

Neues aus der Wissenschaft
Wissenschaftliche Publikationen aus dem Institut für
Ernährungswissenschaften der Friedrich-Schiller-Universität Jena
veröffentlicht von November 2024 bis April 2025

Source of Vitamin B12 in plants of the Lemnaceae family and its production by duckweed-associated bacteria.

Acosta K, Sree KS, Okamoto N, Koseki K, Sorrels S, Jahreis G, Watanabe F, Appenroth KJ, Lam E. *J Food Comp Anal* 135 (2024) 106603. doi.org/10.1016/j.jfca.2024.106603

While most plants are not known to contain significant levels of the essential corrinoid cobalamin (vitamin B12), considerable levels of vitamin B12 were found in the duckweed clone *Wolffia globosa* Mankai. Although endophytes were speculated to be the source of this vitamin B12, it has not been tested yet. In this study, we carried out comparative analysis of vitamin B12 content in 15 duckweed accessions across 11 species. Significant but variable levels of vitamin B12 were found in all unsterile duckweed cultures tested. In contrast, disinfected duckweed cultures with lower levels of bacteria, as monitored by PCR-based methods, contained little vitamin B12. Importantly, two strains of duckweed-associated bacteria were shown to produce vitamin B12. This work provides evidence for bacteria as the source of vitamin B12 in duckweeds. Bioinformatics-aided identification of vitamin B12 producers among duckweed-associated bacteria could facilitate their systematic incorporation into duckweed-based foods to support a planetary health diet.

Transcription blocking properties and transcription-coupled repair of N^2 -alkylguanine adducts as a model for aldehyde-induced DNA damage.

Sarmini L, Kitsera N, Meabed M, Khobta A.

J Biol Chem. 2025 Mar 27;301(5):108459. doi: 10.1016/j.jbc.2025.108459. Onl. ahead of print.

The N^2 position of guanine is a preferential reaction site in DNA for numerous dietary and environmental carcinogens or their electrophilic metabolites, aldehydes arising from lipid peroxidation as well as reactive by-products of normal metabolism. However, DNA repair mechanisms of the resulting covalent adducts in mammalian cells are not well understood, with nucleotide excision repair (NER), base excision repair, and a dioxygenase-mediated damage reversal being discussed as likely pathways. Considering fundamentally different damage recognition principles between the global genome NER and the transcription-coupled (TC)-NER, we here assessed transcription blocking capacities of four synthetic deoxyguanosine (dGuo) adducts of variable size and geometry, using a transfection-based reporter assay. Notably, adducts as different as the aliphatic N^2 -ethylguanine, the exocyclic 1, N^2 -ethenoguanine, and the bulky polycyclic 3-(deoxyguanosin- N^2 -yl)-2-acetylaminofluorene, displayed robust DNA strand-specific transcription-blocking properties. The specific TC-NER components ERCC8/CSA and ERCC6/CSB were consistently required for the removal of all transcription-blocking N^2 -dGuo adducts, whereas the absence of XPC or DDB2/XPE (both specific to global genome NER) did not compromise the repair capacities in the isogenic human cell models. In contrast, no inhibition of the gene expression was detected for reporter constructs carrying N^2 -methylguanine even in the NER-deficient XP-A cell line, suggesting that this adduct is either bypassed with very high efficiency during transcription or repaired by a mechanism different from NER. Collectively, the results identify N^2 -dGuo adducts bigger than methylguanine as a structural subclass of transcription-blocking DNA lesions whose repair heavily relies on the TC-NER pathway.

Exploring design strategies for healthier fruit smoothies.

Donda Zbinden, M., Vignatti, C. I., Faicán Benenaula, M. A., Böhm, V., Pirovani, M. E.
Curr. Food Sci. Technol. Rep. 2025; 3:9. doi.org/10.1007/s43555-025-00053-z

Purpose of review This study examines the development of smoothie formulations by combining fruits and vegetables to optimize bioactive properties. It also reviews recent advances in thermal and high pressure processing technologies that improve the shelf life of smoothies while maintaining bioactive potential.

Recent findings Incorporating dietary fiber into the formulation of fruit smoothies could favor the retention of bioactive compounds in smoothies during their processing and shelf life. Recent studies show that it is feasible to incorporate fiber from post-harvest vegetable processing discards, thereby promoting circular economy practices.

Summary The aim of this study is to develop strategies for formulating smoothies that fully or partially meet the daily requirement of specific bioactive compounds. It will also assess the potential shelf life of these products, taking into account the industrial processing technologies used, and provide insights into optimizing bioactive retention.

Revealing mercury species-specific transfer and toxicity mechanisms in placental trophoblasts.

Michaelis V, Klemens L, Thiel A, Gremme A, Schwarz M, Kipp AP, Zischka H. Chemosphere. 2025 Feb;370:143870. doi: 10.1016/j.chemosphere.2024.143870. Epub 2024 Dec 13.

Environmental mercury (Hg) follows a biogeochemical cycle resulting in a variety of Hg species. Therefore, human exposure to the three Hg species inorganic Hg via crops and air, methyl Hg through fish consumption and ethyl Hg due to the use as antiseptic agent in medical applications is a rising concern. Especially pregnant women and their developing fetus present a vulnerable population. However, little is known about its transfer and toxicity in placental barrier building cells. Here, Hg species-specific transfer and toxicity in placental trophoblasts, which are the main cell type involved in nutrient transfer, were investigated by using the established BeWo b30 in vitro model. The transfer of inorganic Hg was much lower compared to the organic Hg species and all three species were able to perturb barrier integrity. This was accompanied by a less pronounced cytotoxicity of HgCl₂ compared to the two organic species. The energy charge value indicated an increase for inorganic Hg and a decrease for organic Hg compounds. Regarding antioxidative defense, inorganic Hg elevated GSSG levels, while organic Hg decreased GSH. Activity of antioxidative defense related enzymes showed a decrease upon Hg species treatment and all three species induced both apoptotic and necrotic cell death.

Standardizing Nutritional Care for Cancer Patients: Implementation and Evaluation of a Malnutrition Risk Screening.

Mathies V, Kipp AP, Hammersen J, Schrenk KG, Scholl S, Schnetzke U, Hochhaus A, Ernst T. *Oncol Res Treat.* 2025;48(1-2):26-36. doi: 10.1159/000542460. Epub 2024 Nov 7.

Introduction: Cancer-related malnutrition is a highly prevalent, yet often overlooked concern in clinical practice. Although cancer-related management guidelines recommend standardized nutritional care, its implementation is scarce. The aim of this study was to investigate the prevalence of malnutrition and the medical need for nutrition counseling in cancer patients employing a novel standardized nutritional management program (containing malnutrition risk screening, nutritional assessment, and counseling). Furthermore, differences of malnutrition parameters in different cancer patient cohorts were examined.

Methods: Cancer patients were screened for malnutrition using the Patient-Generated Subjective Global Assessment Short Form (PG-SGA SF) on the first day of their inpatient admission to the internal oncology or hematology wards. PG-SGA total score and classification into the three PG-SGA nutrition stages (A, B, C) were used to determine nutritional status. In case of a positive screening, nutritional assessment and individualized counseling by a nutritionist followed. For group comparisons, patients were divided into different groups (e.g., age, gender, tumor entity) and were evaluated accordingly.

Results: A total of 1,100 inpatients were included. 56.8% of the patients had suspected or already existing malnutrition. The most common nutrition impact symptom was loss of appetite (26.7%), followed by fatigue (16.5%) and pain (16.0%). Female ($p < 0.001$), elderly ($p < 0.001$), and patients with upper gastrointestinal tract tumors ($p < 0.001$) showed an unfavorable nutritional status and higher need for counseling. Despite suffering from malnutrition, patients had body mass indices within the upper end of the normal range.

Conclusion: This study shows a high prevalence of malnutrition in hospitalized cancer patients and highlights the need for a standardized nutritional management in the clinical setting. Therefore, it is recommended to provide a malnutrition risk screening for all cancer patients and a following adequate assessment and personalized nutritional care if needed.

PRDX6 as an additional piece in the puzzle of selenoprotein synthesis.

Schwarz M, Kipp AP.

Mol Cell. 2024 Dec 5;84(23):4475-4477. doi: 10.1016/j.molcel.2024.11.010.

In this issue of *Molecular Cell*, Ito et al. and Chen et al. identify peroxiredoxin 6 (PRDX6) as member of the selenoprotein (re)synthesis machinery, thereby linking PRDX6 to ferroptosis susceptibility of cancer cells.

Connecting concentrations of copper, selenium, and zinc with transcriptomic and proteomic data of well-characterized human colorectal cancer cell lines.

Meyer CE, Vukelic N, Mariadason JM, Kipp AP.

J Trace Elem Med Biol. 2025 Mar 28;89:127638. doi: 10.1016/j.jtemb.2025.127638.

Background: Colorectal cancer (CRC) incidence is associated with lower circulating selenium and zinc and elevated copper concentrations. Moreover, copper and selenium accumulate within tumor tissue, indicating a disturbed homeostasis of these essential trace elements in CRC.

Objective: This study aimed to identify associations between CRC characteristics (based on genomic, transcriptomic and proteomic data) and trace element concentrations.

Methods: The concentrations of copper, selenium, and zinc were measured in 83 human CRC cell lines and correlated with transcript and protein expression levels to identify trace element-related gene signatures. By using publicly available gene expression data from The Cancer Genome Atlas we investigated the association between those signatures with the survival probability of CRC patients.

Results: The CRC cell lines differed in their copper (fold change 7.3), selenium (fold change 6), and zinc (fold change 2.6) concentrations. The concentrations were not associated with genetic or cellular characteristics, except for lower copper concentrations in KRAS mutant cells. Expression levels of known copper- and zinc-related proteins correlated significantly with the respective trace element concentrations, serving as a proxy for trace element concentrations in tumors, and with patient survival. This was not the case for selenium and selenoproteins. In addition, an unbiased approach identified novel high and low copper- and zinc-related gene expression signatures significantly associated with patient's outcome.

Conclusion: Herein we identify gene signatures associated with intracellular copper and zinc concentrations in CRC cell lines. Extrapolating these signatures to primary colorectal tumors revealed that they can inform outcome of CRC patients.

Improving the selenium supply of vegans and omnivores with Brazil nut butter compared to a dietary supplement in a randomized controlled trial.

Simon R, Lossow K, Pellowski D, Kipp K, Achatz M, Klasen N, Schwerdtle T, Dawczynski C, Kipp AP.

Eur J Nutr. 2025 Feb 1;64(2):74. doi: 10.1007/s00394-025-03587-z.

Purpose: A vegan diet is associated with health benefits but may also lead to inadequate intake of essential nutrients. Due to the lower selenium content in plant-based compared to animal-based foods, many vegans do not reach the recommended selenium intake in Europe. The only plant-based food with high selenium content is the Brazil nut, even though there is also a high variability. Therefore, we investigated the effectiveness of Brazil nut butter compared to a dietary supplement as selenium source to improve the selenium status of vegans and omnivores.

Methods: 44 vegans and 42 omnivores were randomly assigned to one of three intervention groups, either receiving placebo or consuming additional 55 µg of selenium daily as Brazil nut butter or supplement for two weeks. Serum selenium concentrations, glutathione peroxidase 3 (GPX3), and selenoprotein P (SELENOP) were measured at baseline and after intervention. Additionally, dietary selenium intake was estimated using a five-day dietary protocol.

Results: The estimated selenium intake was significantly lower in vegans compared to omnivores and correlated with all three selenium biomarkers. Independent of the dietary pattern (vegan or omnivore), Brazil nut butter as well as supplement significantly increased serum selenium and SELENOP concentrations, while there were no changes in the placebo groups. Both interventions were equally effective in increasing selenium levels, but the upregulation of SELENOP was more pronounced in vegans than in omnivores.

Conclusion: Brazil nuts are a plant-based source of selenium suitable for vegans and omnivores to improve their selenium status when consumed once in a while.

Validation of Nutritional Approaches to Modulate Cardiovascular and Diabetic Risk Factors in Patients with Hypertriglyceridemia or Prediabetes—The MoKaRi II Randomized Controlled Study. Braun TS, Drobner T, Kipp K, Kiehntopf M, Schlattmann P, Lorkowski S, Dawczynski C. *Nutrients* 2024, 16, 1261. <https://doi.org/10.3390/nu16091261>.

Hypertriglyceridemia and diabetes mellitus type 2 are among the most important metabolic diseases globally. Diet plays a vital role in the development and progression of both clinical pictures. For the 10-week randomized, controlled, intervention study, 67 subjects with elevated plasma triglyceride (TG) concentrations (≥ 1.7 mmol/L) and 69 subjects with elevated fasting glucose concentrations ($\geq 5.6 < 7.0$ mmol/L) were recruited. The intervention groups received specially developed, individualized menu plans and regular counseling sessions to lower (A) TG or (B) fasting glucose and glycated hemoglobin A1c as well as other cardiovascular and diabetic risk factors. The hypertriglyceridemia intervention group was further supplemented with fish oil (3.5 g/d eicosapentaenoic acid + docosahexaenoic acid). The two control groups maintained a typical Western diet. Blood samples were taken every 2 weeks, and anthropometric data were collected. A follow-up examination was conducted after another 10 weeks. In both intervention groups, there were comparable significant reductions in blood lipids, glucose metabolism, and anthropometric parameters. These results were, with a few exceptions, significantly more pronounced in the intervention groups than in the corresponding control groups (comparison of percentage change from baseline). In particular, body weight was reduced by 7.4% (6.4 kg) and 7.5% (5.9 kg), low-density lipoprotein cholesterol concentrations by 19.8% (0.8 mmol/L) and 13.0% (0.5 mmol/L), TG concentrations by 18.2% (0.3 mmol/L) and 13.0% (0.2 mmol/L), and homeostatic model assessment for insulin resistance by 31.8% (1.1) and 26.4% (0.9) ($p < 0.05$) in the hypertriglyceridemia and prediabetes intervention groups, respectively. Some of these changes were maintained until follow-up. In patients with elevated TG or fasting glucose, implementing individualized menu plans in combination with regular counseling sessions over 10 weeks led to a significant improvement in cardiovascular and diabetic risk factors.

Type of diet has no major influence on inflammatory response in a Saddleback pig model.

Wahl L, Rau S, Dawczynski CA, Lorkowski S, Ulrich R, Blüher M, Vervuert I. *Sci Rep* 2025 Mar 11;15(1):8381. doi: 10.1038/s41598-025-92420-y.

Fermentable carbohydrates and resulting short-chain fatty acids (SCFAs) received attention via modifying potential on obesity-associated systemic low-grade inflammation. However, their effects on inflammation remain poorly understood. In this study, the anti-inflammatory properties of pectin or inulin supplementation were investigated in an atherogenic-fed pig obesity model. Pigs were divided into three atherogenic-fed groups with or without 5% pectin/inulin supplementation (AD, ADp, ADi, $n = 10$) and a conventional-fed group (CD, $n = 10$) for a 15-week feeding period. We demonstrated that faecal SCFA concentrations decreased and faecal pH increased in all groups over the feeding period ($P < 0.05$). SCFA concentrations were comparable between colon and faeces in all groups. Liver inflammatory-marker expressions were on average < 1 in all groups, except TNF- α (AD $<$ CD and ADi; $P < 0.01$). Inflammatory-marker expressions in abdominal adipose tissue exceeded subcutaneous marker expressions in all groups. AD showed significantly lower IL-1 β and CD68 mRNA levels than CD ($P < 0.03$). Comparing the atherogenic diet groups, the IL-1 β mRNA levels were higher in ADi versus AD and ADp ($P = 0.02$). Our data indicated that fermentable carbohydrates added to an atherogenic diet cannot resolve low-grade adipose tissue inflammatory associated with obesity.

Comparative analysis of fatty acid profiles across omnivorous, flexitarians, vegetarians, and vegans: insights from the NuEva study.

Klein L, Lenz C, Krüger K, Lorkowski S, Kipp K, Dawczynski C. *Lipids Health Dis* 2025;24:133. doi: 10.1186/s12944-025-02517-6.

Background: Different dietary choices can influence blood fatty acid profiles, which are crucial for maintaining physiological health and reducing disease risk. In particular, the exclusion of animal foods in vegetarian diets is associated with a higher risk of undersupply of long-chain omega (n)-3 fatty acids, which could, potentially, have a negative effect on inflammation. This study aimed to examine differences in plasma and erythrocyte fatty acid profiles as well as inflammation-related biomarkers between various plant-based diets and a regular omnivores diet.

Methods: The Nutritional Evaluation (NuEva) study is a parallel-designed trial. Here screening data was used to investigate differences in plasma and erythrocyte fatty acid profiles across omnivores (Western diet; n = 62), flexitarians (n = 69), vegetarians (n = 64) and vegans (n = 57). Furthermore, markers associated with inflammation are investigated and correlated with selected fatty acids.

Results: Flexitarians showed lower erythrocyte saturated fatty acids (SFA) than omnivores, while vegans had the lowest plasma SFA. Vegans had higher erythrocyte monounsaturated fatty acids proportions, like oleic acid, than flexitarians and vegetarians. n-6 fatty acids, particularly linoleic acid, were highest in vegans and vegetarians. Conversely, omnivores had higher arachidonic acid in erythrocytes. Vegans had lower n-3 fatty acids in both plasma and erythrocytes, also reflected in a lower n-3 index (eicosapentaenoic acid (EPA) + docosahexaenoic acid (DHA)) values, indicating a trend with restriction of animal foods: omnivores/flexitarians > vegetarians > vegans. While interleukin (IL)-6, IL-8, IL-10, tumor necrosis factor (TNF)- α and high-sensitive C-reactive protein (hsCRP) did not differ between groups, and vegans had lower leptin levels compared to omnivores.

Conclusions: The NuEva study revealed significant impact of dietary patterns on fatty acid profiles, with vegans and vegetarians displaying lower concentrations of SFA and n-3 fatty acids, including EPA and DHA, compared to omnivores and flexitarians. Despite the clear differences in fatty acid profiles across the diets, the inflammatory markers measured in our healthy collective are comparable.

Effect of cancer therapy on the uptake and supply of selected micronutrients in acute myeloid leukemia.

Heß M, Huebner J, Dawczynski C, Serzisko J, Erickson N., Micke O, Schnetzke U, Scholl S, Mathies V. *Trace Elements Electrolytes* 2024;41:89-96; doi 10.5414/TE500083.

Objective: Acute myeloid leukemia (AML) is a disease with many challenges that impact nutrition intake. The aim of this pilot study was to assess nutritional problems and deficiencies of micronutrients during AML treatment to gain data for further and larger studies. Materials and

Methods: A questionnaire asked about food intake and symptomatic problems over 7 days. Blood analyses on selected micronutrients, albumin, and urea were collected at 3 fixed timepoints. A questionnaire was used to assess patient-reported data on nutrition and symptomatic problems during ongoing treatment for a pilot cohort of in-patients at a university hospital. This questionnaire was completed by the patients two times during the treatment (at the beginning of the induction therapy and after readmission for consolidation therapy). Also, blood samples were taken at 3 timepoints (at the beginning, at the end, and after readmission for consolidation therapy) and checked for selected micronutrients (vitamin B12, vitamin D, folic acid, vitamin B6, iron, and calcium) and substances synthesized in the body (albumin and urea).

Results: 16 patients participated in the study. The patients ate on average 64% of their ordered menus. The assessment of the ordered menus indicated that the average of all investigated micronutrients was below the recommended reference levels of the German Nutrition Society. The patients' vitamin B6 levels and the albumin concentration were below the reference range. In contrast, some patients had increased vitamin B12 levels.

Conclusion: Diagnosis and treatment of AML have a strong impact on eating habits of patients. Physicians should pay close attention to nutrition status in order to prevent malnutrition. Further studies to verify these data and to assess whether nutrition medicine may prevent malnutrition in this setting are necessary. ^[P]_[SEP]

Improving the selenium supply of vegans and omnivores with Brazil nut butter compared to a dietary supplement in a randomized controlled trial.

Simon R, Lossow K, Pellowski D, Kipp K, Achatz M, Klasen N, Schwerdtle T, Dawczynski C, Kipp AP. *Eur J Nutr* 2025; 64(2):74. doi: 10.1007/s00394-025-03587-z.

Purpose: A vegan diet is associated with health benefits but may also lead to inadequate intake of essential nutrients. Due to the lower selenium content in plant-based compared to animal-based foods, many vegans do not reach the recommended selenium intake in Europe. The only plant-based food with high selenium content is the Brazil nut, even though there is also a high variability. Therefore, we investigated the effectiveness of Brazil nut butter compared to a dietary supplement as selenium source to improve the selenium status of vegans and omnivores.

Methods: 44 vegans and 42 omnivores were randomly assigned to one of three intervention groups, either receiving placebo or consuming additional 55 µg of selenium daily as Brazil nut butter or supplement for two weeks. Serum selenium concentrations, glutathione peroxidase 3 (GPX3), and selenoprotein P (SELENOP) were measured at baseline and after intervention. Additionally, dietary selenium intake was estimated using a five-day dietary protocol.

Results: The estimated selenium intake was significantly lower in vegans compared to omnivores and correlated with all three selenium biomarkers. Independent of the dietary pattern (vegan or omnivore), Brazil nut butter as well as supplement significantly increased serum selenium and SELENOP concentrations, while there were no changes in the placebo groups. Both interventions were equally effective in increasing selenium levels, but the upregulation of SELENOP was more pronounced in vegans than in omnivores.

Conclusion: Brazil nuts are a plant-based source of selenium suitable for vegans and omnivores to improve their selenium status when consumed once in a while.

Reduction of cardiovascular risk factors by the diet – Evaluation of the MoKaRi concept by a parallel-designed randomized study.

Dawczynski C, Drobner T, Weidauer T, Schlattmann P, Kiehntopf M, Weber D, Grune T, März W, Kleber ME, Lorkowski S. *Lipids Health Dis* 2025 Mar 8;24:88. doi: 10.1186/s12944-025-02500-1.

Background and aim: The MoKaRi study aims to evaluate the impact of two nutritional concepts on cardiometabolic risk factors.

Methods: For our 20-week intervention study, 65 participants with moderate elevated low-density lipoprotein cholesterol (LDL-C; ≥ 3 mmol/l) and without lipid-lowering therapy were recruited. The intervention to improve nutritional behavior was based on individualized menu plans which were characterized by defined energy and nutrient intake. To improve compliance, individual nutritional counselling sessions were held every two weeks. In addition to motivation, cooking skills were strengthened and nutritional knowledge was imparted. Follow-up visits were carried out after 10 and 20 weeks.

Results: The MoKaRi diet lowered the concentrations of total cholesterol (menu plan group (MP): -15%; menu plan plus fish oil group (MP-FO): -11%), LDL-C (MP: -14%; MP-FO: -16%) and non-high-density lipoprotein cholesterol (MP: -16%; MP-FO: -13%) ($p < 0.001$). Body weight (MP: -5%; MP-FO: -8%; $p < 0.05$), waist circumference (MP: -6%; MP-FO: -9%) as well as diastolic blood pressure (MP: -8%; MP-FO: -8%), apolipoprotein A1 (MP: -15%; MP-FO: -20%), apolipoprotein B (MP: -15%; MP-FO: -6%) and glycated hemoglobin A_{1c} (HbA_{1c}) (MP: -1.8%; MP-FO: -3.6%) were also reduced in both groups after 20 weeks ($p < 0.05$). In both intervention groups, a maximum reduction in LDL-c of approx. 26% was achieved within the 20 weeks of intervention. Individual participants achieved a reduction of 45-49%. The supplementation of fish oil on top of the menu plans resulted in more substantial effects on body weight (MP: -5% vs. MP-FO: -8%), body fat (MP: -11% vs. MP-FO: -20%), triglycerides (MP: -14% vs. MP-FO: -28%), high-sensitivity C-reactive protein (MP: -19% vs. MP-FO: -43%) and HbA_{1c} (MP: -1.8% vs. MP-FO: -3.6%; $p < 0.05$).

Conclusions: The MoKaRi diet resulted in a significant reduction of cardiometabolic risk factors. Our data highlights the additional benefit of the combination between menu plans and fish oil supplementation, which resulted in more substantial effects on body weight, BMI, TG, HbA_{1c} and hs-CRP.

α -Tocopherol Long-Chain Metabolite α -T-13'-COOH Exhibits Biphasic Effects on Cell Viability, Induces ROS-Dependent DNA Damage, and Modulates Redox Status in Murine RAW264.7 Macrophages.

Liao S, Börmel L, Müller AK, Gottschalk L, Pritsch N, Preisner LZ, Samokhina O, Schwarz M, Kipp AP, Schlörmann W, Gleis M, Schubert M, Schmölz L, Wallert M, Lorkowski S. Mol Nutr Food Res. 2024 Dec;68(23):e2400455. doi: 10.1002/mnfr.202400455.

Scope: The α -tocopherol long-chain metabolite α -tocopherol-13'-hydroxy-chromanol (α -T-13'-COOH) is a proposed regulatory intermediate of endogenous vitamin E metabolism. Effects of α -T-13'-COOH on cell viability and adaptive stress response are not well understood. The present study aims to investigate the concentration-dependent effects of α -T-13'-COOH on cellular redox homeostasis, genotoxicity, and cytotoxicity in murine RAW264.7 macrophages as a model system.

Methods and results: Murine RAW264.7 macrophages are exposed to various dosages of α -T-13'-COOH to determine its regulatory effects on reactive oxygen species (ROS) production, DNA damage, expression of stress-related markers, and the activity of ROS scavenging enzymes including superoxide dismutases, catalase, and glutathione-S-transferases. The impact on cell viability is assessed by analyzing cell proliferation, cell cycle arrest, and cell apoptosis.

Conclusion: α -T-13'-COOH influences ROS production and induces DNA damage in a dose-dependent manner. The metabolite modulates the activity of ROS-scavenging enzymes, with significant changes observed in the activities of antioxidant enzymes. A biphasic response affecting cell viability is noted: sub-micromolar doses of α -T-13'-COOH promote cell proliferation and enhance DNA synthesis, whereas supraphysiological doses lead to DNA damage and cytotoxicity. It hypothesizes an adaptive stress response, characterized by upregulation of ROS detoxification mechanisms, enhanced cell cycle arrest, and increased apoptosis, indicating a correlation with oxidative stress and subsequent cellular damage.

Vitamin E nomenclature: Summary and response to articles published in the FRBM Vitamin E Discussion Forum.

Angelo Azzi, Atkinson J, Ozer NK, Manor D, Wallert M, Galli F. Free Radic Biol Med. 2025 Jul;234:277-282. doi: 10.1016/j.freeradbiomed.2025.04.005. Epub 2025 Apr 6.

The 3rd Vitamin E Satellite Symposium (VESS3) "100 years of vitamin E", held in 2022 during the joint meeting of the Society for Free Radical Research (SFRR)-Europe branch and the Plant Oxygen Group (POG), was an occasion to reunite the scientific community interested in vitamin E and debate on its fundamentals in human nutrition one century after its discovery. This conference initiated a discussion forum dedicated to the revision of the nomenclature of vitamin E that was hosted in this journal (<https://www.sciencedirect.com/special-issue/10GWS76VWXX>). The forum collected 8 papers, including the opening article "Vitamin E discussion forum - position paper on the revision of the nomenclature of vitamin E" (Azzi, Atkinson et al., 2023), that addressed the nomenclature issue essentially suggesting "to restrict to RRR- α -tocopherol the attribute of vitamin E" and to identify "... other related molecules, including chroman-6-ols (i.e. non- α -tocopherols and tocotrienols) and chromen-6-ols by their chemical names until a disease is identified that is prevented by the specific compounds.". The articles published in this forum issue are summarized and their final considerations critically evaluated. The consensus to have come out of these articles favors the original revision proposal, with the modification of including all 2R stereoisomers of α -tocopherol (α -TOH), in addition to RRR- α -TOH (natural form), in the definition of vitamin E. Further and more rigorous studies on the molecular and clinical aspects of vitamin E essentiality were also advised together with studies on the essentiality of other vitamin E-related compounds.

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 Feb 21. doi: 10.1007/s10753-025-02269-6. Online ahead of print.

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- δ -tocotrienol), which is isolated from the *Garcinia kola* seeds. This derivative and potential metabolite of the vitamin E congener δ -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 'kappa-light-chain-enhancer' of activated B-cells (NF- κ 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.

Regulation of nc886 (vtRNA2-1) RNAs is associated with cardiometabolic risk factors and diseases.

Rajić S, Delerue T, Ronkainen J, Zhang R, Ciantar J, Kostiniuk D, Mishra PP, Lyytikäinen LP, Mononen N, Kananen L, Peters A, Winkelmann J, Kleber ME, Lorkowski S, Kähönen M, Lehtimäki T, Raitakari O, Waldenberger M, Gieger C, März W, Harville EW, Sebert S, Marttila S, Raitoharju E.

Clin Epigenetics 2025; 17(1):68. DOI: 10.1186/s13148-025-01871-7.

Non-coding 886 (nc886, vtRNA2-1) is a polymorphically imprinted gene. The methylation status of this locus has been shown to be associated with periconceptional conditions, and both the methylation status and the levels of nc886 RNAs have been shown to associate with later-life health traits. We have previously shown that nc886 RNA levels are associated not only with the methylation status of the locus, but also with a genetic polymorphism upstream from the locus. In this study, we describe the genetic and epigenetic regulators that predict lifelong nc886 RNA levels, as well as their association with cardiometabolic disease (CMD) risk factors and events. We utilised six population cohorts and one CMD cohort comprising 9058 individuals in total. The association of nc886 RNA levels, as predicted by epigenetic and genetic regulators, with CMD phenotypes was analysed using regression models, with a meta-analysis of the results. The meta-analysis showed that individuals with upregulated nc886 RNA levels have higher diastolic blood pressure ($\beta = 0.07$, $p = 0.008$), lower HDL levels ($\beta = -0.07$, $p = 0.006$) and an increased incidence of type 2 diabetes (OR = 1.260, $p = 0.013$). Moreover, CMD patients with upregulated nc886 RNA levels have an increased incidence of stroke (OR = 1.581, $p = 0.006$) and death (OR = 1.290, $p = 0.046$). In conclusion, we show that individuals who are predicted to present elevated nc886 RNA levels have poorer cardiovascular health and are at an elevated risk of complications in secondary prevention. This unique mechanism yields metabolic variation in human populations, constituting a CMD risk factor that cannot be modified through lifestyle choices.

A methodological framework for deriving the German food-based dietary guidelines 2024: Food groups, nutrient goals, and objective functions.

Schäfer AC, Boeing H, Gazan R, Conrad J, Gedrich K, Breidenassel C, Hauner H, Kroke A, Linseisen J, Lorkowski S, Nöthlings U, Richter M, Schwingshackl L, Vieux F, Watzl B.

PLoS One 2025; 20(3):e0313347. DOI: 10.1371/journal.pone.0313347.

Background: For a growing number of food-based dietary guidelines (FBDGs), diet optimization is the tool of choice to account for the complex demands of healthy and sustainable diets. However, decisions about such optimization models' parameters are rarely reported nor systematically studied.

Objectives: The objectives were to develop a framework for (i) the formulation of decision variables based on a hierarchical food classification system; (ii) the mathematical form of the objective function; and (iii) approaches to incorporate nutrient goals.

Methods: To answer objective (i), food groups from FoodEx2 levels 3-7 were applied as decision variables in a model using acceptability constraints (5th and 95th percentile for food intakes of German adults ($n = 10,419$)) and minimizing the deviation from the average observed dietary intakes. Building upon, to answer objectives (ii) and (iii), twelve models were run using decision variables from FoodEx2 level 3 ($n = 255$), applying either a linear or squared and a relative or absolute way to deviate from observed dietary intakes, and three different lists of nutrient goals (allNUT-DRV, incorporating all nutrient goals; modNUT-DRV excluding nutrients with limited data quality; modNUT-AR using average requirements where applicable instead of recommended intakes).

Results: FoodEx2 food groups proved suitable as diet optimization decision variables. Regarding deviation, the largest differences were between the four different objective function types, e.g., in the linear-relative modNUT-DRV model, 46 food groups of the observed diet were changed to reach the model's goal, in linear-absolute 78 food groups, squared-relative 167, and squared-absolute 248. The nutrient goals were fulfilled in all models, but the number of binding nutrient constraints was highest in the linear-relative models (e.g. allNUT-DRV: 11 vs. 7 in linear-absolute).

Conclusion: Considering the various possibilities to operationalize dietary aspects in an optimization model, this study offers valuable contributions to a framework for developing FBDGs via diet optimization.

Global, regional, and national prevalence of adult overweight and obesity, 1990-2021, with forecasts to 2050: a forecasting study for the Global Burden of Disease Study 2021.

GBD 2021 Adult BMI Collaborators.

Lancet 2025; 405(10481):813-838. DOI: 10.1016/S0140-6736(25)00355-1.

Background: Overweight and obesity is a global epidemic. Forecasting future trajectories of the epidemic is crucial for providing an evidence base for policy change. In this study, we examine the historical trends of the global, regional, and national prevalence of adult overweight and obesity from 1990 to 2021 and forecast the future trajectories to 2050.

Methods: Leveraging established methodology from the Global Burden of Diseases, Injuries, and Risk Factors Study, we estimated the prevalence of overweight and obesity among individuals aged 25 years and older by age and sex for 204 countries and territories from 1990 to 2050. Retrospective and current prevalence trends were derived based on both self-reported and measured anthropometric data extracted from 1350 unique sources, which include survey microdata and reports, as well as published literature. Specific adjustment was applied to correct for self-report bias. Spatiotemporal Gaussian process regression models were used to synthesise data, leveraging both spatial and temporal correlation in epidemiological trends, to optimise the comparability of results across time and geographies. To generate forecast estimates, we used forecasts of the Socio-demographic Index and temporal correlation patterns presented as annualised rate of change to inform future trajectories. We considered a reference scenario assuming the continuation of historical trends.

Findings: Rates of overweight and obesity increased at the global and regional levels, and in all nations, between 1990 and 2021. In 2021, an estimated 1·00 billion (95% uncertainty interval [UI] 0·989-1·01) adult males and 1·11 billion (1·10-1·12) adult females had overweight and obesity. China had the largest population of adults with overweight and obesity (402 million [397-407] individuals), followed by India (180 million [167-194]) and the USA (172 million [169-174]). The highest age-standardised prevalence of overweight and obesity was observed in countries in Oceania and north Africa and the Middle East, with many of these countries reporting prevalence of more than 80% in adults. Compared with 1990, the global prevalence of obesity had increased by 155·1% (149·8-160·3) in males and 104·9% (95% UI 100·9-108·8) in females. The most rapid rise in obesity prevalence was observed in the north Africa and the Middle East super-region, where age-standardised prevalence rates in males more than tripled and in females more than doubled. Assuming the continuation of historical trends, by 2050, we forecast that the total number of adults living with overweight and obesity will reach 3·80 billion (95% UI 3·39-4·04), over half of the likely global adult population at that time. While China, India, and the USA will continue to constitute a large proportion of the global population with overweight and obesity, the number in the sub-Saharan Africa super-region is forecasted to increase by 254·8% (234·4-269·5). In Nigeria specifically, the number of adults with overweight and obesity is forecasted to rise to 141 million (121-162) by 2050, making it the country with the fourth-largest population with overweight and obesity.

Interpretation: No country to date has successfully curbed the rising rates of adult overweight and obesity. Without immediate and effective intervention, overweight and obesity will continue to increase globally. Particularly in Asia and Africa, driven by growing populations, the number of individuals with overweight and obesity is forecast to rise substantially. These regions will face a considerable increase in obesity-related disease burden. Merely acknowledging obesity as a global health issue would be negligent on the part of global health and public health practitioners; more aggressive and targeted measures are required to address this crisis, as obesity is one of the foremost avertible risks to health now and in the future and poses an unparalleled threat of premature disease and death at local, national, and global levels.

Global, regional, and national prevalence of child and adolescent overweight and obesity, 1990-2021, with forecasts to 2050: a forecasting study for the Global Burden of Disease Study 2021.

GBD 2021 Adolescent BMI Collaborators.

Lancet 2025; 405(10481):785-812. DOI: 10.1016/S0140-6736(25)00397-6.

Background: Despite the well documented consequences of obesity during childhood and adolescence and future risks of excess body mass on non-communicable diseases in adulthood, coordinated global action on excess body mass in early life is still insufficient. Inconsistent measurement and reporting are a barrier to specific targets, resource allocation, and interventions. In this Article we report current estimates of overweight and obesity across childhood and adolescence, progress over time, and forecasts to inform specific actions.

Methods: Using established methodology from the Global Burden of Diseases, Injuries, and Risk Factors Study 2021, we modelled overweight and obesity across childhood and adolescence from 1990 to 2021, and then forecasted to 2050. Primary data for our models included 1321 unique measured and self-reported anthropometric data sources from 180 countries and territories from survey microdata, reports, and published literature. These data were used to estimate age-standardised global, regional, and national overweight prevalence and obesity prevalence (separately) for children and young adolescents (aged 5-14 years, typically in school and cared for by child health services) and older adolescents (aged 15-24 years, increasingly out of school and cared for by adult services) by sex for 204 countries and territories from 1990 to 2021. Prevalence estimates from 1990 to 2021 were generated using spatiotemporal Gaussian process regression models, which leveraged temporal and spatial correlation in epidemiological trends to ensure comparability of results across time and geography. Prevalence forecasts from 2022 to 2050 were generated using a generalised ensemble modelling approach assuming continuation of current trends. For every age-sex-location population across time (1990-2050), we estimated obesity (vs overweight) predominance using the log ratio of obesity percentage to overweight percentage.

Findings: Between 1990 and 2021, the combined prevalence of overweight and obesity in children and adolescents doubled, and that of obesity alone tripled. By 2021, 93·1 million (95% uncertainty interval 89·6-96·6) individuals aged 5-14 years and 80·6 million (78·2-83·3) aged 15-24 years had obesity. At the super-region level in 2021, the prevalence of overweight and of obesity was highest in north Africa and the Middle East (eg, United Arab Emirates and Kuwait), and the greatest increase from 1990 to 2021 was seen in southeast Asia, east Asia, and Oceania (eg, Taiwan [province of China], Maldives, and China). By 2021, for females in both age groups, many countries in Australasia (eg, Australia) and in high-income North America (eg, Canada) had already transitioned to obesity predominance, as had males and females in a number of countries in north Africa and the Middle East (eg, United Arab Emirates and Qatar) and Oceania (eg, Cook Islands and American Samoa). From 2022 to 2050, global increases in overweight (not obesity) prevalence are forecasted to stabilise, yet the increase in the absolute proportion of the global population with obesity is forecasted to be greater than between 1990 and 2021, with substantial increases forecast between 2022 and 2030, which continue between 2031 and 2050. By 2050, super-region obesity prevalence is forecasted to remain highest in north Africa and the Middle East (eg, United Arab Emirates and Kuwait), and forecasted increases in obesity are still expected to be largest across southeast Asia, east Asia, and Oceania (eg, Timor-Leste and North Korea), but also in south Asia (eg, Nepal and Bangladesh). Compared with those aged 15-24 years, in most super-regions (except Latin America and the Caribbean and the high-income super-region) a greater proportion of those aged 5-14 years are forecasted to have obesity than overweight by 2050. Globally, 15·6% (12·7-17·2) of those aged 5-14 years are forecasted to have obesity by 2050 (186 million [141-221]), compared with 14·2% (11·4-15·7) of those aged 15-24 years (175 million [136-203]). We forecasted that by 2050, there will be more young males (aged 5-14 years) living with obesity (16·5% [13·3-18·3]) than overweight (12·9% [12·2-13·6]); while

for females (aged 5-24 years) and older males (aged 15-24 years), overweight will remain more prevalent than obesity. At a regional level, the following populations are forecast to have transitioned to obesity (vs overweight) predominance before 2041-50: children and adolescents (males and females aged 5-24 years) in north Africa and the Middle East and Tropical Latin America; males aged 5-14 years in east Asia, central and southern sub-Saharan Africa, and central Latin America; females aged 5-14 years in Australasia; females aged 15-24 years in Australasia, high-income North America, and southern sub-Saharan Africa; and males aged 15-24 years in high-income North America.

Interpretation: Both overweight and obesity increased substantially in every world region between 1990 and 2021, suggesting that current approaches to curbing increases in overweight and obesity have failed a generation of children and adolescents. Beyond 2021, overweight during childhood and adolescence is forecast to stabilise due to further increases in the population who have obesity. Increases in obesity are expected to continue for all populations in all world regions. Because substantial change is forecasted to occur between 2022 and 2030, immediate actions are needed to address this public health crisis.

Changing life expectancy in European countries 1990-2021: a subanalysis of causes and risk factors from the Global Burden of Disease Study 2021.

GBD 2021 Europe Life Expectancy Collaborators.

Lancet Public Health 2025; 10(3):e172-e188. DOI: 10.1016/S2468-2667(25)00009-X.

Background: Decades of steady improvements in life expectancy in Europe slowed down from around 2011, well before the COVID-19 pandemic, for reasons which remain disputed. We aimed to assess how changes in risk factors and cause-specific death rates in different European countries related to changes in life expectancy in those countries before and during the COVID-19 pandemic.

Methods: We used data and methods from the Global Burden of Diseases, Injuries, and Risk Factors Study 2021 to compare changes in life expectancy at birth, causes of death, and population exposure to risk factors in 16 European Economic Area countries (Austria, Belgium, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Luxembourg, the Netherlands, Norway, Portugal, Spain, and Sweden) and the four UK nations (England, Northern Ireland, Scotland, and Wales) for three time periods: 1990-2011, 2011-19, and 2019-21. Changes in life expectancy and causes of death were estimated with an established life expectancy cause-specific decomposition method, and compared with summary exposure values of risk factors for the major causes of death influencing life expectancy.

Findings: All countries showed mean annual improvements in life expectancy in both 1990-2011 (overall mean 0.23 years [95% uncertainty interval [UI] 0.23 to 0.24]) and 2011-19 (overall mean 0.15 years [0.13 to 0.16]). The rate of improvement was lower in 2011-19 than in 1990-2011 in all countries except for Norway, where the mean annual increase in life expectancy rose from 0.21 years (95% UI 0.20 to 0.22) in 1990-2011 to 0.23 years (0.21 to 0.26) in 2011-19 (difference of 0.03 years). In other countries, the difference in mean annual improvement between these periods ranged from -0.01 years in Iceland (0.19 years [95% UI 0.16 to 0.21] vs 0.18 years [0.09 to 0.26]), to -0.18 years in England (0.25 years [0.24 to 0.25] vs 0.07 years [0.06 to 0.08]). In 2019-21, there was an overall decrease in mean annual life expectancy across all countries (overall mean -0.18 years [95% UI -0.22 to -0.13]), with all countries having an absolute fall in life expectancy except for Ireland, Iceland, Sweden, Norway, and Denmark, which showed marginal improvement in life expectancy, and Belgium, which showed no change in life expectancy. Across countries, the causes of death responsible for the largest improvements in life expectancy from 1990 to 2011 were cardiovascular diseases and neoplasms. Deaths from cardiovascular diseases were the primary driver of reductions in life expectancy improvements during 2011-19, and deaths from respiratory infections and other COVID-19 pandemic-related

outcomes were responsible for the decreases in life expectancy during 2019-21. Deaths from cardiovascular diseases and neoplasms in 2019 were attributable to high systolic blood pressure, dietary risks, tobacco smoke, high LDL cholesterol, high BMI, occupational risks, high alcohol use, and other risks including low physical activity. Exposure to these major risk factors differed by country, with trends of increasing exposure to high BMI and decreasing exposure to tobacco smoke observed in all countries during 1990-2021.

Interpretation: The countries that best maintained improvements in life expectancy after 2011 (Norway, Iceland, Belgium, Denmark, and Sweden) did so through better maintenance of reductions in mortality from cardiovascular diseases and neoplasms, underpinned by decreased exposures to major risks, possibly mitigated by government policies. The continued improvements in life expectancy in five countries during 2019-21 indicate that these countries were better prepared to withstand the COVID-19 pandemic. By contrast, countries with the greatest slowdown in life expectancy improvements after 2011 went on to have some of the largest decreases in life expectancy in 2019-21. These findings suggest that government policies that improve population health also build resilience to future shocks. Such policies include reducing population exposure to major upstream risks for cardiovascular diseases and neoplasms, such as harmful diets and low physical activity, tackling the commercial determinants of poor health, and ensuring access to affordable health services.

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

Linseisen J, Renner B, Gedrich K, Wirsam J, Holzapfel C, Lorkowski S, Watzl B, Daniel H, Leitzmann M; Working Group "Personalized Nutrition" of the German Nutrition Society. *Adv Nutr* 2025;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.