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**Transcription-Coupled Nucleotide Excision Repair: A Faster Solution or the Only Option?**

Khobta A, Sarmini L.

Biomolecules. 2025 Jul 16;15(7):1026. doi: 10.3390/biom15071026.

A branch of the nucleotide excision repair (NER) pathway, transcription-coupled repair (TCR or TC-NER) specifically operates on the template DNA strand of actively transcribed genes. Initiated by stalling of elongating RNA polymerase complexes at damaged sites, TC-NER has historically been viewed as "accelerated repair", arguably necessary for the maintenance of vital transcription function. Conversely, the conventional "global genome" (GG-NER) mechanism, operating throughout the genome, is usually regarded as a much slower process, even though it has long been found that differences in repair kinetics between transcribed DNA and the rest of the genome are not manifested for all structural types of DNA damage. Considering that damage detection is the rate-limiting step of overall repair reactions in most cases and that the mechanisms of the initial recognition of modified DNA structure are fundamentally different between TC-NER and GG-NER, it is suggestive to attribute the observed kinetic differences to different damage spectra recognized by the two pathways. This review summarizes current knowledge on the differential requirements of TC-NER and GG-NER towards specific damage types, based on their structural rather than spatial characteristics, and highlights some common features of DNA modifications repaired preferentially or exclusively by TC-NER, while evading other repair mechanisms.

**Supranutritional Selenomethionine but not Selenite Reduces Malignant Cell Transformation.**

Meyer CE, Schwarz M, Meyer FB, Thierbach R, Kipp AP.

Biol Trace Elem Res. 2025 Jun 25. doi: 10.1007/s12011-025-04719-6. Online ahead of print.

The trace element selenium is essential to human health and has long been discussed to modulate the carcinogenic process. So far, the functions of selenium and selenoproteins have been mainly studied in already transformed cancer cells. The aim of this study was, therefore, to characterize the role of selenium during the neoplastic transformation process in a concentration- and species-specific manner using the BALB/c cell transformation assay. This assay mimics the initiation and promotion phase of BALB/c cells (murine fibroblasts) treated with a tumor initiator (MCA) and promoter (TPA) leading to malignant cell foci development. In parallel, cells were supplied with selenite or selenomethionine using suboptimal, adequate or supranutritional concentrations (0.01-1  $\mu$ M). The supranutritional selenomethionine concentration reduced malignantly transformed foci, accompanied by higher NQO1 levels suggesting an upregulation of antioxidant NRF2 target genes. In contrast, treatment with the same concentration of selenite appeared to increase malignant transformation which was associated with higher intracellular selenium concentrations. Neither suboptimal nor adequate concentrations of either selenium species affected malignant cell transformation even though selenoprotein expression was modulated. Overall, the current data suggest that high concentrations of selenium have different effects on malignant cell transformation depending on the distinct selenium species applied.

### **Selenium, zinc, and copper intake and status of vegetarian, vegan, and omnivore children and adolescents: results of the VeChi youth study.**

Simon R, Richter E, Lossow K, Fischer M, Längler A, Michalsen A, Weder S, Keller M, Kipp AP, Alexy U. *Eur J Nutr.* 2025 Jul 22;64(5):247. doi: 10.1007/s00394-025-03761-3.

**Purpose:** As animal-derived foods are the main source of selenium, zinc, and copper, children and adolescents on vegetarian or vegan dietary patterns are at risk of an inadequate supply.

**Methods:** Among 342 children and adolescents (6-18 years) with different dietary patterns (86 vegans, 120 vegetarians, 118 omnivores) from the cross-sectional VeChi Youth study serum concentrations of selenium, zinc, and copper and functional biomarkers such as glutathione peroxidase-3 activity (GPX3) and selenoprotein P (SELENOP) for selenium and ceruloplasmin oxidase activity (CPO) for copper were measured. Dietary intake of these trace elements was estimated using a 3-day weighed food record. Group differences were assessed by analysis of covariance, adjusted for age, sex, puberty status, and further covariates.

**Results:** Trace element intake differed across dietary patterns with lower selenium intake in vegans compared to omnivores ( $p < 0.0001$ ), and lower zinc but higher copper intake in vegans ( $p = 0.0487$  and  $p < 0.0001$ ) and vegetarians ( $p = 0.0354$  and  $p < 0.0001$ ) than in omnivores. Lower serum selenium as well as SELENOP concentrations were observed in vegans ( $p < 0.0001$  and  $p < 0.0001$ ) and vegetarians ( $p < 0.0001$  and  $p < 0.0001$ ) in comparison to omnivores, but no difference in GPX3 activity across the dietary groups was observed. Similarly, serum zinc concentrations were lower in vegans ( $p = 0.0122$ ) and vegetarians ( $p = 0.0016$ ) compared to omnivores while serum copper concentrations and CPO did not differ between the dietary patterns.

**Conclusion:** Vegetarian and vegan dietary patterns are associated with lower intake and serum biomarkers of selenium and zinc and should be monitored in children and adolescents on vegan or vegetarian dietary patterns. Trial registration number and date of registration DRKS00012835, 11.07.2018.

### **Nutritional care in metastatic RCC: patient experiences and reported unaddressed needs.**

Kastrati K, Huebner J, Kipp AP, Mathies V.

*Support Care Cancer.* 2025 Aug 4;33(8):754. doi: 10.1007/s00520-025-09801-2.

**Purpose:** Although renal cell carcinoma (RCC) presents unique nutritional challenges due to the disease itself and treatment side effects, little is known about the prevalence of nutritional issues among RCC patients in a real-world setting. This study aimed to investigate the patient-reported prevalence of nutritional issues and the response of healthcare teams to these challenges.

**Methods:** A survey among RCC patients in Germany was developed in collaboration with patient organizations and included 46 questions covering demographics, nutritional issues, and cancer care experiences. It was distributed online from April to July 2022. Responses from 94 German RCC patients were analyzed using descriptive and inferential statistics.

**Results:** Nutritional concerns were reported by 60.6% of participants, with diarrhea (23.4%), loss of appetite (21.3%), and nausea (20.2%) being the most common issues. Unintentional weight loss was reported by 49.4% of patients, but only 13.9% were referred to nutrition specialists. More than two-thirds reported a negative or extremely negative impact due to these problems on their physical condition and quality of life. Additionally, 67% of patients felt that their nutritional needs were not taken seriously by their healthcare teams. Most patients (84%) think that nutritional care should be part of routine cancer care.

**Conclusion:** The findings reveal significant gaps in the nutritional care of RCC patients. Screenings and proactive assessments do not appear to be performed as suggested by nutritional guidelines. Thus, nutritional counseling and support are obviously still not integrated into real-world comprehensive oncological care.

### **Trace elements and risk of diabetes-related vascular complications: results from the EPIC-Potsdam cohort study.**

Eroglu B, Eichelmann F, Kuxhaus O, Kipp AP, Schwerdtle T, Haase H, Schomburg L, Schulze MB.

Cardiovasc Diabetol. 2025 Jul 24;24(1):302. doi: 10.1186/s12933-025-02861-y.

Background: The trace elements selenium, zinc, copper, manganese, iodine, and iron are crucial for various physiological processes, including enzymatic reactions and immune responses. Dyshomeostasis of trace elements is associated with a variety of diseases including diabetes and cardiovascular diseases. It has not been clarified whether blood trace elements associate with the risk of diabetes-related vascular complications. We aimed to investigate the prospective associations between pre-diagnosis serum levels of trace elements with vascular complications in diabetes.

Methods: Participants with incident diabetes and free of micro- and macrovascular disease and with pre-diagnostic serum trace element measurements from the European Prospective Investigation into Cancer and Nutrition (EPIC)-Potsdam cohort (n = 627) were followed for microvascular and macrovascular complications (n = 212 and n = 69, respectively, median follow-up: 12.8 years). We used Cox Proportional Hazard models to investigate the associations between baseline trace element levels (per SD difference) and the risk of developing diabetes-related vascular complications. To investigate the interactions and nonlinear associations between TEs and risk of diabetes-related complications, we applied Bayesian kernel machine regression (BKMR).

Results: In multivariable models, higher iodine levels were associated with higher risk of developing total vascular complications (HR per SD, 95% CI: 1.16, 1.02-1.31) and microvascular complications (1.18, 1.03-1.35). In sex-stratified analyses we observed significant positive associations between zinc and total vascular complications (1.35, 1.06-1.73) and microvascular complications (1.52, 1.15-2.02) in women, while higher zinc was associated with increased risk of macrovascular complications in men (1.33, 1.00-1.77). Copper-to-Zinc ratio was inversely associated with the risk of microvascular complications in women (0.69, 0.54-0.88), but with an increased risk in men (1.54, 1.17-2.02).

Conclusions: Our findings indicate that higher serum levels of iodine measured prior to the diagnosis of diabetes are associated with higher risk of subsequent microvascular complications in diabetes, while copper-to-zinc ratio is associated with microvascular complications in a sex-specific manner.

### **Vitamin A acts as a potent suppressor of selenoprotein P with potential relevance for multivitamin supplementation.**

Karmeli S, Chillon TS, Sane R, Schwarz M, Gröber U, Hackler J, Kipp AP, Schomburg L.

J Nutr Biochem. 2025 Oct 15;148:110142. doi: 10.1016/j.jnutbio.2025.110142. Online ahead of print.

Multivitamin supplementation is a widely used strategy to prevent disease, slow the ageing process, improve quality of life and extend life span, although recent clinical findings do not support these claims. Since selenium (Se) deficiency is associated with morbidity and mortality risk, we tested the hypothesis that certain vitamins interfere with the regular biosynthesis of the Se transporter selenoprotein P (SELENOP). Human liver cancer cells (HepG2) were treated with different concentrations of folic acid, nicotinamide, nicotinic acid, pyridoxal phosphate, thiamine, vitamin A, vitamin C, vitamin D2, vitamin D3, vitamin E, vitamin K and vitamin B12. Secreted SELENOP was quantified by ELISA and characterized by Western blot analysis. SELENOP transcript levels and promoter activity were determined, and resveratrol as a negative and thyroid hormone as a positive modulator were included for comparison. The concentration of extracellular SELENOP decreased twofold in response to micromolar concentrations of vitamin A. The SELENOP transcript concentration decreased to 70% after incubation with 1  $\mu$ M vitamin A, and a moderate concomitant decrease in SELENOP core promoter activity was observed. Co-incubation experiments of vitamin A with the active thyroid hormone T3 revealed dose-dependent effects and suggested competitive activities of these two modifiers of SELENOP expression in opposite directions. We conclude that vitamin A is able to suppress hepatic SELENOP biosynthesis and secretion, which may confer health risks in self-administered or clinically indicated supplementation with retinoids, especially in individuals with marginal Se intake and status.

### **Trace element-linked DNA methylation sites and their association with type 2 diabetes and cardiovascular diseases: EPIC-Potsdam cohort study.**

Eroglu B, Eichelmann F, Kuxhaus O, Kipp AP, Schwerdtle T, Haase H, Schomburg L, Schulze MB. *Clin Epigenetics*. 2025 Oct 16;17(1):172. doi: 10.1186/s13148-025-01991-0.

**Background:** The trace elements (TEs) selenium, zinc, copper, manganese, iodine and iron are essential micronutrients that support essential metabolic functions. Imbalance in their homeostasis might contribute to the pathogenesis of major age-related chronic diseases including type 2 diabetes (T2D) and cardiovascular diseases (CVD). Emerging evidence suggests that TEs may affect health outcomes via epigenetic changes. However, few epigenome-wide association studies (EWAS) have explored TE-associated DNA methylation markers and their links to chronic disease outcomes.

**Methods:** We conducted TE-specific exploratory EWAS using a random subcohort (n = 1030) from the European Prospective Investigation into Cancer and Nutrition (EPIC)-Potsdam cohort. The association between identified CpG sites and incident chronic diseases was evaluated using a case-cohort design comprising random subcohort participants and incident cases of T2D (n = 654) and CVD (n = 334). DNA methylation was measured with the MethylationEPIC BeadChip array. We used Prentice-weighted Cox proportional hazards regression models to estimate multivariable-adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for the associations of TE-associated CpG sites with each incident chronic disease.

**Results:** In the copper EWAS, we identified six CpG sites (cg00398673, cg03957124, cg05736499, cg07573872, cg11503550, and cg18513344) that were significantly associated with serum copper concentrations with a False Discovery Rate < 0.05. All associated CpG sites showed lower methylation levels in association with higher serum copper levels. Higher methylation levels of cg00398673 (HR per SD: 0.74, 95% CI 0.63-0.88), cg03957124 (HR per SD: 0.52, 95% CI 0.41-0.66), cg05736499 (HR Q5 vs Q1: 0.25, 95% CI 0.14-0.47), and cg18513344 (HR Q5 vs Q1: 0.37, 95% CI 0.24-0.57) were associated with decreased risk of developing T2D, and higher methylation levels of cg07573872 were associated with decreased risk of developing CVD (HR per SD: 0.85, 95% CI 0.72-0.99). We did not observe any CpG sites that were significantly associated with other TEs.

**Conclusions:** Serum copper levels are inversely associated with a number of CpG sites. Methylation levels at these CpG sites were inversely associated with developing T2D and CVD. These findings may provide new insights on understanding the increased risk of T2D and CVD with elevated blood copper levels.

### **Vitamin A5: Evidence, definitions, gaps, and future directions**

Bohn T, Rohn S, Böhm V, Despotovic M, de Lera AR, Krezel W, Kucuk O, Bánáti D, Rühl R. *Nutrients*. 2025; 17:2317. doi: 10.3390/nu17142317.

With the emergence of a new vitamin concept—vitamin A5—it is essential to first clarify the basic definition of vitamins, particularly vitamin A. This article summarizes the foundational concepts and definitions of vitamins with particular relevance to the discovery, establishment, and categorization of new vitamin concepts. Vitamin A5 was discovered 80 years after the last vitamin was identified. It serves as an umbrella term for the dietary precursors 9-cis- $\beta$ , $\beta$ -carotene and 9-cis-13,14-dihydroretinol for the endogenous activator of the nuclear hormone receptor RXR, 9-cis-13,14-dihydroretinoic acid. However, several questions arise: Which criteria are typically used to identify a substance as a vitamin? How does vitamin A5 fit into the sometimes misleading definition of vitamin A? This review summarizes key findings and provides a comprehensive assessment of the current understanding, concluding that (a) vitamin A5 is a newly identified micronutrient that plays an important role in the prevention of diet-related diseases and (b) vitamin A5 is an important micronutrient that provides a plausible, mechanistic explanation for why a Western lifestyle diet low in vegetables and especially leafy vegetables can lead to a high prevalence of Western-lifestyle diseases, particularly neurological diseases and poor mental health.

## **Investigating alternative solvents regarding extractability of lipophilic food ingredients in spinach-tomato powder and algae materials**

Schmidt M, Böhm V

Food Analytical Methods 2025; 18: 1850-1862. doi: 10.1007/s12161-025-02821-y.

Extraction of natural products such as carotenoids, vitamin E and chlorophylls is still accompanied with certain challenges. Limitations exist in widespread availability of sophisticated techniques (e.g. supercritical fluid), which are often replaced by conventional approaches such as tissue homogeniser with disperser blades, a sonication bath or vortex mixing. Moreover, an appropriate selection of solvents is a critical step for selective extraction of compounds in complex, severely extractable matrices. The present investigation focussed on a comparison of conventional solvents (e.g. tetrahydrofuran, acetone, hexane) with more sustainable alternatives (e.g. 2-methyl-tetrahydrofuran (2-MeTHF); dimethyl carbonate (DMC); cyclopentyl methyl ether (CPME)) with and without addition of methanol regarding a broad range of analyte polarities. Herein, tetrahydrofuran with methanol resulted in maximum extraction efficiencies for total carotenoids in a spinach tomato powder. 2-MeTHF, DMC and CPME partially combined with MeOH proved to be equivalent alternatives for extraction of xanthophylls and  $\beta$ -carotene isomers. A comparison of renowned and widely available extraction techniques in context of challenging sample matrices (dried, pelletised and fresh microalgae) resulted in preferably powerful approaches such as Ultra-Turrax® homogenisation and sonifier probe application. Necessary pretreatments with methanol combined with powerful extraction techniques were apparently recommendable for dried algae products compared to fresh algae paste, thus reducing the potential extraction repetitions. Finally, a comparison of different syringe filter materials suggested the use of mixed cellulose ester (MCE) membranes for avoiding a significant loss ( $p < 0.05$ ) of analytes (lutein,  $\beta$ -carotene, lycopene, vitamin E) compared to seven other membrane materials. Overall, these results represent a contribution to routine analysis of lipophilic food ingredients with a high transferability and adaptability across applied research.

## **Global burden of 292 causes of death in 204 countries and territories and 660 subnational locations, 1990-2023: a systematic analysis for the Global Burden of Disease Study 2023.**

GBD 2023 Causes of Death Collaborators.

Lancet 2025; 406(10513):1811-1872. DOI: 10.1016/S0140-6736(25)01917-8.

**Background:** Timely and comprehensive analyses of causes of death stratified by age, sex, and location are essential for shaping effective health policies aimed at reducing global mortality. The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2023 provides cause-specific mortality estimates measured in counts, rates, and years of life lost (YLLs). GBD 2023 aimed to enhance our understanding of the relationship between age and cause of death by quantifying the probability of dying before age 70 years (70q0) and the mean age at death by cause and sex. This study enables comparisons of the impact of causes of death over time, offering a deeper understanding of how these causes affect global populations.

**Methods:** GBD 2023 produced estimates for 292 causes of death disaggregated by age-sex-location-year in 204 countries and territories and 660 subnational locations for each year from 1990 until 2023. We used a modelling tool developed for GBD, the Cause of Death Ensemble model (CODEm), to estimate cause-specific death rates for most causes. We computed YLLs as the product of the number of deaths for each cause-age-sex-location-year and the standard life expectancy at each age. Probability of death was calculated as the chance of dying from a given cause in a specific age period, for a specific population. Mean age at death was calculated by first assigning the midpoint age of each age group for every death, followed by computing the mean of all midpoint ages across all deaths attributed to a given cause. We used GBD death estimates to calculate the observed mean age at death and to model the expected mean age across causes, sexes, years, and locations. The expected mean age reflects the expected mean age at death for individuals within a population, based on global mortality rates and the population's age structure. Comparatively, the observed mean age represents the actual mean age at death, influenced by all factors unique to a location-specific population, including its age structure. As part of the modelling process, uncertainty intervals (UIs) were generated using the 2.5th and 97.5th

percentiles from a 250-draw distribution for each metric. Findings are reported as counts and age-standardised rates. Methodological improvements for cause-of-death estimates in GBD 2023 include a correction for the misclassification of deaths due to COVID-19, updates to the method used to estimate COVID-19, and updates to the CODEm modelling framework. This analysis used 55 761 data sources, including vital registration and verbal autopsy data as well as data from surveys, censuses, surveillance systems, and cancer registries, among others. For GBD 2023, there were 312 new country-years of vital registration cause-of-death data, 3 country-years of surveillance data, 51 country-years of verbal autopsy data, and 144 country-years of other data types that were added to those used in previous GBD rounds.

**Findings:** The initial years of the COVID-19 pandemic caused shifts in long-standing rankings of the leading causes of global deaths: it ranked as the number one age-standardised cause of death at Level 3 of the GBD cause classification hierarchy in 2021. By 2023, COVID-19 dropped to the 20th place among the leading global causes, returning the rankings of the leading two causes to those typical across the time series (ie, ischaemic heart disease and stroke). While ischaemic heart disease and stroke persist as leading causes of death, there has been progress in reducing their age-standardised mortality rates globally. Four other leading causes have also shown large declines in global age-standardised mortality rates across the study period: diarrhoeal diseases, tuberculosis, stomach cancer, and measles. Other causes of death showed disparate patterns between sexes, notably for deaths from conflict and terrorism in some locations. A large reduction in age-standardised rates of YLLs occurred for neonatal disorders. Despite this, neonatal disorders remained the leading cause of global YLLs over the period studied, except in 2021, when COVID-19 was temporarily the leading cause. Compared to 1990, there has been a considerable reduction in total YLLs in many vaccine-preventable diseases, most notably diphtheria, pertussis, tetanus, and measles. In addition, this study quantified the mean age at death for all-cause mortality and cause-specific mortality and found noticeable variation by sex and location. The global all-cause mean age at death increased from 46.8 years (95% UI 46.6-47.0) in 1990 to 63.4 years (63.1-63.7) in 2023. For males, mean age increased from 45.4 years (45.1-45.7) to 61.2 years (60.7-61.6), and for females it increased from 48.5 years (48.1-48.8) to 65.9 years (65.5-66.3), from 1990 to 2023. The highest all-cause mean age at death in 2023 was found in the high-income super-region, where the mean age for females reached 80.9 years (80.9-81.0) and for males 74.8 years (74.8-74.9). By comparison, the lowest all-cause mean age at death occurred in sub-Saharan Africa, where it was 38.0 years (37.5-38.4) for females and 35.6 years (35.2-35.9) for males in 2023. Lastly, our study found that all-cause 70q0 decreased across each GBD super-region and region from 2000 to 2023, although with large variability between them. For females, we found that 70q0 notably increased from drug use disorders and conflict and terrorism. Leading causes that increased 70q0 for males also included drug use disorders, as well as diabetes. In sub-Saharan Africa, there was an increase in 70q0 for many non-communicable diseases (NCDs). Additionally, the mean age at death from NCDs was lower than the expected mean age at death for this super-region. By comparison, there was an increase in 70q0 for drug use disorders in the high-income super-region, which also had an observed mean age at death lower than the expected value.

**Interpretation:** We examined global mortality patterns over the past three decades, highlighting—with enhanced estimation methods—the impacts of major events such as the COVID-19 pandemic, in addition to broader trends such as increasing NCDs in low-income regions that reflect ongoing shifts in the global epidemiological transition. This study also delves into premature mortality patterns, exploring the interplay between age and causes of death and deepening our understanding of where targeted resources could be applied to further reduce preventable sources of mortality. We provide essential insights into global and regional health disparities, identifying locations in need of targeted interventions to address both communicable and non-communicable diseases. There is an ever-present need for strengthened health-care systems that are resilient to future pandemics and the shifting burden of disease, particularly among ageing populations in regions with high mortality rates. Robust estimates of causes of death are increasingly essential to inform health priorities and guide efforts toward achieving global health equity. The need for global collaboration to reduce preventable mortality is more important than ever, as shifting burdens of disease are affecting all nations, albeit at different paces and scales.

**Burden of 375 diseases and injuries, risk-attributable burden of 88 risk factors, and healthy life expectancy in 204 countries and territories, including 660 subnational locations, 1990-2023: a systematic analysis for the Global Burden of Disease Study 2023.**

GBD 2023 Disease and Injury and Risk Factor Collaborators.

Lancet 2025 Oct; 406(10513):1873-1922. DOI: 10.1016/S0140-6736(25)01637-X.

**Background:** For more than three decades, the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) has provided a framework to quantify health loss due to diseases, injuries, and associated risk factors. This paper presents GBD 2023 findings on disease and injury burden and risk-attributable health loss, offering a global audit of the state of world health to inform public health priorities. This work captures the evolving landscape of health metrics across age groups, sexes, and locations, while reflecting on the remaining post-COVID-19 challenges to achieving our collective global health ambitions.

**Methods:** The GBD 2023 combined analysis estimated years lived with disability (YLDs), years of life lost (YLLs), and disability-adjusted life-years (DALYs) for 375 diseases and injuries, and risk-attributable burden associated with 88 modifiable risk factors. Of the more than 310 000 total data sources used for all GBD 2023 (about 30% of which were new to this estimation round), more than 120 000 sources were used for estimation of disease and injury burden and 59 000 for risk factor estimation, and included vital registration systems, surveys, disease registries, and published scientific literature. Data were analysed using previously established modelling approaches, such as disease modelling meta-regression version 2.1 (DisMod-MR 2.1) and comparative risk assessment methods. Diseases and injuries were categorised into four levels on the basis of the established GBD cause hierarchy, as were risk factors using the GBD risk hierarchy. Estimates stratified by age, sex, location, and year from 1990 to 2023 were focused on disease-specific time trends over the 2010-23 period and presented as counts (to three significant figures) and age-standardised rates per 100 000 person-years (to one decimal place). For each measure, 95% uncertainty intervals [UIs] were calculated with the 2.5th and 97.5th percentile ordered values from a 250-draw distribution.

**Findings:** Total numbers of global DALYs grew 6.1% (95% UI 4.0-8.1), from 2.64 billion (2.46-2.86) in 2010 to 2.80 billion (2.57-3.08) in 2023, but age-standardised DALY rates, which account for population growth and ageing, decreased by 12.6% (11.0-14.1), revealing large long-term health improvements. Non-communicable diseases (NCDs) contributed 1.45 billion (1.31-1.61) global DALYs in 2010, increasing to 1.80 billion (1.63-2.03) in 2023, alongside a concurrent 4.1% (1.9-6.3) reduction in age-standardised rates. Based on DALY counts, the leading level 3 NCDs in 2023 were ischaemic heart disease (193 million [176-209] DALYs), stroke (157 million [141-172]), and diabetes (90.2 million [75.2-107]), with the largest increases in age-standardised rates since 2010 occurring for anxiety disorders (62.8% [34.0-107.5]), depressive disorders (26.3% [11.6-42.9]), and diabetes (14.9% [7.5-25.6]). Remarkable health gains were made for communicable, maternal, neonatal, and nutritional (CMNN) diseases, with DALYs falling from 874 million (837-917) in 2010 to 681 million (642-736) in 2023, and a 25.8% (22.6-28.7) reduction in age-standardised DALY rates. During the COVID-19 pandemic, DALYs due to CMNN diseases rose but returned to pre-pandemic levels by 2023. From 2010 to 2023, decreases in age-standardised rates for CMNN diseases were led by rate decreases of 49.1% (32.7-61.0) for diarrhoeal diseases, 42.9% (38.0-48.0) for HIV/AIDS, and 42.2% (23.6-56.6) for tuberculosis. Neonatal disorders and lower respiratory infections remained the leading level 3 CMNN causes globally in 2023, although both showed notable rate decreases from 2010, declining by 16.5% (10.6-22.0) and 24.8% (7.4-36.7), respectively. Injury-related age-standardised DALY rates decreased by 15.6% (10.7-19.8) over the same period. Differences in burden due to NCDs, CMNN diseases, and injuries persisted across age, sex, time, and location. Based on our risk analysis, nearly 50% (1.27 billion [1.18-1.38]) of the roughly 2.80 billion total global DALYs in 2023 were attributable to the 88 risk factors analysed in GBD. Globally, the five level 3 risk factors contributing the highest proportion of risk-attributable DALYs were high systolic blood pressure (SBP), particulate matter pollution, high fasting plasma glucose (FPG), smoking, and low birthweight and short gestation-with high SBP accounting for 8.4% (6.9-10.0) of total DALYs. Of the three overarching level 1 GBD risk factor categories-behavioural, metabolic, and environmental and occupational-risk-attributable DALYs rose between 2010 and 2023 only for metabolic risks, increasing by 30.7% (24.8-37.3); however, age-standardised DALY rates attributable to

metabolic risks decreased by 6.7% (2.0-11.0) over the same period. For all but three of the 25 leading level 3 risk factors, age-standardised rates dropped between 2010 and 2023-eg, declining by 54.4% (38.7-65.3) for unsafe sanitation, 50.5% (33.3-63.1) for unsafe water source, and 45.2% (25.6-72.0) for no access to handwashing facility, and by 44.9% (37.3-53.5) for child growth failure. The three leading level 3 risk factors for which age-standardised attributable DALY rates rose were high BMI (10.5% [0.1 to 20.9]), drug use (8.4% [2.6 to 15.3]), and high FPG (6.2% [-2.7 to 15.6]; non-significant).

**Interpretation:** Our findings underscore the complex and dynamic nature of global health challenges. Since 2010, there have been large decreases in burden due to CMNN diseases and many environmental and behavioural risk factors, juxtaposed with sizeable increases in DALYs attributable to metabolic risk factors and NCDs in growing and ageing populations. This long-observed consequence of the global epidemiological transition was only temporarily interrupted by the COVID-19 pandemic. The substantially decreasing CMNN disease burden, despite the 2008 global financial crisis and pandemic-related disruptions, is one of the greatest collective public health successes known. However, these achievements are at risk of being reversed due to major cuts to development assistance for health globally, the effects of which will hit low-income countries with high burden the hardest. Without sustained investment in evidence-based interventions and policies, progress could stall or reverse, leading to widespread human costs and geopolitical instability. Moreover, the rising NCD burden necessitates intensified efforts to mitigate exposure to leading risk factors-eg, air pollution, smoking, and metabolic risks, such as high SBP, BMI, and FPG-including policies that promote food security, healthier diets, physical activity, and equitable and expanded access to potential treatments, such as GLP-1 receptor agonists. Decisive, coordinated action is needed to address long-standing yet growing health challenges, including depressive and anxiety disorders. Yet this can be only part of the solution. Our response to the NCD syndemic-the complex interaction of multiple health risks, social determinants, and systemic challenges-will define the future landscape of global health. To ensure human wellbeing, economic stability, and social equity, global action to sustain and advance health gains must prioritise reducing disparities by addressing socioeconomic and demographic determinants, ensuring equitable health-care access, tackling malnutrition, strengthening health systems, and improving vaccination coverage. We live in times of great opportunity.

### **Global, Regional, and National Burden of Cardiovascular Diseases and Risk Factors in 204 Countries and Territories, 1990-2023.**

Global Burden of Cardiovascular Diseases and Risks 2023 Collaborators.

J Am Coll Cardiol 2025; 86(22):2167-2243. DOI: 10.1016/j.jacc.2025.08.015.

**Background:** Cardiovascular diseases (CVDs) are the leading cause of mortality and are among the foremost causes of disability globally. CVD burden has continued to increase in most countries since 1990, with trends driven by changing exposures to harmful risk factors, population growth, and population aging.

**Objectives:** We report estimates of global, national, and subnational CVD burden, including 18 subdiseases and 12 associated modifiable risk factors. We analyzed change in CVD burden from 1990 to 2023 and identified drivers of change including population growth, population aging, and risk factor exposure.

**Methods:** The Global Burden of Disease (GBD) 2023 study, a multinational collaborative research study, quantified burden due to 375 diseases including CVD burden and identified drivers of change from 1990 to 2023 using all available data and statistical models. GBD 2023 estimated the population-level burden of diseases in 204 countries and territories from 1990 to 2023.

**Results:** CVDs were the leading cause of disability-adjusted life years (DALYs) and deaths estimated in the GBD. As of 2023, there were 437 million (95% UI: 401 to 465 million) CVD DALYs globally, a 1.4-fold increase from the number in 1990 of 320 million (292 to 344 million). Ischemic heart disease, intracerebral hemorrhage, ischemic stroke, and hypertensive heart disease were the leading cardiovascular causes of DALYs in 2023 globally. As of 2023, age-standardized CVD DALY rates were highest in low and low-middle Socio-demographic Index (SDI) settings and lowest in high SDI settings. The number of CVD deaths increased globally from 13.1 million (95% UI: 12.2 to 14.0 million) in 1990

to 19.2 million (95% UI: 17.4 to 20.4 million) in 2023. The number of prevalent cases of CVD more than doubled since 1990, with 311 million (95% UI: 294 to 333 million) prevalent cases of CVD in 1990 and 626 million (95% UI: 591 to 672 million) prevalent cases in 2023 globally. A total of 79.6% (95% UI: 75.7% to 82.5%) of CVD burden is attributable to modifiable risk factors 347 million [95% UI: 318 to 373 million] DALYs in 2023). Globally, high systolic blood pressure, dietary risks, high low-density lipoprotein cholesterol, and air pollution were the modifiable risks responsible for most attributable CVD burden in 2023. Since 1990, changes in exposure to modifiable risk factors have had mixed effects on CVD burden, with increases in high body mass index, high fasting plasma glucose, and low physical activity leading to higher burden, while reductions in tobacco usage have mitigated some of these increases. Population growth and population aging were the main drivers of the increasing burden since 1990, adding 128 million (95% UI: 115 to 139 million) and 139 million (95% UI: 126 to 151 million) CVD DALYs to the increase in CVD burden since 1990.

**Conclusions:** CVD remains the leading cause of disease burden and death worldwide with the greatest burden in low, low-middle, and middle SDI regions. Large variation exists in CVD burden even for countries at similar levels of development, a gap explained substantially by known, modifiable risk factors that are inadequately controlled. The decades-long increase in CVD burden was the result of population growth, population aging, and increased exposure to a subset of risk factors led by metabolic risks. Countries will need to adopt effective health system and public health strategies if they are to progress in achieving global goals to reduce the burden of CVD.

**Protein intake and cardiovascular diseases: an umbrella review of systematic reviews for the evidence-based guideline on protein intake of the German Nutrition Society.**

Egert S, Amini AM, Klug L, Kalotai N, Haardt J, Boeing H, Buyken AE, Kroke A, Lorkowski S, Louis S, Nimptsch K, Schulze MB, Schwingshackl L, Siener R, Stangl GI, Zittermann A, Watzl B, Ellinger S; German Nutrition Society.

Eur J Nutr 2025; 64(6):254. DOI: 10.1007/s00394-025-03746-2.

**Purpose:** This umbrella review aimed to investigate the evidence for an association of dietary intake of total protein as well as animal and plant protein with the incidence of coronary heart disease (CHD), stroke and total cardiovascular diseases (CVD).

**Methods:** PubMed, Embase and Cochrane Database were systematically searched for systematic reviews (SRs) of prospective studies with or without meta-analysis (MA) published between January 2012 and April 2024. Methodological quality, outcome-specific certainty of evidence, and overall certainty of evidence were assessed using established tools and predefined criteria.

**Results:** Ten SRs were considered eligible for the umbrella review; all were based on prospective cohort studies, and six conducted a MA. Dietary intakes of total, animal and plant protein were not associated with the risk of CHD or stroke. For CHD, the overall certainty of evidence for the absence of an association was "probable" for total, animal and plant protein. For stroke and total CVD, the overall certainty of evidence was rated as "possible" for the absence of an association with the intake of total protein and plant protein and insufficient for animal protein intake.

**Conclusion:** Given that most SRs on dietary protein intake did not indicate an association, it seems that protein intake plays no major role in the development of CVD.

### **The vitamin E Derivative garcinoic acid suppresses NLRP3 inflammasome activation and pyroptosis in murine macrophages.**

Börmel L, Geisler AR, Hupfer Y, Liao S, Schubert T, Kluge S, Lorkowski S, Wallert M.

Inflammation 2025; 48(5):3340-3352. DOI: 10.1007/s10753-025-02269-6.

Excessive inflammation in cells are a common cause of inflammation-related diseases such as cardiometabolic diseases. The cellular multiprotein complex nucleotide-binding domain and leucine-rich repeat pyrin domain 3 (NLRP3) inflammasome is a cellular key modulator of inflammatory processes. In addition to classic medications, phytochemicals are known for their anti-inflammatory potential. In African folk medicine the seeds of *Garcinia kola* are used to support the treatment of inflammatory diseases. Of particular interest is the phytochemical garcinoic acid (GA, trans-13'-carboxy- $\delta$ -tocotrienol), which is isolated from the *Garcinia kola* seeds. This derivative and potential metabolite of the vitamin E congener  $\delta$ -tocotrienol (T3) shows anti-inflammatory properties in vitro. However, the underlying mechanisms are largely unknown. To get better insights into the molecular mode of action, murine J774A.1 macrophages were stimulated with lipopolysaccharides (LPS) only or in combination with adenosine triphosphate (ATP), which led to canonical activation of the NLRP3 inflammasome and subsequent pyroptosis. A combined treatment with GA resulted in significantly reduced stimulation of the transcription factor nuclear factor 'k-light-chain-enhancer' of activated B-cells (NF- $\kappa$ B), decreased expression of inflammasome-related genes and marked downregulation of autoproteolytic cleavage of caspase-1 (Casp-1). Consequently, GA had an inhibitory effect on pyroptosis. The results have been validated using the well-known NLRP3 inflammasome inhibitor MCC950. In conclusion, GA was shown to have relevant effects on the regulation of the NLRP3 inflammasome and pyroptosis in vitro. Our study provides new mechanistic insights into the anti-inflammatory mode of action of GA and highlights its relevance as a potential phytochemical drug for the treatment of inflammation.

### **Data in personalized nutrition: bridging biomedical, psycho-behavioral, and food environment approaches for population-wide impact.**

Linseisen J, Renner B, Gedrich K, Wirsam J, Holzappel C, Lorkowski S, Watzl B, Daniel H, Leitzmann M; Working Group "Personalized Nutrition" of the German Nutrition Society.

Adv Nutr 2025; 16(7):100377. DOI: 10.1016/j.advnut.2025.100377.

Personalized nutrition (PN) represents an approach aimed at delivering tailored dietary recommendations, products, or services to support both prevention and treatment of nutrition-related conditions and to improve individual health using genetic, phenotypic, medical, nutritional, and other pertinent information. However, current approaches have yielded limited scientific success in improving diets or in mitigating diet-related conditions. In addition, PN currently caters to a specific subgroup of the population rather than having a widespread impact on diet and health at a population level. Addressing these challenges requires integrating traditional biomedical and dietary assessment methods with psycho-behavioral, and novel digital and diagnostic methods for comprehensive data collection, which holds considerable promise in alleviating present PN shortcomings. This comprehensive approach not only allows for deriving personalized goals ("what should be achieved") but also customizing behavioral change processes ("how to bring about change"). We herein outline and discuss the concept of "Adaptive Personalized Nutrition Advice Systems," which blends data from 3 assessment domains: 1) biomedical/health phenotyping; 2) stable and dynamic behavioral signatures; and 3) food environment data. Personalized goals and behavior change processes are envisaged to no longer be based solely on static data but will adapt dynamically in-time and in-situ based on individual-specific data. To successfully integrate biomedical, behavioral, and environmental data for personalized dietary guidance, advanced digital tools (e.g., sensors) and artificial intelligence-based methods will be essential. In conclusion, the integration of both established and novel static and dynamic assessment paradigms holds great potential for transitioning PN from its current focus on elite nutrition to a widely accessible tool that delivers meaningful health benefits to the general population.

## **Global, regional, and national progress towards the 2030 global nutrition targets and forecasts to 2050: a systematic analysis for the Global Burden of Disease Study 2021.**

Global Nutrition Target Collaborators.

Lancet 2025; 404(10471):2543-2583. DOI: 10.1016/S0140-6736(24)01821-X.

**Background:** The six global nutrition targets (GNTs) related to low birthweight, exclusive breastfeeding, child growth (ie, wasting, stunting, and overweight), and anaemia among females of reproductive age were chosen by the World Health Assembly in 2012 as key indicators of maternal and child health, but there has yet to be a comprehensive report on progress for the period 2012 to 2021. We aimed to evaluate levels, trends, and observed-to-expected progress in prevalence and attributable burden from 2012 to 2021, with prevalence projections to 2050, in 204 countries and territories.

**Methods:** The prevalence and attributable burden of each target indicator were estimated by age group, sex, and year in 204 countries and territories from 2012 to 2021 in the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2021, the most comprehensive assessment of causes of death, disability, and risk factors to date. Country-specific relative performance to date was evaluated with a Bayesian meta-regression model that compares prevalence to expected values based on Socio-demographic Index (SDI), a composite indicator of societal development status. Target progress was forecasted from 2021 up to 2050 by modelling past trends with meta-regression using a combination of key quantities and then extrapolating future projections of those quantities.

**Findings:** In 2021, a few countries had already met some of the GNTs: five for exclusive breastfeeding, four for stunting, 96 for child wasting, and three for child overweight, and none met the target for low birthweight or anaemia in females of reproductive age. Since 2012, the annualised rates of change (ARC) in the prevalence of child overweight increased in 201 countries and territories and ARC in the prevalence of anaemia in females of reproductive age decreased considerably in 26 countries. Between 2012 and 2021, SDI was strongly associated with indicator prevalence, apart from exclusive breastfeeding ( $|r|=0.46-0.86$ ). Many countries in sub-Saharan Africa had a decrease in the prevalence of multiple indicators that was more rapid than expected on the basis of SDI (the differences between observed and expected ARCs for child stunting and wasting were  $-0.5\%$  and  $-1.3\%$ , respectively). The ARC in the attributable burden of low birthweight, child stunting, and child wasting decreased faster than the ARC of the prevalence for each in most low-income and middle-income countries. In 2030, we project that 94 countries will meet one of the six targets, 21 countries will meet two targets, and 89 countries will not meet any targets. We project that seven countries will meet the target for exclusive breastfeeding, 28 for child stunting, and 101 for child wasting, and no countries will meet the targets for low birthweight, child overweight, and anaemia. In 2050, we project that seven additional countries will meet the target for exclusive breastfeeding, five for low birthweight, 96 for child stunting, nine for child wasting, and one for child overweight, and no countries are projected to meet the anaemia target.

**Interpretation:** Based on current levels and past trends, few GNTs will be met by 2030. Major reductions in attributable burden for exclusive breastfeeding and anthropometric indicators should be recognised as huge scientific and policy successes, but the comparative lack of progress in reducing the prevalence of each, along with stagnant anaemia in women of reproductive age and widespread increases in child overweight, suggests a tenuous status quo. Continued investment in preventive and treatment efforts for acute childhood illness is crucial to prevent backsliding. Parallel development of effective treatments, along with commitment to multisectoral, long-term policies to address the determinants and causes of suboptimal nutrition, are sorely needed to gain ground.

**Cardiovascular mortality attributable to dietary risk factors in 54 countries in the WHO European Region from 1990 to 2019: an updated systematic analysis of the Global Burden of Disease Study.**

Pörschmann T, Meier T, Lorkowski S.

Eur J Prev Cardiol 2025; 32(16):1553-1563. DOI: 10.1093/eurjpc/zwae136.

**Aims:** This study aimed to estimate the association between single dietary risk factors and cardiovascular diseases (CVDs) in the WHO European Region (WHO ER) by age and sex using the data of the Global Burden of Diseases Study (GBD) from 1990 to 2019.

**Methods and results:** For this purpose, 13 dietary risks and 13 forms of CVDs were included in the study, and the comparative risk assessment framework of the GBD was used to estimate the deaths attributable to them. The study included four regions, with a total of 54 countries. In 2019, 1.55 million (95 % UI, 1.2-1.9 million) people in the WHO ER died from CVDs attributable to suboptimal diet. Diet-related CVD deaths (DRCDs) accounted for 16.4 % of total deaths and 36.7 % of CVD deaths in 2019. Between 1990 and 2019, there was a DRCDs reduction of 8.1 % and the age-standardized death rate decreased. The deaths were almost equally distributed between women (777 714 deaths) and men (772 519 deaths). The distribution of death numbers between the sexes has changed only slightly over the study period. The largest percentage across the age groups was found in the group 85+ years (32.1 %). Most DRCDs in the WHO ER were caused by a diet low in whole grains (326 755 deaths), followed by a diet low in legumes (232 918 deaths) and a diet high in sodium (193 713 deaths). Overall, 80.3% of deaths were due to ischaemic heart disease, which was the most common cause of death in all countries.

**Conclusion:** In terms of CVD deaths in the WHO ER, more than every third death is attributable to an unbalanced diet, making the diet one of the most important factors in preventing premature CVD death in the WHO ER.

**Arachidonic acid as a potentially critical nutrient for vegetarians and vegans - position paper of the Research Institute for Plant-based Nutrition (IFPE).**

Weder S, Müller S, Dawczynski C, Keller M.

Lipids Health Dis 2025 Jul 19;24(1):244. doi: 10.1186/s12944-025-02645-z.

The long-chain polyunsaturated fatty acid arachidonic acid (ARA, 20:4n-6) is virtually non-existent in plant foods. Concerns have therefore been raised that a predominantly plant-based diet, i.e., a vegetarian or vegan diet, could lead to ARA deficiency. ARA is discussed as conditionally essential, particularly in early infancy and childhood. Therefore, the authors of this position paper provide an overview of the state of scientific research on ARA for Western countries, with a special focus on risk groups, e.g., pregnant and breastfeeding women, infants, and children. We discuss whether ARA is potentially essential in critical life stages and whether a plant-based diet is appropriate in relation to ARA. Preliminary recommendations are derived on the basis of the available literature: healthy adults and pregnant and lactating women are able to synthesize ARA from linoleic acid (LA, 18:2n-6) and, therefore, do not require ARA supplementation, even with plant-based diets. Owing to the importance of ARA in early childhood, infants should be breastfed or given ARA-containing formula. According to current data, it can be assumed that infants, children, and adolescents are also capable of producing sufficient amounts of ARA regardless of their diet. However, these data are sparse. Furthermore, owing to the lack of reference ranges, there are no suitable test methods for diagnosing deficiency. All in all, owing to insufficient data, these recommendations are preliminary, and further studies with risk groups are urgently needed.

Endometriose – Was tun? (Taschenbuch)

Mechsner S (Co-Autoren: B. Knappe-Drzikova, C. Dawczynski)

Taschenbuch, Erscheinungsdatum: 08.10.2025, Verlag: ZS - ein Verlag der Edel Verlagsgruppe, 1.

Auflage, ISBN: 978-3-96584-580-0, Email: buchvertrieb@edel.com

Beschreibung

Nach der Diagnose „Endometriose“ haben die betroffenen Frauen meist viele Fragen: Wie kann mir mein Arzt bzw. meine Ärztin nun helfen? Was kann ich selbst gegen die immer wiederkehrenden Schmerzen tun? Und wie steht es überhaupt um meinen Kinderwunsch? Diese und viele weitere Fragen beantwortet Prof. Dr. Mechsner in diesem Ratgeber auf gewohnt kompetente und einfühlsame Weise. Und mehr noch: Mit ihrem Wissen und ihrer Erfahrung aus der Endometriose-Forschung hat sie einen ganzheitlichen Ansatz entwickelt, der auf den drei Säulen Ernährung, Bewegung und mentalen Bewältigungsstrategien basiert und allen Betroffenen zu mehr Lebensqualität verhelfen kann.

## **Patientenratgeber im Bereich Ernährung & psychische Gesundheit Für Kinder**

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