ABSTRACTS OF THE JOINT INTERNATIONAL SYMPOSIA "VITAMIN D IN PREVENTION AND THERAPY" AND "BIOLOGIC EFFECTS OF LIGHT"

10-12 June, 2026

Schlossberg Hotel, Homburg/Saar, Germany

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Oral presentations (OP)

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OP No. 18
VITAMIN D AND LYMPHOMA: AN UPDATE

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Retrospective analysis from clinical trials have shown improved survival in lymphoma patients with sufficient vitamin D levels. Evidence from animal models and cell-killing assays further indicated that this association was not merely a reflection of better general health but may instead have been related to enhanced treatment efficacy – specifically, improved effectiveness of chemotherapy in Hodgkin lymphoma and of immunotherapy in non-Hodgkin lymphoma among vitamin D–sufficient patients. Multifactorial analysis of lymphoma prognosis including all known risk factors confirmed and independent association between vitamin D status and survival. These findings raised the hope that supplementation of vitamin D given in parallel with chemo-immunotherapy may improve clinical outcomes. Accordingly, rapid, high-dose supplementation protocols were implemented in several clinical trials in both aggressive and indolent non-Hodgkin lymphoma. However, these trials failed to show an improved survival, even though patients had low baseline levels of vitamin D and were supplemented to a median serum vitamin D level within the normal range (65 ng/ml). This led to a more conservative approach to vitamin D supplementation among hematologists. At the same time, results from animal models showed that vitamin D deficiency may change the microbiome, and that this effect can be transmitted between mice by fecal microbiota transfer. This observation raises the hypothesis that vitamin D supplementation alone is not enough to restore all downstream effects of vitamin D deficiency, and that a healthy vitamin D–associated microbiome may also be required to impact on clinical outcomes.

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OP No. 17
LARGE-SCALE TRIALS ON THE IMPACT OF VITAMIN D SUPPLEMENTATION: THE VITAL STUDY AND THE D-HEALTH STUDY REVISITED

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Background/Aim: Vitamin D insufficiency and deficiency remain common in many populations. Large, randomized trials conducted in vitamin D-replete populations in the United States (VITAL) and Australia (D-Health) found that vitamin D supplementation did not significantly reduce major adverse health outcomes. We emulated these trials to estimate the effects that might be expected in populations with lower vitamin D repletion. *Patients and Methods:* We selected subcohorts from the UK Biobank cohort using the inclusion criteria of the VITAL and D-Health trials. Within these subcohorts, we estimated hazard ratios of major health outcomes (total mortality, major cardiovascular events, cancer, hospitalizations due to infections) in relation to increases in serum 25-hydroxy-vitamin D [25(OH)D], using follow-up durations corresponding to those reported in the trials. We repeated these analyses under different assumptions of baseline 25(OH)D. *Results:* When the study participants were weighted to match the serum 25(OH)D distributions of the VITAL and D-Health study populations, the results

were nearly identical to the null findings reported in the trials. By contrast, major, statistically significant reductions of all the assessed adverse health outcomes were obtained when the study populations were restricted to people with vitamin D insufficiency or deficiency. For example, all-cause mortality would have been expected to decrease by 15% (95%CI=9%-21%) and 19% (95%CI=14%-24%), respectively. *Conclusion:* The negative results of the VITAL and D-Health trials were expected, given that the trials were conducted in vitamin D replete populations. Substantial mortality and morbidity reductions would have been expected if the trials had been conducted in populations most likely to benefit from vitamin D supplementation.

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OP No. 2

***IN VIVO* TRANSCRIPTIONAL AND EPIGENETIC RESPONSE OF HUMAN IMMUNE CELLS TO VITAMIN D_3 SUPPLEMENTATION**

Carsten Carlberg

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No abstract submitted.

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OP No. 10

ABSORBED AND ACTIVE? VITAMIN D_2 PHOTOISOMERS – WHAT'S KNOWN?

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UVB irradiation of foods rich in ergosterol (*e.g.*, mushrooms, baker's yeast) is an established process for vitamin D_2 fortification that is approved in the European Union. However, in addition to vitamin D_2, this process also produces photoisomers such as lumisterol$_2$ (L_2) and tachysterol$_2$ (T_2), (seco)steroidal vitamin D-like compounds whose physiological relevance and availability have long been largely ignored. Studies in mice demonstrate that orally ingested L_2 and T_2 are absorbed, detectable in plasma and tissues, and can modulate vitamin D metabolism. Thus, higher intakes are associated with lower circulating calcitriol and altered renal expression of key vitamin D-metabolizing enzymes (including Cyp27b1 and Cyp24a1). Mechanistic data further indicate crosstalk between T_2 and vitamin D signaling *in vivo* and in osseous cell models, T_2 induces fibroblast growth factor 23 (FGF23) in a VDR-dependent manner and modulates osteoblast marker gene expression. These responses are accompanied by changes in mineral homeostasis, including shifts in plasma Ca^{2+} and transcriptional regulation of renal and intestinal Ca^{2+} transport pathways, consistent with potential effects on bone morphology and microarchitecture. Findings from cells suggest that T_2 requires prior hydroxylation involving CYP27A1. L_2 is also an efficient CYP27A1 substrate, and its hydroxylated metabolites are considered biologically active. Emerging cell-based findings further suggest additional molecular actions of L_2, including effects on hepatic cholesterol metabolism and AMPK signaling. Importantly, first-in-human evidence from a randomized intervention study shows that consumption of UVB–treated mushrooms lead to rapid postprandial appearance of L_2 and T_2 in plasma, with sustained detectability upon repeated intake. To conclude, these findings indicate that vitamin D_2 photoisomers are not merely "by-products" of UVB treatment of food, but absorbable compounds with potential biological activity. The presentation summarizes the current animal, cell-based, and first-in-human evidence, on absorption, metabolism, and biological effects of vitamin D_2 photoisomers and discusses plausible mechanisms of action.

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OP No. 20
PHOTOSENSITIVITY OF ANTI-HYPERTENSION MEDICATION AND SKIN CANCER: HOW STRONG IS THE EVIDENCE?

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Background/Aim: The complex relationship between antihypertensive therapies, photosensitivity, and skin cancer remains incompletely understood. *Methods:* We conducted a review of the medical literature until December 2025, identifying preclinical studies, observational clinical studies as well as randomized controlled trials investigating the associations among antihypertensives, photosensitivity and skin cancer. *Results:* Observational studies provide a strong signal suggesting an increased risk of non-melanoma skin cancer in patients taking antihypertensives, especially thiazide diuretics, over a long period. Data on other antihypertensives are less clear. There is conflicting preclinical evidence on the photosensitivity of antihypertensives. Adequately powered randomized controlled trials are scarce. *Conclusion:* Thiazide diuretics in particular appear to be associated with an increased risk of developing non-melanoma skin cancer. Further studies, especially mechanistic investigations, are urgently needed to clarify the interplay among antihypertensives, sunlight and human skin.

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OP No. 44
MURINE URINARY THYMIDINE DIMER EXCRETION AFTER UVA AND UVB EXPOSURE AND DURING LONG-TERM VORICONAZOLE AND PREDNISOLONE TREATMENT

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Background/Aim: Thymidine dimer (TT) is a biomarker of ultraviolet radiation (UVR)-induced DNA damage. Recently, we demonstrated that TT can be quantified in murine urine. This study investigated how urinary excretion of TT depends on UVR source and long-term treatment with voriconazole or prednisolone. *Materials and Methods:* In the UVA/UVB radiation study groups of hairless mice (C3.Cg-Hr^{hr}/TifBomTac; n=7) were irradiated once with either UVB (1, 2, 3, 4 or 5 SED) or UVA (1, 2, 4, 6 or 8 SED) and urine was collected for 5 days post-exposure. In the pharmacological intervention tumor (squamous cell carcinoma, SCC) study, groups of mice (n=25) were treated intraperitoneally with voriconazole (5 mg/kg), prednisolone (30 mg/kg) or corn oil (control) twice weekly and irradiated thrice weekly with 3.5 SED solar simulated UVR. Urine was collected on three occasions for five consecutive days in 10 mice per group. Urinary excretion of TT was measured by liquid chromatography-mass spectrometry. *Results:* Urinary TT excretion followed a linear dose-response with slopes that differed markedly between radiation sources. UVB exposure resulted in a slope of ~8.6 ng TT/ml urine/SED (r^2=0.986, p<0.001) whereas UVA exposure resulted in a slope of ~2.2 ng TT/ml urine/SED (r^2=0.933, p<0.001). The tumor study is ongoing. Preliminary data show a delayed time to first tumor for prednisolone-treated mice (median: 178 days) *vs*. control (median: 155 days) (p<0.01), while no difference was observed for voriconazole-treated mice. TT data from this study will be presented at the conference. *Conclusion:* Murine TT excretion is useful for measuring the DNA damage induced by different radiation sources and may also help describe photocarcinogenic effects of pharmacological treatments.

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OP No. 19

MELANOMA AND VITAMIN D STATUS: FROM RISK TO PROGNOSIS

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Background/Aim: Solar ultraviolet (UV) radiation is the major environmental risk factor for skin cancer. At the same time, UV-B exposure induces cutaneous vitamin D synthesis, and vitamin D has shown anti-proliferative and pro-differentiation effects on melanocytes and melanoma cells in experimental studies. This study systematically assessed whether vitamin D status is associated with malignant melanoma risk and prognosis. *Materials and Methods:* A systematic review with meta-analyses was performed using Medline (via PubMed) and ISI Web of Science (search completed December 31, 2022). Eligible observational studies (cohort and case-control) evaluated serum 25-hydroxyvitamin D [25(OH)D] in relation to melanoma risk and established prognostic markers. Vitamin D deficiency was defined as ≤20 ng/ml. Random-effects models were used to pool standardized mean differences and odds ratios (ORs). *Results:* Melanoma patients showed significantly lower mean 25(OH)D levels than healthy controls (standardized mean difference −0.40; corresponding to approximately −4.6 ng/ml). Vitamin D deficiency was associated with a non-significant trend toward increased melanoma risk (OR=1.79; 95% confidence interval=0.95-3.37), with subgroup analyses in Southern European studies indicating stronger associations. Lower 25(OH)D levels were significantly linked to adverse prognostic features, including greater Breslow thickness, presence of mitoses, and ulceration, whereas the association with higher tumor stage did not reach statistical significance when assessed by mean levels. When analyzed categorically, vitamin D deficiency was associated with greater tumor thickness (OR=1.86), mitotic tumors (OR=2.02), and higher tumor stage (OR=1.54). *Conclusion:* Low vitamin D status is associated with poorer melanoma prognostic characteristics and may be linked to increased melanoma risk, although causality cannot be inferred from available observational evidence. Prospective studies with standardized measurements and careful control of sun-exposure behavior are warranted.

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OP No. 14

THE ROLE OF VITAMIN D IN CARDIOVASCULAR HEALTH

Markus Herrmann

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Vitamin D harbors pleiotropic functions that affect most organs and tissues in the human body. In addition to its canonical role in calcium and phosphate homeostasis, vitamin D modulates cell growth and differentiation, immune function, glucose homeostasis, cognitive function and hormonal actions. Mounting evidence links vitamin D deficiency to a broad spectrum of diseases including cardiovascular disease (CVD). Considering that both vitamin D deficiency and CVD are highly prevalent conditions, it is important to understand the potential interplay between these two. Observational studies consistently show an inverse relationship between the inactive prohormone 25-hydroxyvitamin D [25(OH)D] in serum, which represents the body's vitamin D reservoir, and CVD risk. Specifically, lower 25(OH)D concentrations are associated with a higher risk of CVD events and CVD mortality. Putative mechanisms that contribute to the

pathologic effects of vitamin D deficiency comprise oxidative stress, systemic inflammation, activation of the renin-angiotensin-aldosterone system, endothelial dysfunction, hypertension, and myocardial fibrosis. However, vitamin D supplementation failed to demonstrate significant CVD-related benefits. Although existing randomized, placebo-controlled supplementation studies yielded negative results, most of these studies were not designed to test for CVD outcomes. Another limitation of previous studies is the use of fixed vitamin D dosing regimens, regardless of the achieved serum 25(OH)D concentration. Studies that escalate the vitamin D dose until serum 25(OH)D reaches a prespecified target range are largely lacking. This article reviews the existing literature on the role of vitamin D deficiency in CVD incidence, progression and mortality.

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OP No. 4
VITAMIN D AND IMMUNE FUNCTION

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Over the last 25 years, there has been a dramatic increase in our understanding of the extraskeletal actions of vitamin D. Prominent amongst these are the effects of vitamin D on both innate and adaptive immunity. An association between vitamin D and the immune system initially stemmed from the reported beneficial effects of vitamin D supplementation in mycobacterial diseases such as tuberculosis (TB) and leprosy. Later studies provided a potential mechanistic basis for immunomodulation by vitamin D following the characterization of vitamin D receptor (VDR) expression and 25-hydroxyvitamin D-1α-hydroxylase (CYP27B1) activity in various cells from the immune system. This, in turn, has expanded the repertoire of potential immune activity of vitamin D, from innate antibacterial responses and infectious diseases to adaptive (T cell) modulation and autoimmune diseases. The aim of this presentation is to summarize our current understanding of how vitamin D, specifically tissue-specific generation of active 1,25-dihydroxyvitamin D (1,25D) from 25-hydroxyvitamin D (25), influences the immune system, and how this relates to infectious and autoimmune disease. The review will also highlight recent developments, including studies on cellular metabolism, vitamin D binding protein, and the possible benefits of vitamin D for anti-cancer immunity. Although the presentation will focus on mechanistic aspects of vitamin D and immunity, the relevance of this for prevention and treatment of infectious and autoimmune diseases will also be discussed.

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OP No. 33
HUMAN SKIN BIOPSIES AS AN EXPERIMENTAL MODEL FOR THE ANALYSIS OF DRUG-INDUCED PHOTOSENSITIVITY

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Background/Aim: The diuretic drug hydrochlorothiazide (HCT) has been associated with an increased risk of non-melanoma skin cancer upon ultraviolet (UV) light exposure. This study established a human skin model to assess the underlying molecular mechanisms behind the photocarcinogenic effects of HCT (1). *Materials and Methods:* Human skin biopsies were collected from body donors <24 h after death. Biopsies were treated with 1 mmol/l HCT and irradiated with either 300 mJ/cm^2 UVA (low dosage) or with 5 J/cm^2 UVA (high dosage). *Results:* In HCT-treated biopsies, but not in controls, low dose UVA irradiation resulted in activation and nuclear translocation of the tumor-suppressor protein p53, accompanied by an up-regulated gene expression of p53-negative regulator MDM2 in the absence of DNA damage.

High dose UVA additionally induced pronounced DNA damage, activation of p38 mitogen-activated protein kinase (MAPK), and initiated pro-inflammatory gene expression. Of note, in HCT-incubated biopsies irradiated with 5 J/cm^2 UVA, pre-treatment with a broad-spectrum sunscreen with a sun protection factor of 50+ prevented UVA-induced DNA-damage, reduced p53 activation and inflammatory response. *Conclusion:* In summary, in HCT-treated skin biopsies, activation of the p53-MDM2 axis, induction of DNA-damage, and inflammatory response dependent on UVA-dosage and may influence skin carcinogenesis over time. This human model eliminates the need for animal testing, offering a valuable tool for future drug development and safety testing.

1 Hohl M, Götzinger F, Jäger S, Wagmann L, Tokcan M, Tschernig T, Reichrath J, Federspiel JM, Boor P, Meyer MR, Mahfoud F, Böhm M: Assessing phototoxic drug properties of hydrochlorothiazide using human skin biopsies. Commun Biol 8(1): 705, 2025. DOI: 10.1038/s42003-025-08064-1

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OP No. 1

A D-LIGHTFUL FRIEND RE-VISITED: SUNLIGHT AND VITAMIN D FOR HUMAN HEALTH FROM INCEPTION UNTIL DEATH - A HISTORICAL PERSPECTIVE AND NEW INSIGHTS

Michael F. Holick

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Almost from the beginning of time, organisms including phytoplankton in our vast oceans when exposed to sunlight could produce vitamin D. Throughout evolution, cutaneous production of vitamin D was essential for the evolution of vertebrates, including humans. Although vitamin D is recognized for its importance in bone health, the fundamental function of vitamin D is to maintain serum calcium and phosphate concentrations within a normal range thereby supporting energy-dependent processes, signal transduction, and neuromuscular function. The maintenance of a normal serum concentration of calcium and phosphate ensures an adequate calcium-phosphate product that results in the formation of calcium hydroxyapatite and the mineralization of skeletal collagen matrix required for optimal bone health. The lack of appreciation that sun exposure is important for maximum health resulted in the epidemic of rickets-a devastating growth retardation and bone deforming disease-that began in the 1600s and lasted until the beginning of the 20th century. Insights by Sniadecki, Palm, Steenbock and Hess resulted in the appreciation that sun exposure could prevent and treat rickets. Throughout the 20th century, a multitude of association studies reported that inadequate exposure to sunlight increases the risk of many deadly cancers, autoimmune disorders including multiple sclerosis and type 1 diabetes, and infectious diseases. Many of these observations have since been confirmed by studies related to vitamin D status and by randomized controlled trials of vitamin D supplementation. In addition, other health benefits of sun exposure have been ignored.

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OP No. 16

THE VITAMIN D CONUNDRUM: WHAT IS THE OPTIMAL VITAMIN D STATUS FOR SKELETAL AND NON-SKELETAL HEALTH?

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Before 1998, the recommended daily intake of vitamin D to prevent rickets and to satisfy children and adult requirements was 200 IUs daily. In 1998, the Institute of Medicine recommended, based on the most up-to-date literature, 200 IU/day for children and adults up to the age of 50 years, 400 IU/day for those aged 51-70 years, and 600

IUs daily for those aged 71 years and older, with a tolerable upper intake level (UL) of 2,000 IU/day for adults. In 2010, the Institute of Medicine revised these recommendations to 400 IU/day for infants, 600 IU/day for children and adults, and 800 IU/day for seniors aged 71 years and older, with a UL of 4,000 IU/day. The Endocrine Society Guidelines recommended 400-1,000 IU/day for infants, 600-1,000 IU for children and 1,500-2,000 IU/day for adults, noting that obese individuals may require two to three times higher doses. The 2024 Endocrine Society Guidelines did not focus on evaluation, treatment or prevention of vitamin D deficiency, but rather focused on certain noncalcemic health benefits, noting that higher intakes may reduce the risk of poor birth outcomes, type 2 diabetes, infectious diseases in children. However, they concluded that since the US population is generally considered vitamin D sufficient, the recommended intake levels should be identical to the 2010 Guidelines. It is important to note that the literature suggests that, for optimal bone health, circulating 25-hydroxyvitamin D concentrations should be at least 30 ng/ml (75 nmol/l). Recent association studies have reported that intakes of vitamin D of at least 2,000 IU/day, sufficient to achieve a circulating concentration of 25-hydroxyvitamin D between 40 and 60 ng/ml, may reduce the risk of poor birth outcomes, autoimmune disorders, dying from certain cancers, type 2 diabetes, and infections such as COVID-19 and influenza.

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OP No. 46

HOW MUCH SUNLIGHT DO WE NEED? STANDARD OF CARE AND NOVEL APPROACHES FOR PREVENTING AND TREATING VITAMIN D DEFICIENCY

Michael F. Holick

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For more than 50 years, the sun has been demonized by many national, international, and government agencies because of its association with skin cancer. This has led to the recommendation by some organizations that children and adults should abstain from being exposed to direct sunlight without some type of sun protection. Unfortunately, many of these organizations did not appreciate that the major source of vitamin D for most children and adults is their exposure to sunlight. This lack of appreciation has led to a worldwide pandemic of vitamin D deficiency. It has been estimated that more than 40% of the world's population is vitamin D deficient. This has resulted in disastrous health consequences including metabolic bone disease and increased risk for many chronic illnesses including autoimmune disorders, deadly cancers, cardiovascular disease, neurocognitive dysfunction, poor birth outcomes as well as acute illnesses associated with viral and bacterial infections. A major issue is the lack of understanding for how various factors including latitude, season, time of day, weather conditions, skin pigmentation, and sunscreen use affect this vital cutaneous process. The Sperti lamp, a mercury arc lamp, was routinely used in the 1940s and 1950s by parents to prevent rickets in their children. The development of UVB emitting LEDs provides an energy efficient and user-friendly UVB radiation source that is being developed into vitamin D producing devices. For individuals who wish to meet their vitamin D requirements from sensible sun exposure, an app developed by Ontometrics Inc. is available for both iPhone and Android devices and provides guidance on when sunlight is sufficient vitamin D synthesis, how much vitamin D may be produced based on skin type, and when sun exposure may become excessive.

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OP No. 5

SYNTHESIS OF ^{13}C5 LABELED VITAMIN D_3 FOR EXPLORING VITAMIN D METABOLISM USING LIQUID CHROMATOGRAPHY MASS SPECTROMETRY

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Background/Aim: Simultaneous measurement of the concentration of clinically relevant vitamin D metabolites in human tissue or biofluids by liquid chromatography-tandem mass spectrometry (LC-MS/MS) represents a precise method for exploring vitamin D metabolism and eventually allows for a differentiated diagnosis of vitamin D-related diseases, such as various types of cancer. Vitamin D_3 is significant to be measured, since it is stored in fat tissue, where it is released into the serum for subsequent metabolization. Thus, vitamin D_3 serves as a starting material for the enzymatic conversion into its metabolites. *Materials and Methods:* For its use as internal reference standard for LC-MS/MS-applications, vitamin D_3 must be labeled either with multiple deuterium or ^{13}C atoms. Although deuterated standards are more common than their ^{13}C labeled counterparts, due to their easier chemical accessibility and comparably lower price, multifold ^{13}C labeled standards are preferred, since they lack a kinetic isotope effect, they do not exchange isotope atoms during synthesis or under physiological conditions and show identical retention times relating to their corresponding natural analytes using liquid chromatography. As a representative example, the synthesis of $^{13}C_5$ labeled vitamin D_3 was developed, starting with degradation of commercially readily available vitamin D_2, in a convergent synthetic approach. *Results:* A new efficient chemical synthesis of 5-fold ^{13}C labeled vitamin D_3 (Figure 1) was developed. The product was obtained in good yield, 100% isotopic enrichment and high purity. *Conclusion:* The synthesis of ^{13}C labeled vitamin D_3 enables both chemical and enzymatic synthesis of numerous ^{13}C labeled vitamin D_3 metabolites, which can in turn be used as internal reference standards. These standards facilitate the investigation of vitamin D metabolism and metabolite function by LC-MS/MS and may support the differentiated diagnosis of vitamin D–related diseases.

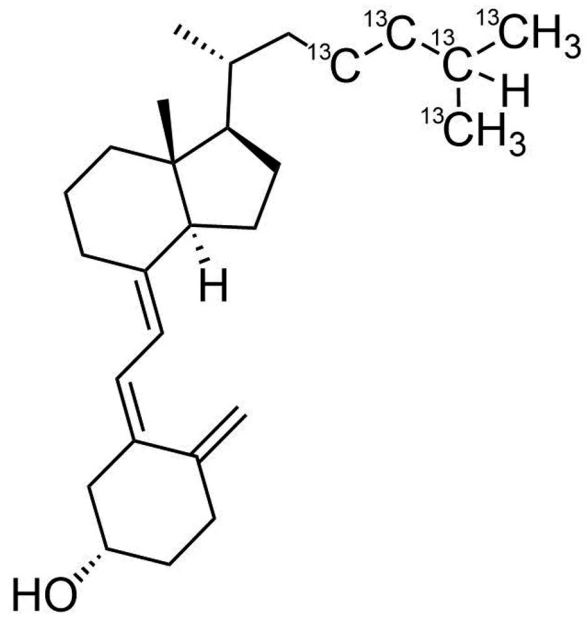

Figure 1. *Chemical structure of vitamin D_3 $^{13}C_5$.*

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OP No. 35

MELATONIN LIMITS UVB-DRIVEN SKIN SENESCENCE BY PRESERVING MITOCHONDRIAL INTEGRITY

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Background/Aim: Cellular senescence is a central driver of skin aging, promoted by ultraviolet radiation (UVR), oxidative stress, and mitochondrial dysfunction. Accumulation of senescent cells impairs epidermal renewal, extracellular matrix homeostasis, and inflammatory balance. Given the pivotal role of mitochondrial integrity in regulating senescence, this study aimed to evaluate whether melatonin mitigates UVB-induced skin aging by preserving mitochondrial function and suppressing senescence-associated pathways. *Materials and Methods: In vitro* studies were

performed using human epidermal keratinocytes exposed to UVB irradiation (50 mJ/cm^2). Mitochondrial function was assessed by measuring mitochondrial membrane potential, reactive oxygen species (ROS) generation, and intracellular ATP levels. Cell proliferation and viability were evaluated using proliferation assays and crystal violet staining. Senescence- and inflammation-related proteins (IL-6, γH2AX, p53) were analyzed by western blotting. *In vivo*, C57BL/6 mice received 30 days subcutaneous melatonin treatment, and skin samples were examined for molecular, inflammatory, proliferative, and extracellular matrix–related parameters associated with skin aging. *Results:* UVB exposure induced mitochondrial dysfunction characterized by depolarized mitochondrial membrane potential, increased ROS production, and reduced ATP levels, accompanied by decreased proliferation and increased expression of IL-6, γH2AX, and p53. Melatonin treatment significantly restored mitochondrial function, reduced oxidative stress, preserved ATP production, and improved cellular proliferation *in vitro. In vivo*, melatonin administration attenuated the hallmarks of skin aging, including inflammatory changes (IL-1α, TNF-α), extracellular matrix degradation (reduced MMP-2, preserved elastin and collagen I), and diminished proliferative capacity (increased Ki-67). Melatonin-treated skin exhibited improved structural integrity and reduced molecular indicators of senescence compared with controls. *Conclusion:* Melatonin counteracts UVB-induced skin aging by preserving mitochondrial function, reducing oxidative stress, and suppressing senescence-associated signaling. Through combined mitochondrial, anti-inflammatory, and extracellular matrix–protective actions, melatonin represents a promising therapeutic strategy for maintaining cutaneous homeostasis and delaying skin aging.

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OP No. 42

URINARY THYMIDINE DIMER EXCRETION AFTER ULTRAVIOLET RADIATION FROM TANNING BEDS COMPARED TO NATURAL SUN EXPOSURE

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Background/Aim: Ultraviolet radiation (UVR) induces cyclobutane pyrimidine dimers (CPDs), including thymidine dimers (T<>T), which are central DNA lesions in photocarcinogenesis. This study compared urinary excretion of repaired T<>Ts after UVR exposure from commercial tanning beds or natural sunlight, evaluating urinary T<>Ts as a non-invasive biomarker of personal UVR exposure. *Materials and Methods:* Two studies were conducted in healthy Danish volunteers using personal UVR dosimeters. Nineteen tanning bed users were monitored for four winter weeks, and 59 individuals were followed for 12 summer weeks. Urinary T<>Ts were quantified using ultra-performance liquid chromatography tandem mass spectrometry (UPLC-MS/MS). *Results:* Urinary T<>Ts were detectable in all participants. Tanning bed users received a mean UVR dose of 1.52 standard erythema doses (SED) per session and excreted a median of 857 ng T<>T/day, reflecting frequent, near full-body exposure. In the summer population, the mean daily dose was 1.46 SED with only partial-body exposure and a mean T<>T excretion of 437 ng/day. Younger participants excreted higher T<>T per unit UVR than older individuals, and individuals with darker skin types excreted lower levels. *Conclusion:* Tanning bed exposure resulted in higher urinary thymidine dimer excretion compared to natural summer sunlight exposure. This increase is largely attributable to the substantially greater body surface area exposed during tanning bed sessions, combined with the high UVR doses delivered.

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OP No. 32

SUN CARE 2040: A NEW FOCUS ON EFFECTIVE SUNBURN PREVENTION

Joseph Levy

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Sun care campaigns centered on sun-avoidance for more than 50 years have failed to make progress at reducing sunburn incidence in the population. More than 50% of adults still experience sunburn, and in some cohorts, sunburn rates have actually increased over this period. After decades of limited success, new evidence now suggests that abstinence-driven messaging may actually be contributing to this failure – causing the problem it was designed to prevent - and that a more nuanced approach to sun care communication is needed, one that recognizes the benefits associated with non-burning sun exposure, while also improving sunburn prevention. Sunshine Health Foundation founder Allen Miller dedicated his final years of life to assisting scientific efforts to restore balance to sun care research. Joe Levy worked with and supported Miller's vision for more than a decade. The emergence of a campaign integrating these ideas is therefore a fitting continuation of Miller's vision. This presentation reviews new evidence documenting decades of failure, supporting the need for new approaches to sunburn prevention, and will be followed by a panel discussion vetting next steps, leading to the development of tangible goals for the coming decade.

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OP No. 28
TO DISTINGUISH SOLARIUM USE WITH AND WITHOUT RISK BEHAVIOR ON MELANOMA INCIDENCE AND ALL-CAUSE MORTALITY. A REPORT FROM THE LARGE MISS COHORT

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Background/Aim: Artificial ultraviolet radiation (UVR) exposure from solarium use has been associated with an increased risk of melanoma in some studies, while other evidence suggests potential beneficial associations with overall mortality. It remains unclear whether melanoma risk is attributable to solarium use per se or to accompanying behaviors indicative of intermittent solar overexposure. *Patients and Methods:* The Melanoma of Southern Sweden (MISS) cohort comprises approximately 29,000 women enrolled in 1990 and followed for up to 34 years. Information on solarium use and sun exposure habits was collected at baseline and updated after 10 years. Participants were classified as non-users of solarium, solarium users without indicators of intermittent solar overexposure, or solarium users with such indicators. Age was used as the underlying time scale in Cox proportional hazards models estimating hazard ratios (HRs) and 95% confidence intervals (CIs) for melanoma incidence and all-cause mortality. Multiple sensitivity analyses were conducted to address reverse causation, exposure changes, and comorbidity. Restricted mean survival time (RMST) over 25 years of follow-up was estimated to provide an absolute measure of mortality differences. *Results:* Solarium use without indicators of intermittent solar overexposure was not associated with an increased risk of melanoma compared with non-use. In contrast, solarium users with indicators of overexposure had a 60% higher risk of melanoma (HR=1.60, 95%CI=1.30-2.00). Both solarium user groups exhibited lower all-cause mortality compared with non-users (HR=0.83, 95%CI=0.79-0.88 and HR=0.81, 95%CI=0.76-0.87). Thirty-three percent of solarium melanomas were attributed to solar overexposure. Over 25 years, RMST was 23.96 years among solarium users and 23.12 years among non-users, corresponding to an

absolute difference of approximately 10 months. *Conclusion:* Melanoma risk among solarium users appears to be driven by behaviors indicative of intermittent solar overexposure rather than solarium use per se. At the same time, solarium use was associated with lower all-cause mortality. These findings suggest that preventive efforts should prioritize reducing UV overexposure behaviors rather than targeting solarium use alone.

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OP No. 6
VITAMIN D ANALOGS: LESSONS LEARNED FROM CHEMICAL RESEARCH AND STRUCTURAL INSIGHTS

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The pleiotropic nature of VDR signaling has positioned it as an attractive therapeutic target. However, clinical translation of natural vitamin D metabolites – particularly calcitriol – has been hampered by dose-limiting hypercalcemia, a consequence of its potent effects on calcium absorption and bone resorption. To overcome this obstacle and selectively exploit the non-classical actions of VDR, intense synthetic chemistry efforts have provided VDR ligands (vitamin D analogs and non-secoesteroidal elements) with selective properties and no calcemic actions. In the presentation, a selection of outstanding VDR ligands (vitamin D analogs) will be described together with their biological properties and their interaction with VDR.

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OP No. 20
VITAMIN D AND CARDIO-VASCULAR HEALTH

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The impact of vitamin D on the risk of cardiovascular disease (CVD) has extensively been examined for two decades. Observational data indicate a strong non-linear association between vitamin D and CVD, with the highest CVD risk at severe vitamin D deficiency. Preclinical data and randomized controlled trials (RCTs) show beneficial effects of vitamin D on surrogate parameters of vascular and cardiac function. Mendelian randomization report studies report no significant effect of vitamin D supplementation on CVD risk. Large RCTs in the general population had also been neutral, but more recent results point at the role of vitamin D in primary and secondary prevention. In the large D-Health study with more than 21,200 participants, vitamin D_3 (60,000 IU monthly) produced a small reduction in heart attacks of borderline statistical significance. Also, new research suggests that individually adjusted vitamin D dosing, based on regular blood level monitoring, could significantly reduce the risk of a second heart attack (≈ 50% lower risk in the treated group). In conclusion, the current evidence regarding the beneficial vitamin D effects on CVD risk, both in the general population and in high-risk groups, is controversial. Yet, indications beyond CVD may justify vitamin D supplementation and specific subgroups – such as adolescents, individuals with metabolic syndrome, and older adults – may derive particular benefit.

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OP No. 27
27 DAYS *VERSUS* MORE THAN 6 YEARS – WHAT THE BURDEN OF DISEASE REVEALS ABOUT THE TRUE MEANING OF SUNLIGHT

Manfred Matzel

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Background/Aim: Epidemiological studies consistently report lower all-cause mortality among individuals with higher sun exposure. This analysis aimed to quantify the mathematical basis for this observation using burden of disease (BoD) data, comparing the disease burden attributable to ultraviolet (UV) radiation with that of conditions positively influenced by sunlight exposure. *Materials and Methods:* We analyzed German BoD data published by the Robert Koch Institute (RKI, 2021) and Australian Institute of Health and Welfare BoD data. Life-years lost were calculated for skin cancer *versus* sunlight-responsive diseases, including cardiovascular disease, stroke, cancer, and autoimmune disorders. A theoretical maximum benefit scenario assuming 30% reduction in skin cancer mortality through complete UV avoidance was modeled. *Results:* In Germany, skin cancer accounts for an average loss of 27 days of life per person, while sunlight-responsive diseases account for more than 6 years' loss. Even assuming a 30% reduction in skin cancer mortality through strict UV avoidance – a scenario unsupported by evidence – the theoretical maximum gain would be 8 days. Australian data confirm this pattern: malignant melanoma contributes 0.55% and non-melanoma skin cancer 0.26% to the total BoD, yielding a combined UV-preventable fraction of only 0.81%. *Conclusion:* The BoD data demonstrate that strict UV avoidance offers minimal potential benefit while carrying substantial potential harm. These findings provide the mathematical foundation explaining why epidemiological studies observe reduced all-cause mortality with increased sun exposure. Those who avoid the sun may gain days – but may lose years.

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OP No. 49

HIGH SUN PROTECTION FACTOR, LOW EVIDENCE: WHY SUNSCREEN NEEDS A RETHINK

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Background/Aim: A study of the widespread endorsement of sun protection strategies based on progressively higher sun protection factor (SPF) values reveals scientific inconsistencies and ecological concerns. This presentation challenges the prevailing SPF-centric paradigm and highlights its unintended consequences for human health and ecosystems. *Materials and Methods:* We reviewed the biophysical basis of SPF measurement, analyzed the law of diminishing returns in ultraviolet (UV) filtration, and evaluated epidemiological evidence on sunscreen efficacy in melanoma prevention. Additionally, we assessed photostability, endocrine-disrupting potential, environmental persistence, and systemic absorption of chemical UV filters based on published biomonitoring data. *Results:* The SPF quantifies the delay in erythema onset under standardized laboratory UVB exposure but does not linearly correspond to the reduction of biologically effective UV radiation under real-world conditions. According to the law of diminishing returns, SPF 4 products filter approximately 75% of UVB, SPF 10 around 90%, SPF 30 approximately 97%, and SPF 50 about 98%. Beyond SPF 10, filtration gains are minimal yet require exponentially higher concentrations of chemical UV filters. The World Health Organization's recommendation to apply SPF 30-50 sunscreens at a UV Index above 3 lacks biophysical plausibility and neglects intrinsic human photoadaptation. Epidemiological evidence remains inconclusive regarding the efficacy of sunscreens in reducing malignant melanoma incidence. Chemical filters vary widely in photostability and endocrine-disrupting potential and have been implicated in aquatic toxicity and coral reef bleaching. Several organic filters have been detected in human urine, blood, and breast milk in a dose-dependent manner, confirming systemic absorption. *Conclusion:* The current SPF-centric sunscreen paradigm lacks robust scientific support and carries unintended consequences for human health and ecosystems. An evidence-based, photobiologically balanced approach to sun exposure is needed that protects both humans and the environment while minimizing ecological impact.

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OP No. 29
**REDEFINING PHOTOPROTECTION:
SUN PROTECTION BEYOND SUNBURN**

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Excessive sun exposure causes both acute and chronic ultraviolet (UV) damage and represents the primary risk factor for the development of skin cancer. In most Western countries, the topical application of sunscreens to UV-exposed skin areas is by far the most common preventative measure against sunburn and skin cancer development. However, recent studies indicate that clinically relevant DNA damage occurs well below the threshold of 1 minimal erythema dose (MED). These findings contribute to the ongoing discussion regarding the true clinical value of high SPF levels and the read out of the MED as an endpoint for SPF determination. *Ex vivo* and *in vivo* studies on human skin and volunteers have demonstrated strong DNA damage below 1 MED. SPF 30 reduces DNA damage by approximately 53% during a full day of sun exposure (24 MED), whereas SPF100 provides a significantly stronger reduction of about 73%. While sunscreens with SPF30 or SPF50+ already provide solid UVB protection for most purposes, our findings suggest that SPF100 offers significantly enhanced protection for particularly vulnerable groups, such as immunosuppressed individuals or patients with a history of skin cancer. Furthermore, noninvasive techniques such as the hybrid diffuse reflectance spectroscopy, which is now a new ISO standard for SPF measurement, might be used to find a better definition of a healthy dose of sun irradiation.

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OP No. 43
WAVELENGTH, DOSE, SKIN TYPE AND SKIN MODEL RELATED RADICAL FORMATION IN SKIN

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Background/Aim: Exposure to solar radiation is essential for human health; however, prolonged or intense exposure can cause cellular damage, erythema, premature skin aging, and contribute to the development of skin tumors. One key underlying mechanism is the formation of free radicals, which can trigger oxidative stress when present at high concentrations. *Materials and Methods:* Various skin models – including porcine, murine, and human *ex vivo* skin, reconstructed human skin, and human skin *in vivo* – were examined during and after irradiation using X-band and L-band electron paramagnetic resonance spectroscopy across different wavelength ranges [ultraviolet (UV)C to near infrared]. Radical formation was quantified using a 3-(carboxy)-2,2,5,5-tetramethylpyrrolidin-1-oxyl spin probe, while the specific radical types were identified *ex vivo* using spin trap 3,4-dihydro-2,3-dimethyl-2H-pyrrole 1-oxide. *Results:* The radiation dose plays a decisive role in determining the types of radicals produced in the skin. At low doses, reactive oxygen species dominated, whereas higher doses led to increased formation of lipid oxygen species. Although the types of radicals generated were not dependent on the irradiation wavelength, the overall amount of radicals varied with wavelength. Heat-pre-stressed porcine skin exhibited elevated lipid oxygen species levels from the outset.

Conclusion: The ratio of radical types may serve as an indicator of stress, with the shift from reactive oxygen species to lipid oxygen species marking the transition from beneficial to harmful stress. Compared to lighter skin types, darker skin types generated fewer radicals under UV radiation, similar levels under visible light, and higher levels under infrared radiation. This highlights the importance of tailoring sun protection to individual skin types.

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OP No. 40
MANAGEMENT OF PHOTODERMATOSES

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Photodermatoses are a group of skin diseases resulting from an abnormal response to sunlight, particularly the ultraviolet component. These diseases are categorized as phototoxic or photoallergic reactions to known photosensitizers, or as idiopathic photodermatoses when the exact pathomechanism is unclear. Diagnosis can be challenging due to overlapping symptoms and confusing terminology. Some types are extremely rare, such as *Hydroa vacciniforme* (with a prevalence of 0.34 per 100,000), while others are very common, such as polymorphic light eruption (with a prevalence of 10-20%). The management of photodermatoses begins with the clinical recognition of characteristic lesions that are predominantly localized to areas of the skin that are exposed to light. A detailed case history, phototesting and photopatch testing are required to make an accurate diagnosis, particularly if patients present during disease-free intervals. Although photodermatoses are not life-threatening, they can cause considerable suffering. Prevention is therefore just as important as treatment.

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OP No. 12
IMPAIRED VITAMIN D METABOLISM IN LIVER DISEASE: CURRENT PERSPECTIVES ON CONSEQUENCES FOR VITAMIN D STATUS AND CLINICAL IMPLICATIONS

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Background/Aim: Vitamin D status is frequently overlooked in patients with chronic liver disease (CLD), despite the liver being a central organ in vitamin D hydroxylation, storage, and transport. Hepatic conversion of vitamin D to 25-hydroxyvitamin D and the synthesis of vitamin D-binding protein (DBP) are key steps in maintaining vitamin D homeostasis, suggesting that liver dysfunction may directly affect vitamin D availability. Nevertheless, assessment of vitamin D status in clinical practice is largely limited to conventional markers of status, and the relevance of altered vitamin D metabolism remains incompletely understood. Across different etiologies and stages of CLD, including metabolic-associated steatotic liver disease, alcohol-related liver disease, viral hepatitis, and cirrhosis, numerous studies consistently report a high prevalence of vitamin D deficiency. Low vitamin D levels have been associated with disease severity and a broad range of hepatic and extrahepatic complications, including infections, sarcopenia, hepatic encephalopathy, disease decompensation, and reduced survival. Despite these associations, randomized clinical trials investigating vitamin D supplementation in CLD have yielded mixed and often inconclusive results, raising questions about current assessment strategies and therapeutic approaches. *Methods and Results:* Recent pathway-wide analyses from our group demonstrate that advanced liver disease is characterized by a profound disruption of vitamin D metabolism. In patients with decompensated

cirrhosis, multiple components of the vitamin D pathway were markedly altered, including reduced circulating vitamin D metabolites, reduced concentration of DBP, loss of seasonal variation, and dysregulation of endocrine regulators such as fibroblast growth factor 23, largely independently of vitamin D supplementation. Importantly, the use of conventional concentrations of 25-hydroxyvitamin D_3 showed limited prognostic value, whereas a low level of 1,25-dihydroxyvitamin D, and a particularly low level of vitamin DBP, were associated with clinically relevant complications and impaired short-term survival. *Conclusion:* This presentation provides an overview of the current literature on vitamin D deficiency in CLD and integrates recent data on altered vitamin D metabolism in advanced disease stages. Prevalence, clinical consequences, potential underlying mechanisms, and implications for vitamin D assessment and therapeutic strategies are discussed.

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OP No. 45

NEW ACTION SPECTRA FOR VITAMIN D AND THYMIDINE DIMERS FORMATION IN HUMAN SKIN – DOES THIS ALTER THE RISK – BENEFIT BALANCE?

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Background/Aim: Ultraviolet radiation (UVR) causes DNA damage in human skin, most commonly cyclobutane pyrimidine dimers (CPDs), but UVR also has a beneficial effect on vitamin D_3 synthesis. The biological effect after UVR is dependent on wavelength and can be described by weighting functions named action spectra. Until now action spectra have been obtained in separate studies and exposure regimes. The aim of the study was to accurately quantify the action spectra of vitamin D_3 and CPD obtained under identical exposure regimes. *Materials and Methods:* Waistband skin from five persons was obtained immediately after surgery. A total of 82 biopsies were prepared from each person's skin tissue: 80 were irradiated with one of 10 UV-LEDs with wavelengths from 280 to 335 nm and two non-irradiated controls. For each wavelength, four doses with linear increments were given and a linear dose–response was calculated. The regression slopes are presented as action spectra. Quantification of CPDs and vitamin D_3 in the skin were performed by liquid chromatography–tandem mass spectrometry. *Results:* The action spectrum of vitamin D_3 was found to have a maximal peak at 296 nm with a decrease with both lower and higher wavelengths. The action spectrum of CPD had a maximal peak at 291 nm, decreasing with higher wavelengths. From 294 to 310 nm, the normalized action spectrum for vitamin D_3 was higher than that for CPD, with a peak of 1.4 at 301 nm. *Conclusion:* There is a window from 294 to 310 nm where vitamin D_3 production is relatively higher than CPD production.

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OP No. 34

TAPE STRIP-DERIVED GENE EXPRESSION OF BASAL CELL CARCINOMA IS ASSOCIATED WITH FEATURES OF IMAGES BY LINE-FIELD OPTICAL COHERENCE TOMOGRAPHY

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Background/Aim: We explored associations between gene expression and tumor morphology in basal cell carcinoma (BCC) using two non-invasive approaches: tape stripping for gene-expression profiling and line-field confocal optical coherence tomography (LC-OCT) for tumour morphology. Our aim was to see if combining spatial and molecular information can enhance our understanding of skin cancer biology. *Materials and Methods:* Histology-confirmed BCCs (n=53) were tape-stripped for mRNA analysis and compared to control skin of the same anatomical region. Differentially expressed genes (DEGs) were identified. All lesions and control skin were scanned and compared with LC-OCT to assess tumor features. *Results:* Seventy-two DEGs were identified in BCC (false-discovery rate <0.001). Forward binary logistic regression using all 72 DEGs revealed that 8 remained significant (p<0.05), with a sensitivity and specificity of 92%. LC-OCT scans revealed seven BCC-specific LC-OCT image features (p≤0.004). Of the 72 BCC DEGs, 27 were associated with two BCC-specific LC-OCT features: the millefeuille pattern with a 4-fold increase in expression, and collagen alterations with a 12-fold increase in expression. *Conclusion:* This imaging–transcriptomic approach demonstrates the feasibility of tape stripping for detecting BCC-specific gene expression and the application of LC-OCT-based imaging transcriptomics for new insights into BCC pathobiology.

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OP No. 24

SUN-SIMULATED LOW-DOSE UV EXPOSURE TO RESTORE THE VITAMIN D_3 LEVEL

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Background/Aim: Exposure of the skin to sun causes the body to synthesize vitamin D_3. To maintain health effects, blood serum levels of 25(OH)D_3 >20 ng ml^{-1} are recommended. However, many people suffer from deficiency due to their lifestyle, showing values below 15 ng ml^{-1}. Compensatory effects of oral vitamin D supplementation are limited due to short degradation times, while endogenously produced 25(OH)D_3 slowly degrades. However, UV skin exposure is controversial due to risks of unwanted side-effects. We investigated vitamin D_3 synthesis by solar-simulated UV considering current radiation protection guidelines. *Materials and Methods:* Twenty non-adapted healthy volunteers (skin phototypes I-IV; ages: 22-59 years) underwent 15 whole-body irradiations during winter. Daily doses ranged from 30-65% of the individual erythema dose. The concentration of 25(OH)D_3 was measured from blood samples. *Results:* 25(OH)D_3 levels increased from baseline deficiency (13.4±7.46 ng ml^{-1}) after completion of the irradiation series but varied individually and depended on age. Increases were greater the lower the baseline concentrations were, but the increase weakened from week to week. After finishing the series, the 25(OH)D_3 concentration was 32.4±6.9 ng ml^{-1} in persons up to 45 years of age, and 17.9±9.2 ng ml^{-1} in individuals aged 49-59 years. *Conclusion:* The results demonstrate the potential of sun-simulated, low-dose UV-skin exposure to induce sufficient vitamin D_3 status, particularly for young up to middle-aged individuals.

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OP No. 50

WATER-FILITERED INFRARED-A IRRADIATION AS A POTENT RADIOSENSITIZER IN THE TREATMENT OF SUPERFICIAL MALIGNANCIES: PHYSICAL AND PHOTOBIOLOGICAL BASICS

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Background/Aim: Mild hyperthermia (mHT, 39-42°C for 30-60 min) is a potent sensitizer in oncological radiotherapy when applied immediately before the treatment of superficial malignancies. The suitability of water-filtered infrared-A (wIRA) irradiation immediately before oncological radiotherapy was investigated. *Materials and Methods:* The physical and photobiological basics of wIRA irradiation were investigated using model calculations and *in vivo* measurements. Comparisons were made with unfiltered IR-A- and IR-C irradiation. *Results:* By adjusting incident irradiance to maximum skin surface temperatures of 42-43°C, the effective heating depths were ≈15 mm (40°C), and ≈25 mm (39°C). *Conclusion:* Results using wIRA are in accordance with the guidelines of the European Society for Hyperthermic Oncology for (a) effective tissue heating and (b) to avoid acute heat damage. In contrast, exposure of the skin to conductive or convective heat, or unfiltered infrared-A or infrared-C radiation led to hot spots at the skin surface and large temperature gradients, which prevent therapeutically relevant temperatures being achieved in deeper tissue layers.

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OP No. 47

THE ICARUS PROJECT: THE IMPACT OF HEAT TOLERANCE AND SKIN CHARACTERISTICS ON VITAMIN D, URINARY PHOTOLESIONS, AND STEROID HORMONES FOLLOWING EXPOSURE TO HEAT AND ULTRAVIOLET RADIATION

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Background/Aim: Accelerating heat stress driven by global warming presents a critical societal challenge. Heat waves are associated with increased morbidity and mortality, while the incidence of keratinocyte carcinoma has markedly increased over the past decade, highlighting the harmful effects of excessive sun exposure. This ongoing study aims to investigate how heat tolerance and skin characteristics influence biological outcomes following combined heat and ultraviolet radiation (UVR) exposure. *Materials and Methods:* Healthy participants are being recruited based on self-reported heat tolerance (25 heat-intolerant and 25 heat-tolerant individuals). Prior to the experimental protocol, skin pigmentation and individual typology angle (ITA) skin type are objectively assessed using reflectance spectroscopy, and minimal erythema dose is determined. Participants undergo exposure to 40°C heat in a climate chamber for 4 h, including 1 h of UVR exposure (3 standard erythema doses administered to the front and back). Blood samples are collected before and after exposure for assessment of vitamin D [25(OH)D] and steroid hormone levels. In addition, participants collect morning urine samples for one week following exposure for analysis of cyclobutane pyrimidine dimers (thymidine dimers). *Expected Results and Significance:* Data collection and biological analyses are currently ongoing. Biological outcomes will be correlated with heat tolerance levels and skin characteristics to identify factors that may contribute to individual susceptibility to heat and UVR exposure. The findings are expected to improve understanding of physiological responses to combined environmental stressors and their potential implications for skin health and disease risk.

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OP No. 25
ENDOCRINE SOCIETY GUIDELINE FOR PREVENTING AND TREATING VITAMIN D DEFICIENCY: A CRITICAL APPRAISAL

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Background/Aim: An Endocrine Society Clinical Practice Guideline on vitamin D was published in 2024. The methodology followed the Grading of Recommendations, Assessment, Development, and Evaluation methodology and the Evidence-to Decision framework. Evidence from randomized controlled trials retrieved by a systematic review was prioritized to inform this guideline. It was concluded that vitamin D supplementation reduces rickets and respiratory tract infections in children, mortality in individuals aged 75 years or older, pregnancy complications (outcomes), and progression of prediabetes to diabetes mellitus. Consequently, empiric vitamin D supplementation was recommended for all individuals under 18 years, adults aged ≥75 years, pregnant women, and individuals with prediabetes. Empiric vitamin D supplementation was defined as vitamin D intake that exceeds the Dietary Reference Intake, implemented without testing for 25-hydroxyvitamin D. *Materials and Methods:* This is a narrative review on systematically searched scientific publications and expert opinions regarding the quality, limitations, and implications of the 2024 Endocrine Society Clinical Practice Guideline on vitamin D. *Results:* Several publications reviewed and discussed the 2024 Endocrine Society Clinical Practice Guideline on vitamin D. Main criticisms and discussion points were related to unclear vitamin D dosages, guideline applicability to certain populations, potential overlap and controversy with previous vitamin D guidelines, and indications of 25-hydroxyvitamin D testing. *Conclusion:* The 2024 Endocrine Society Clinical Practice Guideline on vitamin D followed a rigorous methodological approach with high quality standards but the recommendations of this guideline leave many open questions and room for interpretation regarding their applicability and implementation.

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OP No. 51
SUNLIGHT/UV EXPOSURE AND MORTALITY: WHAT IS THE EVIDENCE?

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Background/Aim: Public health recommendations regarding sunlight exposure must consider beneficial and adverse effects. Data on sunlight exposure and mortality are useful to provide an overall outcome measure that reflects the totality of health effects with relevance to survival. *Materials and Methods:* This is a narrative expert review on measures of sunlight or ultraviolet (UV) radiation exposure and mortality, with a focus on all-cause and total-cancer mortality. This work adhered to the Scale for the Quality Assessment of Narrative Review Articles (SANRA) recommendations. *Results:* Existing literature on sunlight or UV radiation exposure and mortality is heterogeneous in terms of how exposure was assessed, how the data were analyzed, and was usually lacking adequate adjustments for potential confounders with an overall high risk of bias and thus relatively low quality of evidence. Most existing analyses suggest that more sunlight exposure is associated with reduced all-cause mortality but there are also studies showing opposite associations. The only large study on indoor tanning devices showed significantly reduced risk of all-cause mortality in solarium users *versus* non-users. Most studies showed reduced total

cancer mortality with higher sunlight exposure. *Conclusion:* The evidence on sunlight or UV exposure and mortality is inconsistent, with a high risk of bias, but most studies suggest that more sunlight or UV exposure is associated with reduced all-cause and total mortality. High-quality observational studies with accurate individual level measures of sunlight or UV exposure and randomized trials are urgently required to inform the next revision of public health recommendations regarding this issue.

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OP No. 11
24,25-DIHYDROXYVITAMIN D IN A GENETIC KIDNEY STONE DISEASE

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Background/Aim: Dent Disease (DD) is X-linked and affected males often exhibit hypercalciuria and low-molecular-weight proteinuria, with high risks for early onset of kidney stones, kidney calcification, and progressive kidney failure. DD is caused by pathogenic variants of the voltage-gated Cl^-/H^+ antiporter 5 (*CLCN5*), which alters renal calcium regulation and contributes to pathogenic manifestations of DD. Renal calcium reabsorption is regulated, in part, by 1,25-diyhdroxyvitamin D [$1,25(OH)_2D$] and fibroblast growth factor 23 (FGF23). We investigated the interrelationship of 24,25-dihydroxyvitamin D, $1,25(OH)_2D$ and FGF23 in DD manifestations. *Patients and Methods:* Serum and 24-h urine collections were compared between adult patients with DD (DD-A, n=10) and adults with history of idiopathic kidney stones (iKS, n=9). Adult participants completed an oral phosphate supplementation intervention (1 g/day for 14 days) with pre and post clinical measurements. Pediatric patients with DD (DD-P: aged 6-12 years, n=9) underwent only a cross-sectional baseline assessment. *Results:* FGF23 was significantly lower in DD-A than in iKS (p=0.006). Concentrations of $24,25(OH)_2D$ in DD-A and DD-P were low, with conversion ratios ($25OHD:24,25(OH)_2D$) ranging from 18 to 180. Participants in the iKS cohort had normal ratios ranging from 9 to 20. Phosphorus supplementation reduced calcium excretion in DD-A (p=0.02) and iKS (p=0.04). DD-A patients with low $24,25(OH)_2D$ (ratio ≥25, n=5) had lower FGF23, higher $1,25(OH)_2D$, greater urine calcium, and greater urine protein than those with normal $24,25(OH)_2D$ (ratio <25, n=5). *Conclusion:* Analysis of $24,25(OH)_2D$ may have clinical relevance for evaluating the severity, progression, and treatment of DD.

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OP No. 48
SEASONALITY OF UV RADIATION: ANALYSIS, *METHODS AND* FINDINGS

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Background/Aim: Investigating seasonal fluctuations in ultraviolet (UV) radiation and associated changes in disease is crucial for understanding the health-related effects of UV exposure. However, the myriads of epidemiological methodologies developed to study seasonality and to account for confounding factors make it difficult to select the most appropriate approach for a given research question. Here, we provide an overview of methodological strategies used to evaluate seasonal effects of UV exposure on health outcomes. *Materials and Methods:* We reviewed and contrasted commonly used methodological approaches, outlining their underlying assumptions, strengths, and limitations. Illustrative examples are provided to demonstrate how these methods have been applied to study

the health effects of UV exposure and related meteorological variables. *Results:* The methods discussed include core time-series approaches, distributed lag non-linear models (DLNM), ecological designs, and case-crossover analyses. Each approach offers distinct advantages depending on the research question and data structure. However, all methods are subject to important limitations, particularly with respect to residual confounding and model specification. These must be carefully considered during study design and interpretation. Correspondingly, findings on the seasonality and health effects of UV exposure remain inconsistent across studies. *Conclusion:* No single methodological approach is optimal for assessing seasonal health effects of UV exposure. Method choice should be guided by the specific research question, outcome of interest, temporal resolution, and data availability, as well as by an explicit consideration of potential biases. A clear understanding of methodological assumptions and limitations is essential to avoid overinterpretation of seasonal patterns.

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OP No. 3

RESEARCH PROGRESS IN VDR AGONISTS AND ANTAGONISTS

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Background/Aim: The biological actions of 1,25-dihydroxyvitamin D ($1,25D_3$) are mediated by the nuclear vitamin D receptor (VDR), which has emerged as a therapeutic target in a spectrum of diseases, including not only bone disorders, but also autoimmune diseases and cancer. Since the discovery of $1,25D_3$, extensive efforts have been made towards the synthesis and development of highly active and non-calcemic analogs of the natural hormone; however, a limited number have reached clinical use. *Methods and Results:* Herein, we provide a comprehensive examination of the multifaceted role of VDR in diverse physiological and pathophysiological conditions, accompanied by an in-depth exploration of novel VDR agonists, bifunctional molecules and VDR antagonist ligands. Moreover, peptide inhibitors and proteolysis-targeting chimeras offer new possibilities for enhancing the therapeutic efficacy of VDR inactivation. *Conclusion:* These advancements are crucial for increasing the efficacy and safety of VDR-targeted therapies.

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OP No. 21

MAIN RESULTS OF THE VICTORIA-RCT: PERSONALIZED VITAMIN D_3 SUPPLEMENTATION INCREASED 25-HYDROXYVITAMIN D LEVELS AS PLANNED BUT DID NOT REDUCE FATIGUE IN PATIENTS WITH COLORECTAL CANCER

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Background/Aim: Many patients with colorectal cancer (CRC) suffer from major fatigue. We aimed to test whether vitamin D_3 supplementation improved the 25-hydroxyvitamin [25(OH)D] level and the Functional Assessment of Chronic Illness Therapy Fatigue Scale in patients with CRC. *Patients and Methods:* In the randomized, double-blind, controlled VICTORIA trial, 350 patients with CRC (175 in the vitamin D and 175 in the placebo group) were recruited up to 1 year post surgery or chemo/radiotherapy at five German rehabilitation clinics. Study inclusion required a 25(OH)D level <60 nmol/l. Personalized loading doses (range: 40,000-420,000 IU) were calculated from the baseline 25(OH)D level and the body mass index, administered in daily doses of 20,000-40,000 IU during in-patient rehabilitation and followed by a maintenance dose of 2,000 IU vitamin D_3

daily until the end of the trial (12 weeks). *Results:* In the placebo group, mean 25(OH)D levels remained almost unchanged from baseline [33.1 nmol/l, 95% confidence interval (CI)=31.1-35.2 nmol/l] to 12 weeks (35.9 nmol/l, 95% CI=33.2-38.6). In contrast, in the vitamin D group, mean 25(OH)D levels were increased over this 12-week period (from 32.8 nmol/l, 95% CI=30.9-34.6at baseline to 74.2 nmol/l, 95% CI=70.9-77.4 at week 12). The between-group difference in mean change was 38.3 nmol/l (95% CI=34.1-42.5; $p<0.0001$). The mean FACIT-F-FS fatigue scale scores did not differ between the vitamin D (38.3, 95% CI=36.6-40.0) and placebo group (37.8, 95% CI=35.9-39.6) at the end of the trial. The between-group difference was 0.5 points (95% CI=−2.0-3.1; $p=0.97$). *Conclusion:* Personalized vitamin D supplementation almost perfectly reached the target mean 25(OH)D level of 75 nmol/l, whereas 81.5% of patients with CRC in the placebo group had an insufficient 25(OH)D level (<50 nmol/l) at the end of the trial. However, the vitamin D_3 intervention did not influence cancer-related fatigue within the 12-week observation period.

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OP No. 8

GENOMIC EFFECTS OF NEW BIOLOGICALLY ACTIVE VITAMIN D AND LUMISTEROL METABOLITES

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Background/Aim: The discovery of vitamin D and lumisterol pathways initiated by cytochrome P 450 family 11 subfamily A member 1 (CYP11A1) or CYP27A1, which generate biologically active secosteroids, extends classical concepts on vitamin D and lumisterol biology. This presentation summarizes key findings on how these hydroxy metabolites modify gene expression and cellular homeostasis. *Overview:* Hydroxylated vitamin D_3 and lumisterol derivatives formed by the action of CYP11A1 or CYP27A1 interact with nuclear receptors including the vitamin D receptor (VDR), retinoic acid orphan receptors (RORs), aryl hydrocarbon receptor (AhR), liver X receptors (LXRs), peroxisome proliferator-activated receptor gamma (PPARG) and potentially others. These interactions lead to modulation of transcriptional networks governing cell proliferation and differentiation, immune activity, oxidative stress responses and metabolism, and stimulate DNA repair and protective mechanisms. These actions lead to the regulation of skin functions and integrity, systemic homeostatic effects, immunoregulatory effects and anticancer activities. *Conclusion:* Vitamin D_3 and lumisterol hydroxy metabolites form an integrated genomic regulatory network involving selective interactions with nuclear receptors, with implications in dermatology, immunology, metabolism, and oncology.

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OP No. 37

REGULATION OF THE CENTRAL NEUROENDOCRINE AND IMMUNE SYSTEM BY ULTRAVIOLET RADIATION: IMPLICATIONS FOR THE REGULATION OF BODY HOMEOSTASIS

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Background/Aim: Ultraviolet (UV) radiation (UVR) influences systemic physiology through skin-initiated neuroendocrine and immune pathways. This presentation will summarize how integrated skin–brain–endocrine-immune communication networks contribute to the

maintaince of whole-body homeostasis. *Materials and Methods:* UVR, particularly UVB, induces the production of different neuropeptides, including corticotropin-releasing hormone (CRH), adrenocorticotropic hormone (ACTH), α-melanocyte-stimulating hormone (α-MSH), and β-endorphin. These mediators influence the central hypothalamic–pituitary axis (HPA) as well as its peripheral equivalents, thereby modulating innate and adaptive immune response, as well as contributing to the maintaince of local and systemic homeostasis. UVB exposure also stimulates the production of other neuromediators and cytokines affecting HPA. It can also stimulate steroidogenesis locally and systemically. Importantly, UVB drives the synthesis of vitamin D, lumisterol and tachysterol, whose metabolites exert localized cutaneous effects or systemic actions following entry into systemic circulation. *Conclusion:* UV, especially UVB, is a key regulator of the neuro-endocrine–immune networks that regulate body homeostasis and allostasis. UVR exposure can be used theapeutically for inflammatory, neuropsychiatric, metabolic and endocrine disorders. A critical emerging challenge is to delinate which UVB-mediated effects are dependent on vitamin D and/or its phoderivatives, and which occur through vitamin D-independent mechanism.

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OP No. 23
INDIVIDUAL VITAMIN D SUPPLEMENTATION TO OVERCOME THE NATIONAL VITAMIN D DEFICIENCY IN GERMANY

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Background/Aim: In 2008, the German DEGSY1 study found an average vitamin D level of just under 20 ng/ml in the adult German population. Only a few participants (<4%) were taking vitamin D supplements at that time. This finding raised the question of whether and how a general vitamin D deficiency in the German population could be overcome. *Materials and Methods:* A total of 2.1 million vitamin D data were collected from four different laboratories across Germany, covering the period from 2008 to 2017. The anonymized data comes from patients aged between one and 90 years old. *Results:* The evaluation showed a significant increase of the mean vitamin D-level to approximately 30 ng/ml in the elderly people (>60 years) in 2017 compared to the data from 2008. In 2023, additional data from one of these labs reveal a further increase of the mean vitamin D level in the elderly people to 35 ng/ml. In the year 2024 a consumer survey in Germany stated, that 42% of respondents had taken vitamin D supplements in the last 12 months. *Conclusion:* The long-term trend in vitamin D levels in Germany suggests that it is possible to overcome nationwide vitamin D deficiency without changing official dietary or medical guidelines, but rather by improving the health literacy of the population with the help of all types of media.

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OP No. 7
VITAMIN D AND INFLAMMATION: AN UPDATE

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Background/Aim: Low vitamin D levels are clinically associated with the enhanced incidence of inflammatory diseases such as rheumatoid arthritis, atherosclerosis, inflammatory bowel disease, asthma or multiple sclerosis (MS). From cellular studies, it is well known that the active metabolite $1,25(OH)_2D_3$ regulates the expression of genes involved in the innate immune system and in cell differentiation. Typical vitamin D responding genes involved in host defense reactions are human

5-lipoxygenase and CD14. TGFβ, another regulator of immune reactions, is known to interact with vitamin D signaling and to modulate expression of vitamin D target genes. Regarding human 5-lipoxygenase, there is strong synergistic mode of action on the upregulation of 5-lipoxygenase expression. *Materials and Methods:* We systematically investigated the interaction between the TGFβ pathway and vitamin D signaling in human monocytic cell lines and their modulation by inhibitors of histone deacetylases (HDACs) and CDK9, which is the kinase involved in the regulation of transcript elongation. *Results:* We found that many genes are sensitive to CDK9 inhibition indicating that transcriptional elongation is a critical process which controls the expression level of many vitamin D and TGFβ target genes. Furthermore, we observed differential effects of HDAC inhibitors on vitamin D target genes. In the talk, results will be presented on the genome-wide analysis of the TGFβ/vitamin D responsive gene expression, the bioinformatic pathway analyses and the modulation of the vitamin D and TGFβ effects by HDAC inhibitors and by compounds interfering with different signaling pathways. *Conclusion:* These findings suggest an involvement of complex regulatory networks mediating the actions of both agents.

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OP No. 39

HYPOTHETICAL *VERSUS* PROVEN EXTRACUTANEOUS EFFECTS OF UVB PHOTOTHERAPY FOR SKIN DISEASES - WHAT CAN BE GATHERED FROM THE SCIENTIFIC LITERATURE?

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Sunlight is known to exert an abundance of biological effects on human skin, both harmful and beneficial. Whereas the effects of the visible and infrared spectrum of sunlight on human skin are still poorly investigated, there is unequivocal evidence that the ultraviolet spectrum of sunlight is a major driver of skin photoaging and skin cancer development. Conversely, ultraviolet (UV) B radiation is essential for vitamin D formation in the skin and phototherapy with artificial UV light is widely and effectively used for the treatment of a broad range of inflammatory skin diseases. The prevailing type of currently practiced dermatological phototherapy is narrow-band UVB (NB UVB) phototherapy which employs a narrow band of longer wave UVB radiation between 310-315 nm. Besides affecting the skin, UVB radiation from sunlight also induces an array of extracutaneous effects and has been implicated in the modification of autoimmune diseases (multiple sclerosis, type 1 diabetes), asthma, neurodevelopmental disorders (schizophrenia and autism), as well as metabolic and cardiovascular diseases. However, exposure to the UVB spectrum of sunlight differs in many respects from the therapeutic exposure to artificial NB UVB radiation (e.g., spectral composition of the UVB light, fluence rate, pattern of exposure) and thus their biological effects cannot be equated. The lecture will delve into this topic and give an overview of which of the manifold theoretical systemic effects of UVB have been observed or systematically evaluated in patients receiving NB UVB phototherapy for the management of skin conditions.

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OP No. 13

VITAMIN D_3, 25-HYDROXYVITAMIN D_3, AND 1,25-DIHYDROXYVITAMIN D_3 UPTAKE IN CULTURED HUMAN MATURE ADIPOCYTES

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Background/Aim: Vitamin D_3 is predominantly stored in the adipose tissue, where it is slowly mobilized under conditions of deficiency *in vivo*. However, the kinetics of its uptake, release and interaction with its major metabolites, $25(OH)D_3$ and $1,25(OH)_2D_3$, remain poorly understood. This study aimed to characterize the time-dependent intracellular handling of vitamin D_3 and its metabolites in differentiated human adipocytes. *Materials and Methods:* Human pre-adipocytes were differentiated into mature adipocytes and incubated with either vitamin D_3, $1,25(OH)D_3$ or in combination with vitamin D_3, $25(OH)D_3$ and $1,25(OH)_2D_3$. Intracellular concentrations were quantified through high performance liquid chromatography (HPLC) at multiple time-points up to 96 h and normalized to triglyceride content. Vitamin D_3 efflux was assessed using radiolabeled vitamin D_3 under basal and isoproterenol-stimulated lipolytic conditions. *Results:* Vitamin D_3 exhibited a gradual and sustained intracellular accumulation over 96h, consistent with sequestration within lipid-rich compartments. In contrast, $25(OH)D_3$ and $1,25(OH)_2D_3$ rapidly peaked within 1h and declined sharply thereafter. Isoproterenol stimulation significantly enhanced vitamin D_3 release into the extracellular medium from the adipocytes, indicating increased efflux during lipolytic activation. *Conclusion:* Human adipocytes selectively retain vitamin D_3 while rapidly clearing their hydroxylated metabolites. These findings highlight the distinct intracellular handling of vitamin D metabolites and suggest that tailored supplementation strategies, particularly in individuals with excess adiposity, may improve bioavailability and metabolic efficacy.

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OP No. 31

LONG-LATENCY DISEASE PREVENTION AND ADVICE TO THE PUBLIC ABOUT THE ROLE OF SUNSHINE EXPOSURE AND/OR VITAMIN D

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Long-latency diseases include melanoma, osteoporosis, bowel cancer, cardiovascular disease, arthritis, physical and cognitive decline, susceptibility to infection, and autoimmune conditions. Epidemiology strongly relates higher sun exposure and vitamin D levels to lower mortality from these long-latency diseases. However, no double-blind randomized clinical trial (RCT) exists demonstrating the primary prevention of any long-latency disease. Such an RCT would require healthy individuals, younger than 50 years, to be randomized to an intervention or control group with decades of follow-up to track a pre-specified disease outcome. Without such "causal evidence" for the benefits of sunshine and/or vitamin D, policy makers fixate on the acute risks of skin cancer and hypercalcemia instead. Using power calculations, this presentation will show the practical problems with conducting studies seeking causal evidence. For now, current consensus recommends maintaining serum 25(OH)D higher than 50 nmol/l. To ensure this floor, the population average serum 25(OH)D levels must be near 75 nmol/l. To achieve this, at least 2000 IU of vitamin D or daily sunshine is required consistently.

If possible, individuals should stay outdoors in the sun for at least 10 minutes every day, year-round. Finally, the evidence shows that chronic, non-burning sun exposure does not increase melanoma risk, whereas intermittent high sun exposure and sunburn double the risk. Gradual seasonal transitions in sunlight help to prime the skin, building biological protection to block harm from UVB.

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OP No. 26
GEOGRAPHY AND SKIN COLOUR MUST DETERMINE SUNLIGHT ADVICE

Richard Weller

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Excess sunlight exposure is the major environmental risk factor for skin cancer in white skinned individuals, but balanced health policy also needs to recognise that sunlight has significant health benefits and probably most of these occur independently of vitamin D synthesis. Observational studies from northern Europe all show that increased sunlight exposure associates with reduced all cause, and particularly cardiovascular mortality. In the largest and most tightly defined of these studies, using data from the UK Biobank and two independent estimates of ultraviolet (UV) exposure, validated against serum vitamin D levels and adjusted for confounders, we showed that higher UV exposure was associated with lower all-cause, cardiovascular and cancer mortality. Extending this study and adding two further indicators of UV exposure we were able to divide the ca 395,00 participants into low (47%), medium (43%) and high (9%) sun exposure cohorts. Fifteen years after recruitment, strong dose-dependent reductions in all-cause, cardiovascular and cancer mortality with sunlight exposure were seen, together with dose dependent increases in incident keratinocyte cancer. Reducing sunlight exposure enough to reduce one death from skin cancer would lead to 75 excess deaths from other causes. Serum vitamin D is a biomarker for sunlight exposure. The disparity between strong inverse associations between measured vitamin D and health outcomes, with the largely negative results of large scale randomised clinical trials of supplementation show that vitamin D cannot replace the overall health benefits of sunlight. UV-released NO gives cardiovascular benefits and effects on T cell status may account for reduced cancer mortality.

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OP No. 38
PROTEOMIC MEDIATION ANALYSIS IDENTIFIES VITAMIN D INDEPENDENT PATHWAYS DRIVING UV HEALTH BENEFITS

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Background/Aim: We have previously identified reduced all cause, cardiovascular and cancer mortality with sunlight exposure in the UK population using the UK Biobank. Numerous clinical trials of vitamin D supplementation show little effect. Other pathways must be relevant. The proteomic extension of this study examined biological pathways that may mediate the associations between habitual ultraviolet (UV) exposure and reduced cardiovascular and non-skin cancer mortality. *Materials and Methods:* In a subcohort of 44,712 UK Biobank participants with Olink® Explore 1536 plasma proteomic profiles (2,494 proteins), we applied a prespecified two-stage mediation framework. First, Cox models estimated the total effect of UV exposure on mortality and the direct effect after adjusting for each protein; the difference represented the indirect (mediated) effect, with bootstrapped confidence intervals used to assess significance. Proteins with sparse or unstable data were excluded. Second, UV–protein associations were evaluated using multivariable linear

regression with false discovery rate correction. Proteins were considered putative mediators only if they showed both a significant indirect effect and a strong UV–protein association (FDR <0.01). *Results:* Eight proteins met these criteria for both cardiovascular and cancer mortality: PIGR, NHLRC3, MMP-7, CD302, FGF23, REN, LGALS4, and IL-22. These markers implicate immunoregulatory, mucosal-barrier, and cardiorenal–neuroendocrine pathways as potential mechanisms linking UV exposure to systemic health outcomes. Mediation proportions ranged from 7.7% to 18.0% for cardiovascular mortality and 6.9% to 11.9% for cancer mortality. *Conclusion:* Because these proteins operate within overlapping networks, mediation percentages reflect relative influence rather than independent pathway effects.

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OP No. 30

SUN EXPOSURE AND TREND IN SUN PROTECTION

Hans Christian Wulf

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Background/Aim: Skin cancer is clearly related to skin type and ultraviolet radiation (UVR) exposure. UVR exposure is primarily from sun exposure and solarium use. *Materials and Methods:* Sun exposure has been measured by UVR dosimeters in groups of people with different occupations. The dose is measured in Standard Erythema Dose (SED). The exposure dose from solaria can be measured accordingly. Use of sun protection by sunscreens was measured at Danish beaches in the Greater Copenhagen area from 1992-2025 to monitor the development in sunscreen use and trends in sun protection factor (SPF). *Results:* The average Dane receives a yearly dose of 173 SED, but people's sun exposure varies by a factor 50 which explains why some people are at high risk of developing skin cancer. Exposure from one solarium treatment may provide about 3 SED, depending on cabin type. The use of sunscreen has increased to 90% among women and 70% among men at the Danish beaches, with a median SPF of 30 - an exponential increase over the last 40 years. *Conclusion:* Sun exposure, especially in combination with use of solarium, may lead to very high cumulative UVR doses. However, the pronounced increase in use of sunscreen and higher SPF among the Danish population seeking the sun may, to some degree, counteract the risk of skin cancer from over-exposure.

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OP No. 36

MEASUREMENT OF SKIN TYPE AND ITS RELATION TO SKIN CANCER RISK

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Background/Aim: People with light skin are more sensitive to ultraviolet radiation (UVR) and sunlight than people with darker skin, regarding both sunburn and skin cancer risk. Estimation of UVR tolerance is essential. *Materials and Methods:* UVR tolerance can be measured in 3 different ways. The 1st method is Fitzpatrick's Skin Type (FST) which subdivides people into white-, brown-, and black-skinned. White-skinned people are again subdivided into 4 types based on a questionnaire about tendency to burn and ability to tan. 2nd method is determination of minimal erythema dose (MED), a labor-heavy method. During the MED test, the patient is exposed to increasing doses of UVR to determine the erythema-provoking UVR dose the day after exposure. The 3rd method, which only takes a few seconds to perform, measures melanin in the skin and converts it to a pigment protection factor (PPF). *Results:* Method 1 is poorly correlated to MED but with modified questions it may be used to classify a skin cancer phototype. Method 2 is considered gold standard to

determine MED directly linked to UVR dose. The precision depends on dose increments, typically 25%. As a side-effect, it leaves long-lasting spots of hyperpigmentation in the tested skin areas. Method 3 is very fast and reliable. It measures PPF in all skin types on a scale from 1-25 standard erythema doses (SED) and is highly significantly correlated to MED and skin cancer risk. The skin cancer risk is about 35 times higher in the most fair-skinned ethnic Dane compared to the most dark-skinned ethnic Dane. *Conclusion:* FST may be modified to classify skin cancer phototype but measuring PFF is a much more exact and fine-meshed method both for skin cancer patients and the general population than both the MED test and the modified FST test.

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OP No. 41

PHOTODYNAMIC THERAPY OF ACTINIC KERATOSES: AN UPDATE

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Background/Aim: Actinic keratosis (AK) skin lesions are increasingly prevalent due to cumulative ultraviolet exposure. Photodynamic therapy (PDT) is widely used by trained dermatologists for the treatment of multiple AKs and large skin areas (field cancerization). *Materials and Methods:* Conventional PDT consists of superficial curettage by application of 5-aminolevulinic acid (5-ALA), or the methyl aminolevulinate esther (MAL), with red light exposure 3 h later, allowing accumulation of protoporphyrin IX (PpIX) causing photosensitivity in the precancerous cells. In daylight PDT, PpIX is activated by natural or artificial visible light. The procedure includes superficial curettage, ALA or MAL application, a 30-min incubation, and subsequent 2-h continuous illumination, either outdoors or indoors. *Results:* Conventional PDT is effective to treat AK, but is associated with severe pain and inflammation, whereas daylight PDT using 2 h illumination is nearly painless but still as effective. The illumination time may possibly be shortened. Combination of PDT with topical corticosteroids decreases inflammation, and in some cases, curettage may be omitted. After pretreatment in the clinic, daylight PDT can be performed in non-clinical outdoor location. *Conclusion:* Continuous activation of PpIX by daylight or artificial visible light can replace conventional PDT without loss of efficacy. Clinical efficacy is maintained in the absence of pain and inflammation, highlighting daylight PDT as a more tolerable and practical approach.

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OP No. 9

SIMULTANEOUS MEASUREMENT OF 1-HYDROXYLATED AND 24-HYDROXYLATED VITAMIN D METABOLITES BY LIQUID-CHROMATOGRAPHY-TANDEM-MASS-SPECTROMETRY – AN INNOVATIVE TOOL IN CHRONIC KIDNEY DISEASE MANAGEMENT

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Background/Aim: Bone and mineral metabolism is profoundly altered in patients with chronic kidney disease (CKD). As kidney function declines renal 1-alpha- and 24-hydroxylation of vitamin D metabolites decrease progressively, limiting the utility of serum 25-hydroxyl-vitamin D (25[OH]D) as a biomarker for patients' vitamin D

status. The simultaneous analysis of additional metabolites allows a functional assessment of vitamin D status that potentially correlates better than 25(OH)D with bone and mineral metabolism in CKD patients. Therefore, this project aimed to develop a liquid-chromatography-tandem-mass-spectrometry (LC-MS/MS) method for the simultaneous assessment of 1-alpha- and 24-hydroxylation of vitamin D metabolites in CKD patients. *Materials and Methods:* An LC-MS/MS method for the measurement of 25(OH)D3, 25(OH)D2, 1,25-dihydroxy vitamin D (1,25[OH]2D), 24,25-dihydroxyvitamin D (24,25[OH]2D), and 1,24,25-trihydroxyvitamin D (1,24,25[OH]3D) was developed. Sample preparation combines protein precipitation, liquid-liquid-extraction and derivatization with 4-phenyl-1,2,4-triazole-3,5-dione (PTAD). For chromatographic separation, a Nexera UHPLC from SHIMADZU (Kyoto, Japan) equipped with a Kinetex® 5 µm F5 100 Å LC column (150×4.6 mm, Phenomenex, Torrance, CA, USA) was used. A SCIEX QTRAP 6500 triple quadrupole instrument (Applied Biosystems, Framingham, MA, USA) with electrospray ionisation (ESI) was employed for detection. This method was validated according to CLSI EP-10 standards. Serum samples from individuals with 24-hydroxlase deficiency, CKD patients and kidney donors with blood collection before and after kidney transplantation were analyzed to demonstrate the ability of our method to capture functional derangements in vitamin D metabolism. *Results:* Our novel LC-MS/MS method has a linear range from 1.5 to 250 nmol/l for 25(OH)D3, 1.5-48 nmol/l for 24,25(OH)2D and 25(OH)D2, 15.6 to 500 pg/ml for 1,25(OH)2D, and 15.6 to 500 pg/ml for 1,24,25(OH)D3D. The limits of detection (LOD) and quantitation (LoQ) were 1.5/3.1 nmol/l for 25(OH)D, 0.3/1.0 nmol/l for 24,25(OH)2D, 3.9/7.8 pg/mll for 1,25(OH)2D, and 3.9/7.8 pg/ml for 1,24,25(OH)D3D. Recovery ranged between 90.8 to 105.5% for all four metabolites. Intra- and inter-assay imprecisions (CV) were ≤9.4% and ≤11.5%, respectively, across the entire analytical range for all metabolites. Analysis of human serum samples from 24-hydroxylase deficient patients revealed pronounced reductions of 24,25(OH)2D, 1,24,25(OH)3D, and the respective vitamin D metabolite ratios. Measurement of the vitamin D metabolites in serum samples before and after kidney transplantation showed a reduction in 24-hydroxylation, but no change in 1-alpha hydroxylation. *Conclusion:* This novel vitamin D metabolite detection method permits the accurate and precise measurement of 25(OH)D and its 1-alpha and 24-hydroxlated metabolites. With this method it is possible to capture dynamic changes in vitamin D metabolism due to renal impairment or enzyme deficiencies.

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OP No. 22

VITAMIN D DEFICIENCY IN BREAST CANCER PATIENTS

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Background/Aim: Vitamin D plays an important role in many types of cancer. The aim of the "BEGYN" study was to analyze serum 25-hydroxyvitamin D (25(OH)D) levels in newly diagnosed breast cancer patients over a year, the association with prognostic and lifestyle factors, and supplementation strategies. *Patients and Methods:* A total of 110 nonmetastatic breast cancer patients were included in the prospective observational "BEGYN" study. Serum 25(OH)D levels were assessed at baseline and quarterly thereafter. Clinical, pathological, nutritional, vitamin supplementation, and lifestyle data were recorded. *Results:* At baseline, 68.5%

of patients were vitamin D deficient (<30 ng/ml). Over the year, the median vitamin D levels increased to 48 ng/ml (range=22.0-76.7 ng/ml). At baseline 25(OH)D was higher in patients that reported use of vitamin D supplements (43 ng/ml *vs.* 22 ng/ml; $p<0.001$), and in summer compared to other seasons ($p=0.03$). Patients with moderate vitamin D deficiency were less likely to have triple negative breast cancer ($p=0.047$). *Conclusion:* 25(OH)D levels should be monitored regularly to adjust substitution individually. While variables such as seasons, age, very low-density lipoprotein, magnesium, diet, and oncological interventions affect 25(OH)D levels, supplementation has the greatest impact. However, vitamin D deficiency does not appear to be a relevant prognostic factor for breast cancer.

Poster presentations (PP)

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PP No. 1
MELANOMA AND SUN PROTECTION: WHERE DO WE STAND?

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Background/Aim: Ultraviolet (UV) radiation is a major modifiable risk factor for skin cancer, yet melanoma incidence has increased despite widespread use of sunscreens. We evaluated whether sunscreen use is associated with melanoma risk in human studies. *Materials and Methods:* A systematic review and meta-analysis were performed using PubMed. Eligible randomized controlled trials, cohort studies, and case-control studies assessed sunscreen use in relation to malignant melanoma. For comparability, sunscreen exposure was harmonized primarily as "ever" *versus* "never/rarely," with a secondary analysis restricted to studies reporting a distinct "never" category. Study quality was assessed with the Newcastle–Ottawa Scale, and level of evidence was classified according to the Oxford Centre for Evidence-Based Medicine. Crude odds ratios (ORs) with 95% confidence intervals (CIs) were pooled using random-effects models. Moderator analyses explored the impact of sex, geographical region, and study quality. *Results:* Twenty-three studies met inclusion criteria. In the main analysis (ever *vs*. never/rarely), the pooled effect estimate showed no significant association between sunscreen use and melanoma risk (OR=0.98, 95% CI=0.79-1.21). In the restricted analysis (ever *vs.* never), results were consistent (OR=0.95, 95% CI=0.75-1.20). A substantial between-study heterogeneity was present, and moderator analyses did not meaningfully explain variability. Funnel plot asymmetry and a significant Egger test suggested small-study effects; therefore, findings should be interpreted with caution. *Conclusion:* Across available evidence, sunscreen use (ever *vs.* never/rarely) was not associated with a measurable reduction in melanoma risk. More robust studies capturing application quantity, reapplication frequency, sun exposure behavior, and sun protection factor (SPF) are needed to clarify if any protective effect is present under real-world conditions.

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PP No. 2
VITAMIN D SYNTHESIS UNDER X-RAY IRRADIATION

Julia Kühn and Gabriele I. Stangl

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Background/Aim: Vitamin D synthesis is traditionally attributed to ultraviolet B (UVB)-induced photochemical

conversion of the sterol precursors 7-dehydrocholesterol (7-DHC) and ergosterol. In contrast, ionizing radiation has not been considered a relevant pathway for vitamin D formation. X-ray irradiation is widely used for the sterilization of food and feed to ensure microbial safety. This study investigated whether X-ray irradiation can induce the conversion of sterol precursors into vitamin D. *Materials and Methods:* Crystalline 7-DHC and ergosterol, sterols dissolved in oil (50 μg/ml), and matrices naturally containing sterol precursors, such as mushrooms, yeast, and rodent feed were exposed to X-ray irradiation at a dose of 25 kGy. Vitamin D_2 and vitamin D_3 concentrations were quantified by high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS) and compared to vitamin D levels generated under UVB irradiation at 20 mJ/cm^2 and 200 mJ/cm^2. *Results:* At a dose of 25 kGy, X-rays produced 94 μg/g of vitamin D_3 from crystalline 7-dehydrocholesterol and 74 μg/g of vitamin D_2 from crystalline ergosterol. When the precursors were dissolved in oil (50 μg/ml), X-ray exposure yielded 70 ng/g vitamin D_3 and 45 ng/g vitamin D_2. Similar increases were also observed in mushrooms, yeast, and rodent feed. Compared with UVB irradiation, X-ray exposure produced vitamin D amounts similar to those generated by 20 mJ/cm^2 UVB. High-dose UVB (200 mJ/cm^2) yielded substantially more; 151 μg/g vitamin D_3 and 188 μg/g vitamin D_2 from crystalline precursors. *Conclusion:* These results demonstrate that X-ray irradiation can generate vitamin D at levels comparable to UVB, revealing a previously unexpected and unrecognized pathway of vitamin D formation that warrants consideration in the context of feed sterilization.

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PP No. 3

SEASONAL FLUCTUATIONS OF CARDIOVASCULAR RISK MARKERS IN PATIENTS REFERRED TO CORONARY ANGIOGRAPHY

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Background/Aim: Seasonal variation in cardiovascular disease (CVD) is well documented. Data on seasonal fluctuations in cardiovascular risk markers are relatively sparse but may be relevant for CVD risk classification and treatment. We aimed to quantify the presence, magnitude, and timing of seasonality across various cardiovascular risk markers in patients referred to coronary angiography. *Materials and Methods:* In this retrospective, cross-sectional study, we analysed cardiovascular risk markers in 3,316 patients referred to coronary angiography between July 1997 and January 2000 from the Ludwigshafen Risk and Cardiovascular Health (LURIC) study. Seasonal patterns were assessed using robust cosinor regression, adjusting for age and sex. For each cardiovascular risk marker, we evaluated seasonality, peak date and magnitude (difference between peak and nadir) of seasonal fluctuations. In total, 24 different cardiovascular risk markers were analyzed, with correction for the false discovery rate (FDR). *Results:* Overall, 16 cardiovascular risk markers showed significant seasonal variation. Among these, the following exhibited effect sizes (Cohen's d) greater than 0.2 (peak-magnitude difference): 25-hydroxyvitamin D (10.28 ng/ml), LDL cholesterol (15.36 mg/dl), HbA1c (0.31 %), Omega-3 Index (0.45 %), HDL (3.18 mg/dl), HOMA Index

(0.54), calcium (0.03 mmol/l), and ApoB (5.6 mg/dl). The timing of peak values varied substantially. *Conclusion:* Seasonal variation in cardiovascular risk markers among patients referred to coronary angiography suggests that diagnostic and therapeutic thresholds may need to account for the timing of assessment. The heterogeneity in peak timing indicates that underlying mechanisms are likely multifactorial. Further research is needed to evaluate the individual and environmental factors driving these seasonal fluctuations.

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PP No. 4

MODERATE EXPOSURE TO ULTRAVIOLET (UV) RADIATION AND HUMAN HEALTH

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Most life forms on earth have evolved under the influence of solar radiation and are directly or indirectly dependent on it. There are only a few known life forms that can exist completely independently of the sun, such as organisms in the oceans that receive their energy from hydrothermal sources. Although the sun is an essential prerequisite for higher life forms like humans, too much ultraviolet (UV) radiation is harmful. In dermatology, for example, sunburns or cumulative UV exposure are significant for skin cancer and photoaging and have been well known for a long time. However, this should not lead to completely avoiding UV radiation, as even moderate or low doses of UV radiation can have negative effects on the human body. The significant effects of UV light have a positive impact on overall well-being. Additionally, well-known mechanisms that occur in the skin, such as the UV-dependent production of hormones, chemokines, and other substances, which can also have effects on the entire organism through endocrine, autocrine, or paracrine actions, are important. An important example of this is vitamin D and its derivatives. Furthermore, photoimmunological research has shown that UV radiation can suppress the adaptive immune system in the skin and, conversely, stimulate the innate immune system.

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PP No. 5

UMBRELLA REVIEW ON VITAMIN D AND CANCER

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Background/Aim: Cancer is a major public health problem and is linked to vitamin D through several mechanisms. However, recent umbrella reviews on the extraskeletal effects of vitamin D have not specifically addressed cancer. *Materials and Methods:* An umbrella review (PROSPERO: CRD42021244758) was conducted to provide an overview of the relationship between vitamin D (intake and blood levels) and the incidence and mortality of five common cancers. Forty-one systematic reviews comprising 281 individual studies were included (breast n=14, colorectal n=15, pancreatic n=3, prostate n=11, lung n=10). *Results:* Inverse associations between vitamin D levels and mortality were observed for all five cancer types examined. For pancreatic, breast, colorectal, and lung cancer there is also evidence suggesting a possible reduction in incidence associated with higher vitamin D levels. The associations between vitamin D intake and incidence are less clear. Only a small number of meta-analyses on breast, colorectal, and lung cancer indicate a protective effect of vitamin D intake. No associations are reported between mortality and vitamin D intake (no

data available for pancreatic and lung cancer). Except for prostate cancer incidence, there were no signs of harmful associations of higher 25(OH)D levels or vitamin D intake regarding cancer. *Conclusion:* Circulating vitamin D levels show inverse correlations with cancer risk and mortality for most studied cancers. Evidence regarding vitamin D intake is less consistent. As most reviews include observational studies, causal relationships cannot generally be inferred. Despite methodological limitations, the review strengthens the evidence that adequate vitamin D levels may have protective effects regarding cancer.

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PP No. 6

DISRUPTION OF THE CUTANEOUS INTEGRATED NEUROENDOCRINE SYSTEM (CINE): THE IMPACT OF CHEMICAL UV FILTERS ON AHR VDR CROSSTALK AND SKIN HOMEOSTASIS

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Background/Aim: The incidence of skin diseases is rising globally. While ultraviolet (UV) radiation is a known primary risk factor for skin cancer, the role of chemical UV filters as potential endocrine disruptors is gaining research focus worldwide. The skin is a highly active organ governed by the Cutaneous Integrated Neuroendocrine System (CINE), a complex network of signaling pathways essential for cell proliferation, differentiation, and DNA repair. This study aimed to investigate the effects of the widely used UV filters oxybenzone and octocrylene on CINE homeostasis, using the banned filter 3-benzylidene camphor (3-BC) as a positive control for endocrine disruption. *Materials and Methods:* Using human skin biopsies obtained from body donors, we analyzed the expression of genes involved in the CINE axis – specifically the vitamin D receptor (VDR) and estrogen related receptors – alongside the aryl hydrocarbon receptor (AhR) signaling pathway. Furthermore, the biopsies were subjected to UV irradiation to assess cellular viability, proliferation, and DNA damage. *Results:* Based on our prior work demonstrating significant functional crosstalk between AhR and VDR in human keratinocytes, we hypothesize that these UV filters disrupt this specific inter-receptor communication. We further anticipate that such interference impairs the skin's protective mechanisms, thereby increasing susceptibility to disease. *Conclusion:* The findings of this study are expected to improve understanding of the risks associated with topically applied UV filters and provide an evidence-based foundation for public health recommendations. By offering new insights into the etiology of skin diseases, this research may contribute to the development of safer sunscreen products.

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