also according to these latitude strata. The association of skin pigmentation and latitude with odds ratios was estimated using linear regression. RESULTS: Overall, there was no statistically significant effect of use of sunscreens on risk of melanoma (odds ratio 1.2, 95% confidence interval [95% CI] 0.9-1.6; p for heterogeneity < 0.0001). However, there was an interaction with latitude. At >40 degrees from the equator, the odds ratio was 1.6 (95% C.I. 1.3-1.9; p for heterogeneity = 0.006), whereas it was 0.7 at <or=40 degrees (95% C.I. 0.4-1.0; p for heterogeneity = 0.0002). CONCLUSIONS: Use of common sunscreen formulations that absorb UVB almost completely, but transmit large quantities of UVA, may contribute to risk of melanoma in populations at latitudes >40 degrees.
Schlagwörter	Case-Control Studies; Geography; Humans; Melanomaepidemiologyetiologyprevention & control; Neoplasms, Radiation-Inducedepidemiologyetiologyprevention & control; Risk Factors; Skin Neoplasmsepidemiologyetiologyprevention & control; Skin Pigmentationdrug effectsradiation effects; Sunscreening Agentsadministration & dosageadverse effects; Ultraviolet Raysadverse effects

Grant, William B.; Cross, Heide S.; Garland, Cedric F.; Gorham, Edward D.; Moan, Johan; Peterlik, Meinrad et al. (2009): Estimated benefit of increased vitamin D status in reducing the economic burden of disease in western Europe. In: Progress in biophysics and molecular biology. Online verfügbar unter doi:10.1016/j.pbiomolbio.2009.02.003.

Abstract	Vitamin D has important benefits in reducing the risk of many conditions and diseases. Those diseases for which the benefits are well supported and that have large economic effects include many types of cancer, cardiovascular diseases, diabetes mellitus, several bacterial and viral infections, and autoimmune diseases such as multiple sclerosis. Europeans generally have low serum 25-hydroxyvitamin D [25(OH)D] levels owing to the high latitudes, largely indoor living, low natural dietary sources of vitamin D such as cold-water ocean fish, and lack of effective vitamin D fortification of food in most countries. Vitamin D dose-disease response relations were estimated from observational studies and randomized controlled trials. The reduction in direct plus indirect economic burden of disease was based on increasing the mean serum 25(OH)D level to 40ng/mL, which could be achieved by a daily intake of 2000-3000IU of vitamin D. For 2007, the reduction is estimated at euro187,000 million/year. The estimated cost of 2000-3000IU of vitamin D3/day along with ancillary costs such as education and testing might be about euro10,000 million/year. Sources of vitamin D could include a combination of food fortification, supplements, and natural and artificial UVB irradiation, if properly acquired.

Additional randomized controlled trials are warranted to evaluate the benefits and risks of vitamin D supplementation. However, steps to increase serum 25(OH)D levels can be implemented now based on what is already known.

Grant, William B.; Garland, Cedric F.; Gorham, Edward D. (2007): An estimate of cancer mortality rate reductions in Europe and the US with 1,000 IU of oral vitamin D per day. In: Recent results in cancer research. Fortschritte der Krebsforschung. Progrès dans les recherches sur le cancer, Jg. 174, S. 225–234.

Abstract: Solar ultraviolet B (UVB) irradiance and/or vitamin D have been found inversely correlated with incidence, mortality, and/or survival rates for breast, colorectal, ovarian, and prostate cancer and Hodgkin's and non-Hodgkin's lymphoma. Evidence is emerging that more than 17 different types of cancer are likely to be vitamin D-sensitive. A recent meta-analysis concluded that 1,000 IU of oral vitamin D per day is associated with a 50% reduction in colorectal cancer incidence. Using this value, as well as the findings in a multifactorial ecologic study of cancer mortality rates in the US, estimates for reductions in risk of vitamin D-sensitive cancer mortality rates were made for 1,000 IU/day. These estimates, along with annual average serum 25-hydroxyvitamin D levels, were used to estimate the reduction in cancer mortality rates in several Western European and North American countries that would result from intake of 1,000 IU/day of vitamin D. It was estimated that reductions could be 7% for males and 9% for females in the US and 14% for males and 20% for females in Western European countries below 59 degrees. It is proposed that increased fortification of food and increased availability of supplements could help increase vitamin D intake and could augment small increases in production of vitamin D from solar UVB irradiance. Providing 1,000 IU of vitamin D per day for all adult Americans would cost about $1 billion; the expected benefits for cancer would be in the range of $16-25 billion in addition to other health benefits of vitamin D.

Schlagwörter: Administration, Oral; Europe; Humans; Neoplasmsmortalityprevention & control; Risk Reduction Behavior; United States; Vitamin Dadministration & dosage

Mohr, S. B.; Garland, C. F.; Gorham, E. D.; Garland, F. C. (2008): The association between ultraviolet B irradiance, vitamin D status and incidence rates of type 1 diabetes in 51 regions worldwide. In: Diabetologia, Jg. 51, H. 8, S. 1391–1398. Online verfügbar unter doi:10.1007/s00125-008-1061-5.

Abstract: AIMS/HYPOTHESIS: This study is an analysis of the relationship between ultraviolet B (UVB) irradiance, the primary source of circulating vitamin D in humans, and age-standardised incidence rates of type 1 diabetes mellitus in children, according to region of the world. METHODS: The association of UVB irradiance adjusted for cloud cover to incidence rates of type 1 diabetes in children aged <14 years during 1990--1994 in 51 regions worldwide was assessed using multiple regression. Incidence data were obtained from the Diabetes Mondial Project Group. RESULTS: Incidence rates were generally higher at higher latitudes ($R2 = 0.25$, $p < 0.001$). According to multiple regression, UVB irradiance adjusted for cloud cover was inversely associated with incidence rates ($p < 0.05$), while per capita health expenditure ($p < 0.004$) was positively associated (overall $R2 = 0.42$, $p < 0.0001$). CONCLUSIONS/INTERPRETATION: An association was found between low UVB irradiance and high incidence rates of type 1 childhood diabetes after controlling for per capita health expenditure. Incidence rates of type 1 diabetes approached zero in regions worldwide with high UVB irradiance, adding new support to the concept of a role of vitamin D in reducing the risk of the disease.

Schlagwörter: Adolescent; Calcifedioltherapeutic use; Child; Diabetes Mellitus, Type 1complicationsepidemiologyprevention & control; Geography; Humans; Regression Analysis; Ultraviolet Rays; Vitamin Dtherapeutic use; Vitamin D Deficiencycomplicationsepidemiology

Mohr, S. B.; Garland, C. F.; Gorham, E. D.; Grant, W. B.; Garland, F. C. (2008): Could ultraviolet B irradiance and vitamin D be associated with lower incidence rates of lung cancer. In: Journal of epidemiology and

community health, Jg. 62, H. 1, S. 69–74. Online verfügbar unter doi:10.1136/jech.2006.052571.

Abstract	BACKGROUND: This study examines whether insufficient ultraviolet B (UVB) irradiance, a marker of vitamin D inadequacy, might contribute to lung cancer incidence. METHODS: The association of latitude and UVB irradiance with age-adjusted incidence rates of lung cancer in 111 countries was investigated. Independent associations with UVB irradiance, cloud cover, anthropogenic aerosols, and cigarette smoking, were assessed using multiple regression. RESULTS: Latitude was positively related to incidence rates in men ($R(2) = 0.55$, $p<0.01$) and women ($R(2) = 0.36$, $p<0.01$). In men, cigarette consumption ($p<0.001$) was positively related to risk, whereas UVB irradiance was inversely associated ($p = 0.003$). There were positive associations with UVB absorbers, in particular cloud cover ($p = 0.05$) and aerosol optical depth ($p = 0.005$). The $R(2)$ for the model was 0.78 ($p<0.001$). UVB irradiance was also inversely associated with incidence rates in women ($p = 0.0002$), whereas cigarette consumption ($p<0.001$), total cloud cover ($p = 0.02$) and aerosol optical depth ($p = 0.005$) were positively associated. The $R(2)$ for the model was 0.77 ($p<0.001$). CONCLUSIONS: Lower levels of UVB irradiance were independently associated with higher incidence rates of lung cancer in 111 countries.
Schlagwörter	Aerosols; Atmospherechemistry; Environmental Exposureanalysis; Epidemiologic Methods; Female; Humans; Lung Neoplasmsepidemiologyetiologyprevention & control; Male; Smokingadverse effectsepidemiology; Sunlight; Ultraviolet Rays; Vitamin D Deficiencycomplicationsepidemiology

Mohr, Sharif B. (2009): A brief history of vitamin d and cancer prevention. In: Annals of epidemiology, Jg. 19, H. 2, S. 79–83. Online verfügbar unter doi:10.1016/j.annepidem.2008.10.003.

Abstract	PURPOSE: To review the history of vitamin D and its use in cancer prevention. METHODS: The literature on published studies of vitamin D and its role in human health was reviewed and summarized. RESULTS: The modern history of vitamin D began in the mid-1800s, when it was noticed that city children were more likely to have rickets than rural children. Half a century later, Palm reported that children raised in sunny climates virtually never developed rickets. McCollum isolated vitamin D, and Windaus its precursors, receiving the Nobel Prize. Other scientists later observed that people with skin cancer had lower prevalence of nonskin cancers, and that lower overall mortality rates from all internal cancers combined existed in sunnier areas. These observations went largely unnoticed, and the field stagnated until 1970, when maps were created of cancer mortality rates. Through study of these maps, Cedric and Frank Garland of Johns Hopkins University reported a strong latitudinal gradient for colon cancer mortality rates in 1980, and hypothesized that higher levels of vitamin D compounds in the serum of people in the south were responsible, and that calcium intake also would reduce incidence. Edward Gorham and colleagues carried out cohort and nested studies, including the first study that found an association of a serum vitamin D compound with reduced cancer risk. William B. Grant then carried out numerous ecologic studies that extended the vitamin D-cancer theory to other cancers. CONCLUSIONS: The history of the role of vitamin D in human health is rich and much of that history is yet to be written not only by scientists, but by policy makers with the vision and leadership necessary to bridge the gap between research and policy.
Schlagwörter	History, 19th Century; History, 20th Century; History, 21st Century; Humans; Neoplasmsbloodhistoryprevention & control; Vitamin Dbloodhistory; Vitamin D Deficiencyblood

Mohr, Sharif B.; Garland, Cedric F.; Gorham, Edward D.; Grant, William B.; Garland, Frank C.: Relationship between low ultraviolet B irradiance and higher breast cancer risk in 107 countries. In: The breast journal, Jg. 14, H. 3, S. 255–260. Online verfügbar unter doi:10.1111/j.1524-4741.2008.00571.x.

Abstract	Epidemiological data show an inverse relationship between vitamin D levels and breast cancer incidence. This study investigates the relationship of modeled and

	measured serum 25-hydroxyvitamin D [25(OH)D] levels with age-standardized incidence rates of breast cancer in 107 countries. The hypothesis being tested is that breast cancer incidence is inversely related to geographically-dependent cutaneous sunlight exposure. A multiple regression approach was used to examine the contributions of ultraviolet B (UVB) irradiance to age-standardized incidence rates of breast cancer in the 107 countries with data on these covariates-total column ozone thickness, per capita intake of alcohol and energy from animal and vegetable sources, cigarettes, proportion of female population overweight, and total fertility. Age-standardized incidence rates were substantially higher at latitudes distant from the equator (R2 = 0.43, p < 0.0001). The dose-response gradient between modeled serum 25(OH)D levels and incidence rates of breast cancer followed a standard inverse dose-response curve. Increasing increments in serum 25(OH)D in the range above 22 ng/mL were associated with incrementally lower incidence rates of breast cancer. According to multiple regression, UVB irradiance adjusted for cloud cover was inversely associated with incidence rates (p = 0.04) after controlling for covariates. Intake of energy from animal sources was also positively associated with incidence rates (p < 0.01). The overall coefficient of determination, R2, was 0.81 (p < 0.0001). There was a protective effect of UVB irradiance on risk of breast cancer that was independent of fertility rate, proportion of the population overweight, alcohol intake, animal energy intake, and other covariates.
Schlagwörter	Adult; Breast Neoplasmsbloodetiology; Female; Humans; Middle Aged; Risk Factors; Sunlight; Ultraviolet Rays; Vitamin Danalogs & derivativesblood; Vitamin D Deficiencycomplications

Mohr, Sharif B.; Garland, Cedric F.; Gorham, Edward D.; Grant, William B.; Garland, Frank C. (2007): Is ultraviolet B irradiance inversely associated with incidence rates of endometrial cancer: an ecological study of 107 countries. In: Preventive medicine, Jg. 45, H. 5, S. 327–331. Online verfügbar unter doi:10.1016/j.ypmed.2007.01.012.

Abstract	OBJECTIVE: The purpose of this study was to perform an ecological analysis of the relationship between low levels of ultraviolet B (UVB) irradiance and age-standardized incidence rates of endometrial cancer by country, controlling for known confounders. METHODS: The contributions of UVB irradiance, cloud cover, intake of energy from animal sources, proportion of population overweight, skin pigmentation, per capita cigarette consumption, per capita health expenditure, and total fertility rates, to age-standardized incidence rates of endometrial cancer in 107 countries were assessed using multiple regression. RESULTS: Incidence rates were higher at higher latitudes (R2=0.47, p<0.01). According to multiple regression, UVB irradiance adjusted for cloud cover was negatively associated with incidence rates (p=0.02), while proportion of population overweight (p=0.004), intake of energy from animal sources (p=0.01) and per capita health expenditure (p<0.0001) were positively associated with incidence rates (overall R2=0.73, p<0.0001). CONCLUSION: An association was found between low UVB irradiance, high intake of energy from animal sources, per capita health expenditure, proportion of population overweight, and incidence rates.
Schlagwörter	Endometrial Neoplasmsepidemiology; Epidemiologic Research Design; Female; Food Habits; Health Expenditures; Humans; Incidence; Overweight; Ultraviolet Rays; Vitamin Dphysiology; World Health

Mohr, Sharif B.; Gorham, Edward D.; Garland, Cedric F.; Grant, William B.; Garland, Frank C. (2006): Are low ultraviolet B and high animal protein intake associated with risk of renal cancer. In: International journal of cancer. Journal international du cancer, Jg. 119, H. 11, S. 2705–2709. Online verfügbar unter doi:10.1002/ijc.22213.

Abstract	Incidence rates of kidney cancer are thought to be highest in places situated at high latitudes and in populations with high intake of energy from animal sources. This suggests that low 25-hydroxyvitamin D status, due to lower levels of UVB

	irradiance, and energy from animal sources might be involved in etiology. The association of latitude with age-adjusted incidence rates was determined for all 175 countries in a UN cancer database, GLOBOCAN. The independent association of UVB irradiance, cloud cover and intake of calories from animal sources with age-adjusted incidence rates was assessed using multiple regression in 139 countries that provided dietary data. Renal cancer incidence rates were highest in countries situated at the highest latitudes, in men (R(2) = 0.64, p < 0.01) and women (R(2) = 0.63, p < 0.01). According to multivariate analysis in men, UVB irradiance was inversely associated with renal cancer incidence rates (p = 0.0003), while cloud cover (p = 0.003) and intake of calories from animal sources (p < 0.0001) were independently positively associated (R(2) for model = 0.73, p < 0.0001). In women, UVB irradiance was inversely associated with incidence rates (p = 0.04), while total cloud cover (p = 0.0008) and calories from animal sources (p < 0.0001) were positively associated (R(2) = 0.68, p < 0.0001). Lower levels of UVB irradiance and higher intakes of calories from animal sources were independently associated with higher incidence rates of kidney cancer.
Schlagwörter	Animals; Dietary Proteinsadministration & dosage; Female; Humans; Incidence; Kidney Neoplasmsetiology; Male; Risk Factors; Ultraviolet Rays

Wei, Melissa Y.; Garland, Cedric F.; Gorham, Edward D.; Mohr, Sharif B.; Giovannucci, Edward (2008): Vitamin D and prevention of colorectal adenoma: a meta-analysis. In: Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology, Jg. 17, H. 11, S. 2958–2969. Online verfügbar unter doi:10.1158/1055-9965.EPI-08-0402.

Abstract	BACKGROUND: Vitamin D status is associated inversely with risk of colorectal cancer, but the association with adenoma risk is less clear. This meta-analysis examined the overall relationship between circulating (plasma or serum) 25-hydroxyvitamin D [25(OH)D], vitamin D intake (dietary, supplemental, or total), and colorectal adenoma incidence in published studies. METHODS: A meta-analysis composed of 17 epidemiologic studies [1 cross-sectional, 9 case-control, and 7 cohort or nested case-control studies; 7 on 25(OH)D and 12 on vitamin D intake] published before December 2007 was done to examine the association between circulating 25(OH)D, vitamin D intake, and colorectal adenomas. Summary Peto odds ratios (OR) were computed for overall and stratified analyses. RESULTS: Circulating 25(OH)D was inversely associated with risk of colorectal adenomas: the OR was 0.70 [95% confidence interval (95% CI), 0.56-0.87] for high versus low circulating 25(OH)D. The highest quintile of vitamin D intake was associated with an 11% marginally decreased risk of colorectal adenomas compared with low vitamin D intake (OR, 0.89; 95% CI, 0.78-1.02). For recurrent adenomas, there was a decreased risk of 12% (95% CI, 0.72-1.07) among individuals with high versus low vitamin D intake. The inverse associations appeared stronger for advanced adenoma [OR, 0.64; 95% CI, 0.45-0.90 for serum 25(OH)D and OR, 0.77; 95% CI, 0.63-0.95 for vitamin D intake], but the number of studies was small. CONCLUSIONS: Both circulating 25(OH)D and vitamin D intake were inversely associated with colorectal adenoma incidence and recurrent adenomas. These results further support a role of vitamin D in prevention of colorectal adenoma incidence and recurrence.
Schlagwörter	Adenomaepidemiologyprevention & control; Chi-Square Distribution; Colorectal Neoplasmsepidemiologyprevention & control; Humans; Incidence; Neoplasm Recurrence, Local; Risk; Vitamin Dadministration & dosageanalogs & derivativesblood