#### Neues aus der Wissenschaft

#### Wissenschaftliche Publikationen aus dem Institut für Ernährungswissenschaften der Friedrich-Schiller-Universität Jena veröffentlicht von Mai 2022 bis Oktober 2022

Impact of in vitro digested zinc oxide nanoparticles on intestinal model systems Mittag A, Singer A, Hoera C, Westermann M, Kämpfe A, Glei M Part Fibre Toxicol. **2022** May 30;19(1):39. doi: 10.1186/s12989-022-00479-6

**Background**: Zinc oxide nanoparticles (ZnO NP) offer beneficial properties for many applications, especially in the food sector. Consequently, as part of the human food chain, they are taken up orally. The toxicological evaluation of orally ingested ZnO NP is still controversial. In addition, their physicochemical properties can change during digestion, which leads to an altered biological behaviour. Therefore, the aim of our study was to investigate the fate of two different sized ZnO NP (< 50 nm and < 100 nm) during in vitro digestion and their effects on model systems of the intestinal barrier. Differentiated Caco-2 cells were used in mono- and coculture with mucus-producing HT29-MTX cells. The cellular uptake, the impact on the monolayer barrier integrity and cytotoxic effects were investigated after 24 h exposure to 123-614  $\mu$ M ZnO NP.

**Results**: In vitro digested ZnO NP went through a morphological and chemical transformation with about 70% free zinc ions after the intestinal phase. The cellular zinc content increased dose-dependently up to threefold in the monoculture and fourfold in the coculture after treatment with digested ZnO NP. This led to reactive oxygen species but showed no impact on cellular organelles, the metabolic activity, and the mitochondrial membrane potential. Only very small amounts of zinc (< 0.7%) reached the basolateral area, which is due to the unmodified transepithelial electrical resistance, permeability, and cytoskeletal morphology.

**Conclusions**: Our results reveal that digested and, therefore, modified ZnO NP interact with cells of an intact intestinal barrier. But this is not associated with serious cell damage.

# Dietary PUFA Preferably Modify Ethanolamine-Containing Glycerophospholipids of the Human Plasma Lipidome

Dawczynski C, Plagge J, Jahreis G, Liebisch G, Höring M, Seeliger C, Ecker J Nutrients **2022** Jul 26;14(15):3055. doi: 10.3390/nu14153055

The content of polyunsaturated fatty acids (PUFA) in complex lipids essentially influences their physicochemical properties and has been linked to health and disease. To investigate the incorporation of dietary PUFA in the human plasma lipidome, we quantified glycerophospholipids (GPL), sphingolipids, and sterols using electrospray ionization coupled to tandem mass spectrometry of plasma samples obtained from a dietary intervention study. Healthy individuals received foods supplemented with different vegetable oils rich in PUFA. These included sunflower, linseed, echium, and microalgae oil as sources of linoleic acid (LA: FA 18:2 n-6), alpha-linolenic acid (ALA: FA 18:3 n-3), stearidonic acid (SDA: FA 18:4 n-3), and docosahexaenoic acid (DHA; FA 22:6 n-3). While LA and ALA did not influence the species profiles of GPL, sphingolipid, and cholesteryl ester drastically, SDA and DHA were integrated primarily in ethanolamine-containing GPL. This significantly altered phosphatidylethanolamine and plasmalogen species composition, especially those with 38-40 carbons and 6 double bonds. We speculate that diets enriched with highly unsaturated FA more efficiently alter plasma GPL acyl chain composition than those containing primarily diand tri-unsaturated FA, most likely because of their more pronounced deviation of FA composition from typical western diets.

#### SEMO-1, a novel methanethiol oxidase in Caenorhabditis elegans, is a pro-aging factor conferring selective stress resistance

Philipp TM, Gong W, Köhnlein K, Ohse VA, Müller FI, Priebs J, Steinbrenner H, Klotz LO Biofactors. 2022 May;48(3):699-706. doi: 10.1002/biof.1836

Methanethiol is a toxic gas produced through bacterial degradation of sulfur-containing amino acids. Applying a novel enzymatic assay, we here identified a methanethiol oxidase (MTO) that catalyzes the degradation of methanethiol in the nematode Caenorhabditis elegans (C. elegans). The corresponding protein, Y37A1B.5, previously characterized as a C. elegans ortholog of human selenium-binding protein 1 (SELENBP1), was renamed SEMO-1 (SELENBP1 ortholog with methanethiol oxidase activity). Worms rendered deficient in SEMO-1 not only showed decreased hydrogen sulfide production from methanethiol catabolism but they were also more resistant to oxidative stress and had an elevated life span. In contrast, resistance to selenite was significantly lowered in SEMO-1-deficient worms. Naturally occurring mutations of human SELENBP1 were introduced to recombinant SEMO-1 through site-directed mutagenesis and resulted in loss of its MTO activity, indicating a similar enzymatic mechanism for SELENBP1 and SEMO-1. In summary, SEMO-1 confers resistance to toxic selenite and the ability to metabolize toxic methanethiol. These beneficial effects might be a trade-off for its negative impact on C. elegans life span.

## Altered Capacity for H2S Production during the Spontaneous Differentiation of Caco-2 Cells to Colonocytes Due to Reciprocal Regulation of CBS and SELENBP1

Scheller AS, Philipp TM, Klotz LO, Steinbrenner H. Antioxidants 2022 September; 11(10):1957. doi: 10.3390/antiox11101957

Hydrogen sulfide (H2S) has been proposed to promote tumor growth. Elevated H2S levels have been detected in human colorectal cancer (CRC) biopsies, resulting from the selective upregulation of cystathionine β-synthase (CBS). In contrast, the recently identified novel H2Sgenerating enzyme, selenium-binding protein 1 (SELENBP1), is largely suppressed in tumors. Here, we provide the first comparative analysis of the four human H2S-producing enzymes and the key H2S-catabolizing enzyme, sulfide: guinone oxidoreductase (SQOR), in Caco-2 human colorectal adenocarcinoma cells. The gene expression pattern of proliferating Caco-2 cells parallels that of CRC, while confluent cells undergo spontaneous differentiation to a colonocyte-like phenotype. SELENBP1 and SQOR were strongly upregulated during spontaneous differentiation, whereas CBS was downregulated. Cystathionine y-lyase and 3mercaptopyruvate sulfurtransferase remained unaffected. Terminally differentiated cells showed an enhanced capacity to produce H2S from methanethiol and homocysteine. Differentiation induced by exposure to butyrate also resulted in the upregulation of SELENBP1. accompanied by increased SELENBP1 promoter activity. In contrast to spontaneous differentiation, however, butyrate did not cause downregulation of CBS. In summary, SELENBP1 and CBS are reciprocally regulated during the spontaneous differentiation of Caco-2 cells, thus paralleling their opposing regulation in CRC. Butvrate exposure, while imitating some aspects of spontaneous differentiation, does not elicit the same expression patterns of genes encoding H2S-modulating enzymes.

#### Nutrient Intake and Nutrition Status in Vegetarians and Vegans in Comparison to Omnivores - the Nutritional Evaluation (NuEva) Study

Dawczynski C, Weidauer T, Richert C, Schlattmann P, Dawczynski K, Kiehntopf M Front Nutr **2022** May 16;9:819106. doi: 10.3389/fnut.2022.819106

**Introduction:** In recent years, vegetarian and vegan diets became increasingly important as they are associated with beneficial health outcomes. Therefore, the NuEva study compares the impact of flexitarian, vegetarian, or vegan diets with omnivorous nutritional habits on nutrient intake and risk factors for non-communicable diseases.

**Methods**: A dietary protocol was kept over five days and blood and 24h urine samples were collected to examine the impact of dietary habits [omnivores, n = 65 (Median/Interquartile range: 33/17 yrs.), flexitarians, n = 70 (30/17 yrs.), ovo-lacto vegetarians, n = 65 (28/14 yrs.), vegans, n = 58 (25/10 yrs.)] on nutrient intake, nutrient concentrations in plasma, serum or 24h urine, body composition, and blood lipids.

**Results**: The increased exclusion of animal based foods in the diet (omnivores < flexitarians < vegetarians < vegans) is associated with a decreased intake of energy, saturated fat, cholesterol, disaccharides, and total sugar as well an increased intake of dietary fibers, beta carotene, vitamin E and K. The combined index of the B12 status (4cB12 score) in vegetarians (0.02/0.75) was lower compared to omnivores (0.34/0.58;  $p \le 0.05$ ) and flexitarians (0.24/0.52;  $p \le 0.05$ ). In omnivores vitamin A, vitamin E, ferritin, and the urinary excretion of selenium, iodine, and zinc were higher than in vegans ( $p \le 0.05$ ). In contrast, vegans had the highest concentrations of biotin, folate, and vitamin C. Flexitarians, vegetarians, and vegans had a lower body weight, BMI, and body fat percentage in comparison to omnivores ( $p \le 0.05$ ). In omnivores the concentrations on total cholesterol, total cholesterol/HDL cholesterol ratio, LDL cholesterol, LDL cholesterol/HDL cholesterol ratio, apolipoprotein B, and apolipoprotein B/ apolipoprotein A1 ratio were higher than in vegetarians and vegans ( $p \le 0.05$ ).

**Conclusion**: The NuEva study confirms the position of the Academy of Nutrition and Dietetics that adequately planned vegetarian diets are healthy, nutritionally adequate, and may provide health benefits in the prevention and treatment of non-communicable diseases. Nevertheless, critical nutrients were identified for all groups studied. This highlights the need to develop individual nutritional concepts to ensure an adequate nutrient intake.

#### Dramatic Decrease of Vitamin K2 Subtype Menaquinone-7 in COVID-19 Patients

Mangge H, Prueller F, Dawczynski C, Curcic P, Sloup Z, Holter M, Herrmann M, Meinitzer A. Antioxidants (Basel). **2022** Jun 24;11(7):1235.doi: 10.3390/antiox11071235

**Background**: Vitamin K (VK) is a fat-soluble compound with a common chemical structure, a 2-methyl-1,4-naphthoquinone ring, and a variable aliphatic side-chain. VK is involved in the synthesis of blood-clotting proteins, bone stability, anti-oxidative, and immune inflammatory-modulatory functions. Vitamin K also activates protein S, which acts as an antioxidant and anti-inflammatory. The fact that cytokine overproduction, oxidative stress, and disturbed microcirculation by thrombogenicity play a central role in severe COVID-19 prompted us to analyze this vitamin.

**Methods**: We analyzed by a validated liquid-chromatography tandem mass-spectrometry method serum vitamin K1, MK4, MK7, and VK epoxide levels in 104 healthy controls, 77 patients with non-COVID-19 pneumonia, and 135 hospitalized COVID-19 patients with potentially fatal outcomes admitted to our University Hospital between April and November 2020. We included the quotient between VK and triglyceride (TG, nmol/mmol/L) values in the analyses with respect to the TG transporter function for all VK subtypes. Additionally, we assessed anthropometric, routine laboratory, and clinical data from the laboratory and hospital information systems.

**Results:** The COVID-19 patients had significantly lower MK7 levels than non-COVID-19 pneumonia patients and healthy controls. COVID-19 and non-COVID-19 pneumonia patients had significantly lower vitamin K1 and significantly higher MK4 compared to healthy controls, but did not differ significantly from each other. Between COVID-19 non-survivors (n = 30) and survivors (n = 105) no significant differences were seen in all vitamin K subtypes, despite the fact that non-survivors had higher peak concentrations of IL-6, CRP, d-dimer, and higher oxygen needs, respectively.

**Conclusions**: The present data identified significantly decreased vitamin K1, K2 (MK7), and increased MK4 levels in patients with COVID-19 compared to healthy controls. Vitamin K2 (MK7) was lowest in COVID-19 patients irrespective of potentially fatal courses, indicating consumption of this VK subtype by COVID-19 immanent effects, most probably inflammatory and oxidative stress factors.

### Interlaboratory exercise for the analysis of carotenoids and related compounds in dried mango fruit (Mangifera indica L.)

Villacís-Chiriboga, J, Jacobs, G, Van Camp, J, Elst, K, Ruales, J, Marcillo-Parra, V, Böhm, V, Bunea, A, Cirlini, M, Craft, N, De Meulenaer, B, Graça Dias, M, Lazzarino, G, Meléndez-Martínez, A J, Versloot, P, Mercadante, A Z, Olmedilla-Alonso, B, Ortiz-Ulloa, J, Stinco, C. M, Voorspoels, S

J. Food Comp. Anal. 2022, 111, 104616.

An interlaboratory comparison was done for the analysis of carotenoids in freeze-dried mango. The study was performed from July to September 2018. Mango fruit was freeze-dried, homogenized, and packaged under vacuum conditions in portions of 6 g (test sample). Two test samples were sent to the participating laboratories for analysis. Laboratory results were rated using Z-scores in accordance with ISO 13528 and ISO 17043. The standard deviation for proficiency assessment (also called target standard deviation) was determined using a modified Horwitz function and varied between 10% and 25%, depending on the analyte. Out of 14 laboratories from 10 different countries, 9 laboratories (64%) obtained a satisfactory performance (Z ≤ 2) for the analysis of  $\beta$ -carotene. While for 7 laboratories (57%) obtained a satisfactory performance for lutein. Based on the comparability of the analytical results, this study concludes that freeze-dried mango pulp can be used as a reference material for the analysis of  $\alpha$  and  $\beta$ -carotene, (9Z)- $\beta$ -carotene,  $\beta$ -cryptoxanthin, and zeaxanthin by applying different analysis of  $\alpha$  and  $\beta$ -carotene, (9Z)- $\beta$ -carotene,  $\beta$ -cryptoxanthin, and zeaxanthin by applying different analysis of  $\alpha$  and  $\beta$ -carotene, (9Z)- $\beta$ -carotene,  $\beta$ -cryptoxanthin, and zeaxanthin by applying different analysis of  $\alpha$  and  $\beta$ -carotene, (9Z)- $\beta$ -carotene,  $\beta$ -cryptoxanthin, and zeaxanthin by applying different analysis of  $\alpha$  and  $\beta$ -carotene, (9Z)- $\beta$ -carotene,  $\beta$ -cryptoxanthin, and zeaxanthin by applying different analysis of  $\alpha$  and  $\beta$ -carotene, (9Z)- $\beta$ -carotene,  $\beta$ -cryptoxanthin, and zeaxanthin by applying different analysis of  $\alpha$  and  $\beta$ -carotene, for their extraction and quantification.

### Phytochemical analysis, antioxidant, cytotoxic and antimicrobial activities of golden chamomile (Matricaria aurea (Loefl.) Schultz Bip)

Yousefbeyk, F, Hemmati, G, Gholipour, Z, Ghasemi, S, Evazalipour, M, Schubert, C, Koohi, D E, Böhm, V

Z. Naturforsch. C 2022, 77, 331-342

Matricaria aurea (Loefl.) Schultz Bip. (Asteraceae), known as golden chamomile, has been traditionally used for the treatment of various diseases. In this study, total phenolic, flavonoid, and tannin contents of total extract and different fractions of this plant were determined. The antioxidant, cytotoxic, and antimicrobial activities were also evaluated. Moreover, the phenolic profiles of selected fractions were determined by HPLC and LC-MS/MS analysis. Results demonstrated total phenolic contents of 37.8-57.2 mg GAE/g and total flavonoid contents of 3.0–111.2 mg QE/g. The ethyl acetate and methanol fractions (EF and MF) had the highest concentrations of phenolic, tannin, and flavonoid compounds. In both DPPH radical scavenging assay and phosphomolybdenum reduction assay, EF showed the best antioxidant activity, followed by MF. EF and MF indicated also the best antibacterial activities against Bacillus subtilis (MIC 1.56 and 12.5 mg ml-1) and Staphylococcus aureus (MIC 0.78 and 12.5 mg ml-1). Hexane fraction (HF) had no antibacterial effect. None of the samples had antifungal effect. MTT (3-(4,5-dimethyl-thiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay revealed for EF and HF the highest antiproliferative activities (IC<sub>50</sub> values ranged from 111.8 to 294.6 µg ml-1). The presence of chlorogenic acid, ferulic acid, and luteolin-7-O-glucoside in MF, and p-coumaric acid in EF was confirmed and quantified.

#### High pressure processing and heat sterilization of kale: Impact on extractability, antioxidant capacity and storability of carotenoids and vitamin E

Schmidt, M, Hopfhauer, S, Schwarzenbolz, U, Böhm, V Appl. Res. **2022**, 1, e202200025

Food process engineering represents a rapidly evolving discipline traditionally focussing on thermal treatments including objectives such as preservation and stabilization. Innovative and gentle preservation techniques such as high-pressure processing (HPP) may potentially improve or replace conventional methods by enhancing nutritional and health aspects, flavor and taste, sustainability, and more consumer-targeted, minimally processed food items. As information about the impact of HPP (600 MPa, 5-40 min) on lipophilic food ingredients (e.g., carotenoids, vitamin E) in kale is limited, a comparison to heat sterilization (20 min, 121°C) may result in new insights related to lipophilic, antioxidant capacity (L-AOC), extractability and storage stability (8 weeks, 5°C). HPP of chopped kale resulted in significantly increased (p < 0.05) total carotenoid and chlorophyll contents in contrast to declined concentrations of vitamin E. Significantly decreased extractabilities were observed for total carotenoids and chlorophylls in heat sterilized kale, showing no significant change (p > 0.05) in vitamin E content. Moreover, 2 months of storage of HP-treated kale resulted in a major loss of vitamin E and total carotenoid contents compared to thermally treated samples. Elevated  $\alpha$ -tocopherol equivalent antioxidant capacities (αTEAC) and lipophilic oxygen radical antioxidant capacities (L-ORAC) correlated with an increased pressure holding time.

**Obesity Hinders the Protective Effect of Selenite Supplementation on Insulin Signaling** Hauffe R, Rath M, Agyapong W, Jonas W, Vogel H, Schulz TJ, Schwarz M, Kipp AP, Blüher M, Kleinridders A

Antioxidants (Basel). 2022 Apr 28;11(5):862. doi: 10.3390/antiox11050862

The intake of high-fat diets (HFDs) containing large amounts of saturated long-chain fatty acids leads to obesity, oxidative stress, inflammation, and insulin resistance. The trace element selenium, as a crucial part of antioxidative selenoproteins, can protect against the development of diet-induced insulin resistance in white adipose tissue (WAT) by increasing glutathione peroxidase 3 (GPx3) and insulin receptor (IR) expression. Whether selenite (Se) can attenuate insulin resistance in established lipotoxic and obese conditions is unclear. We confirm that GPX3 mRNA expression in adipose tissue correlates with BMI in humans. Cultivating 3T3-L1 pre-adipocytes in palmitate-containing medium followed by Se treatment attenuates insulin resistance with enhanced GPx3 and IR expression and adipocyte differentiation. However, feeding obese mice a selenium-enriched high-fat diet (SRHFD) only resulted in a modest increase in overall selenoprotein gene expression in WAT in mice with unaltered body weight development, glucose tolerance, and insulin resistance. While Se supplementation improved adipocyte morphology, it did not alter WAT insulin sensitivity. However, mice fed a SRHFD exhibited increased insulin content in the pancreas. Overall, while selenite protects against palmitate-induced insulin resistance in vitro, obesity impedes the effect of selenite on insulin action and adipose tissue metabolism in vivo.

Vitamin E and Metabolic Health: Relevance of Interactions with Other Micronutrients Liao S, Omage SO, Börmel L, Kluge S, Schubert M, Wallert M, Lorkowski S Antioxidants (Basel). **2022** Sep 9;11(9):1785. doi: 10.3390/antiox11091785

A hundred years have passed since vitamin E was identified as an essential micronutrient for mammals. Since then, many biological functions of vitamin E have been unraveled in both cell and animal models, including antioxidant and anti-inflammatory properties, as well as regulatory activities on cell signaling and gene expression. However, the bioavailability and physiological functions of vitamin E have been considerably shown to depend on lifestyle, genetic factors, and individual health conditions. Another important facet that has been considered less so far is the endogenous interaction with other nutrients. Accumulating evidence indicates that the interaction between vitamin E and other nutrients, especially those that are enriched by supplementation in humans, may explain at least some of the discrepancies observed in clinical trials. Meanwhile, increasing evidence suggests that the different forms of vitamin E metabolites and derivates also exhibit physiological activities, which are more potent and mediated via different pathways compared to the respective vitamin E precursors. In this review, possible molecular mechanisms between vitamin E and other nutritional factors are discussed and their potential impact on physiological and pathophysiological processes is evaluated using published co-supplementation studies.

**100 Jahre Vitamin-E-Forschung: Status, Ausblick und zukünftige Entwicklungen** Wallert M, Eggersdorfer M Ernährung & Medizin. **2022**. doi: 10.1055/a-1743-6605

Neue Ansätze zur Rolle von Vitamin E in verschiedenen Bereichen der menschlichen Gesund-

heit werden in verschiedenen Arbeitsgruppen untersucht und versprechen neue Anwendungen in der gesundheitlichen Unterstützung von Risikogruppen. Nach 100 Jahren Forschung zu und über Vitamin E eröffnen neue Technologien und Studien auch für die Zukunft vielversprechende zusätzliche Funktionen und Anwendungsmöglichkeiten in der Risikoprävention. Population-level risks of alcohol consumption by amount, geography, age, sex, and year: a systematic analysis for the Global Burden of Disease Study 2020 Lancet 2022; 400(10347):185-235. DOI: 10.1016/S0140-6736(22)00847-9 GBD 2020 Alcohol Collaborators

**Background:** The health risks associated with moderate alcohol consumption continue to be debated. Small amounts of alcohol might lower the risk of some health outcomes but increase the risk of others, suggesting that the overall risk depends, in part, on background disease rates, which vary by region, age, sex, and year.

**Methods:** For this analysis, we constructed burden-weighted dose-response relative risk curves across 22 health outcomes to estimate the theoretical minimum risk exposure level (TMREL) and non-drinker equivalence (NDE), the consumption level at which the health risk is equivalent to that of a non-drinker, using disease rates from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2020 for 21 regions, including 204 countries and territories, by 5-year age group, sex, and year for individuals aged 15-95 years and older from 1990 to 2020. Based on the NDE, we quantified the population consuming harmful amounts of alcohol.

**Findings:** The burden-weighted relative risk curves for alcohol use varied by region and age. Among individuals aged 15-39 years in 2020, the TMREL varied between 0 (95% uncertainty interval 0-0) and 0.603 (0.400-1.00) standard drinks per day, and the NDE varied between 0.002 (0-0) and 1.75 (0.698-4.30) standard drinks per day. Among individuals aged 40 years and older, the burden-weighted relative risk curve was J-shaped for all regions, with a 2020 TMREL that ranged from 0.114 (0-0.403) to 1.87 (0.500-3.30) standard drinks per day and an NDE that ranged between 0.193 (0-0.900) and 6.94 (3.40-8.30) standard drinks per day. Among individuals consuming harmful amounts of alcohol in 2020, 59.1% (54.3-65.4) were aged 15-39 years and 76.9% (73.0-81.3) were male.

**Interpretation:** There is strong evidence to support recommendations on alcohol consumption varying by age and location. Stronger interventions, particularly those tailored towards younger individuals, are needed to reduce the substantial global health loss attributable to alcohol.

### Genetics and epigenetics in personalized nutrition: evidence, expectations, and experiences

Holzapfel C, Waldenberger M, Lorkowski S, Daniel H, Working Group "Personalized Nutrition" of the German Nutrition Society

Mol Nutr Food Res 2022; 66(17):e2200077. DOI: 10.1002/mnfr.202200077

With the presentation of the blueprint of the first human genome in 2001 and the advent of technologies for high-throughput genetic analysis, personalized nutrition (PN) becomes a new scientific field and the first commercial offerings of genotype-based nutrition advice emerge at the same time. Here, the state of evidence for the effect of genetic and epigenetic factors in the development of obesity, the metabolic syndrome, and resulting illnesses such as non-insulin-dependent diabetes mellitus and cardiovascular diseases is summarized. This study also critically value the concepts of PN that are built around the new genetic avenue from both the academic and a commercial perspective and their effectiveness in causing sustained changes in diet, lifestyle, and for improving health. Despite almost 20 years of research and commercial direct-to-consumer offerings, evidence for the success of gene-based dietary recommendations is still generally lacking. This calls for new concepts of future PN solutions that incorporate more phenotypic measures and provide a panel of instruments (e.g., self- and bio-monitoring tools, feedback systems, algorithms based on artificial intelligence) that increases compliance based on the individual's physical and social environment and value system.

# Estimates, trends, and drivers of the global burden of type 2 diabetes attributable to PM2.5 air pollution, 1990-2019: an analysis of data from the Global Burden of Disease Study 2019

GBD 2019 Diabetes and Air Pollution Collaborators Lancet Planet Health **2022**; 6(7):e586-e600. DOI: 10.1016/S2542-5196(22)00122-X

**Background:** Experimental and epidemiological studies indicate an association between exposure to particulate matter (PM) air pollution and increased risk of type 2 diabetes. In view of the high and increasing prevalence of diabetes, we aimed to quantify the burden of type 2 diabetes attributable to PM2·5 originating from ambient and household air pollution.

**Methods:** We systematically compiled all relevant cohort and case-control studies assessing the effect of exposure to household and ambient fine particulate matter (PM2·5) air pollution on type 2 diabetes incidence and mortality. We derived an exposure-response curve from the extracted relative risk estimates using the MR-BRT (meta-regression-Bayesian, regularised, trimmed) tool. The estimated curve was linked to ambient and household PM2·5 exposures from the Global Burden of Diseases, Injuries, and Risk Factors Study 2019, and estimates of the attributable burden (population attributable fractions and rates per 100 000 population of deaths and disability-adjusted life-years) for 204 countries from 1990 to 2019 were calculated. We also assessed the role of changes in exposure, population size, age, and type 2 diabetes incidence in the observed trend in PM2·5-attributable type 2 diabetes burden. All estimates are presented with 95% uncertainty intervals.

**Findings:** In 2019, approximately a fifth of the global burden of type 2 diabetes was attributable to PM2·5 exposure, with an estimated 3·78 (95% uncertainty interval 2·68-4·83) deaths per 100 000 population and 167 (117-223) disability-adjusted life-years (DALYs) per 100 000 population. Approximately 13·4% (9·49-17·5) of deaths and 13·6% (9·73-17·9) of DALYs due to type 2 diabetes were contributed by ambient PM2·5, and 6·50% (4·22-9·53) of deaths and 5·92% (3·81-8·64) of DALYs by household air pollution. High burdens, in terms of numbers as well as rates, were estimated in Asia, sub-Saharan Africa, and South America. Since 1990, the attributable burden has increased by 50%, driven largely by population growth and ageing. Globally, the impact of reductions in household air pollution was largely offset by increased ambient PM2·5.

**Interpretation:** Air pollution is a major risk factor for diabetes. We estimated that about a fifth of the global burden of type 2 diabetes is attributable PM2·5 pollution. Air pollution mitigation therefore might have an essential role in reducing the global disease burden resulting from type 2 diabetes.

### Long known and mostly unused: lifestyle measures to support lipid-lowering therapy Lorkowski S

Dtsch Med Wochenschr 2022; 147(12):796-806. DOI: 10.1055/a-1516-2581

Dyslipidemias are common metabolic disorders in Western industrialized countries. Lifestyle measures such as increasing physical activity and improving diet were for many years the only measure for their treatment. Because of their health-promoting effects, guidelines for the treatment of dyslipidemias consider lifestyle measures to be the basis of any drug therapy. Due to the numerous efficient options for intensive lipid-lowering medication, lifestyle measures are recommended by responsible physicians, but their implementation is usually not intensively pursued due to the large time commitment; in contrast to sustained recommendations for increasing physical activity and normalizing body weight, nutritional therapists are too rarely consulted as specialists despite the significant effects our diet has on cardiovascular risk factors such as LDL-cholesterol, triglycerides and blood pressure. In this review, the principles of nutritional therapy of dyslipidemias are described, and it is outlined how recent studies support the plausibility and evidence of the individual measures.