Scientific reference list on UV and sunbed use from 2006 to today

We have sorted the research by category as follows:

A. Epidemiological studies showing the importance of moderate sun/UV exposure for good health

B. UV exposure and health effects

C. Indoor UV exposure and vitamin D3

D. UV exposure and melanoma

E. Other published peer reviewed studies stressing the importance of sun/UV exposure for maintaining good health.

A. Epidemiological studies showing the importance of moderate sun/UV exposure for good health

1. Pierre Engel et al, 2010

Inserm, CESP Centre for Research in Epidemiology, Paris South University, France
Cancer Epidemiol Biomarkers Prev 2011;20:187-198. Published OnlineFirst December 2, 2010.
in Cancer Epidemiol Biomarkers Prev; 20(1); 187–98. _2011 American Association for Cancer Research.

Title: Joint Effects of Dietary Vitamin D and Sun Exposure on Breast Cancer Risk: Results from the French E3N Cohort (Tracking 67,721 women for ten years)

Conclusion: 43% less breast cancer for the women who did not avoid the sun.

2. **Pelle Lindqvist et al. 2014**

Karolinska University Hospital, Stockholm, Sweden
J Intern Med 2014; 276;77-86 DOI: 10.1111/joim.12251

Title: Avoidance of sun exposure is a risk factor for all-cause mortality: results from the MISS cohort(Tracking 29,518 women for twenty years)

Conclusion: We conclude that women who avoid sun exposure are at an increased risk of all-cause death with a two-fold increased mortality rate as compared to those with the highest sun exposures. The implementation of restrictive sun exposure advice in countries with low solar intensity might not be beneficial to women's health.

3. **Chowdhury R, Kunutsor S, Vitezova A, Oliver-Williams C, Chowdhury S, Kiefte-de-Jong JC et al. Vitamin D and risk of cause specific death: systematic review and meta-analysis of observational cohort and randomized intervention studies. BMJ 2014;348:g1903 (Published 1 April 2014)**

A systematic review of 73 cohort studies and 849,412 participants published in 2014 found that adults with lower levels of vitamin D had a 35% increased risk of death from heart disease, 14% greater likelihood of death from cancer and an all-cause mortality risk of 35%. Based on population prevalence estimates 12.8% of all deaths in the United States could be attributed to vitamin D deficiency. This ranks vitamin D deficiency as the second leading cause of premature death in the USA behind smoking at 20%, but ahead of physical inactivity (11%) and alcohol consumption (9%).

Conclusion: This reinforces the potential importance of scalable, cost effective public health strategies (such as moderate sun exposure, supplementation, and food fortification) in improving the overall vitamin D status to reduce premature deaths worldwide.

4. **Garland CF et al,. Meta-analysis of All-Cause Mortality According to Serum 25-Hydroxyvitamin D. Am J Public Health. 2014 Jun 12:e1-e8**

The hazard ratio for all cause mortality comparing the lowest (0–9 nanograms per milliliter [ng/mL]) to the highest (> 30 ng/mL) category of 25(OH)D was 1.9 (95% confidence interval = 1.6, 2.2; P < .001).

5. **Schottker et al,. Vitamin D and mortality: meta-analysis of individual participant data from a large consortium of cohort studies from Europe and the United States. BMJ 2014;348:g3656**

Comparing bottom versus top quintiles resulted in a pooled risk ratio of 1.57 (95% CI 1.36 to 1.81) for all-cause mortality.

6. **Busse B et al. Vitamin D Deficiency Induces Early Signs of Aging in Human Bone, Increasing the Risk of Fracture. Sci Transl Med. 2013 Jul 10;5(193):193ra88.**

In situ fracture mechanics measurements and synchrotron radiation micro–computed tomography of the crack path indicated that vitamin D deficiency increases both the initiation and propagation of cracks by 22 to 31%. Thus, vitamin D deficiency is not simply associated with diminished bone mass.

7. **Chen W, Clements M, Rahman B, Zhang S, Qiao Y, Armstrong BK. Relationship between cancer mortality/incidence and ambient ultraviolet B irradiance in China. Cancer Causes Control. 2010 Oct;21(10):1701-9.**

Conclusion: Mortality from all cancers together and most major cancers in China was inversely associated with solar UVB. These associations were similar to those observed in a number of populations of European origin. Incidence of some cancer types had the same correlation with UVB. They suggest the possibility that vitamin D may reduce the incidence or improve the outcome of cancer in Chinese people.

8. **Li M, Chen P, Li J, Chu R, Xie D, Wang H. Review: The Impacts of Circulating 25-Hydroxyvitamin D Levels on Cancer Patient Outcomes: A Systematic Review and meta-Analysis. J Clin Endocrinol Metab. 2014 Jul;99(7):2327-36.**

The pooled hazard ratio for the highest vs the lowest quartile of circulating 25(OH)D levels was 0.55 (95% confidence interval [CI] _ 0.33–0.91) for overall survival of colorectal cancer patients, 0.63 (95% CI _ 0.51–0.77) for breast cancer patients, and 0.48 (95% CI _ 0.36–0.64) for lymphoma patients.

Conclusions: The results indicate that cancer patients with higher circulating 25(OH)D levels at or near the time of diagnosis have better outcomes.

9. **Anderson LN, Cotterchio M, Kirsh VA, Knight JA. Ultraviolet Sunlight Exposure During Adolesence and Adulthood and Breast Cancer Risk: A Population-based Case-Control Study Among Ontario Women. Am J Epidemiol. 2011 Aug 1;174(3):293-304**

The associations among ultraviolet radiation from sunlight, factors related to cutaneous vitamin D production, and breast cancer risk were evaluated in a population-based case-control study conducted in Ontario, Canada, between 2003 and 2004 (n ¼ 3,101 cases and n ¼ 3,471 controls). Time spent outdoors was associated with reduced breast cancer risk during 4 periods of life (>21 vs. _6 hours/week age adjusted odds ratio (OR) ¼ 0.71, 95% confidence interval (CI): 0.60, 0.85 in the teenage years; OR ¼ 0.64, 95% CI: 0.53, 0.76 in the 20s–30s; OR ¼ 0.74, 95% CI: 0.61, 0.88 in the 40s–50s; and OR ¼ 0.50, 95% CI: 0.37, 0.66 in the 60s–74 years). Sun protection practices and ultraviolet radiation were not associated with breast cancer risk. A combined solar vitamin D score, including all the variables related to vitamin D production, was significantly associated with reduced breast cancer risk. These associations were not confounded or modified by menopausal status, dietary vitamin D intake, or physical activity. This study suggests that factors suggestive of increased cutaneous production of vitamin D are associated with reduced breast cancer risk.

10. **Knight JA, Lesosky M, Barnett H, Raboud JM, Vieth R. Vitamin D and Reduced Risk of Breast Cancer: A Population-Based Case-Control Study. Cancer Epidemiol Biomarkers Prev 2007;16(3):422-9**

Reduced breast cancer risks were associated with increasing sun exposure from ages 10 to 19 (e.g., OR, 0.65; 95% CI, 0.50-0.85 for the highest quartile of outdoor activities versus the lowest; P for trend = 0.0006).

11. **Abbas S, Linseisen J, Slanger T, Kropp S, Mutschelknauss EJ, Flesch-Janys D, Chang-Claude J. Serum 25-hydroxyvitamin D and risk of post-menopausal breast cancer – results of a large case-control study. Carcinogenesis. 2008 Jan;29(1):93-9.**

Compared with the lowest category (<30 nM), OR [95% confidence intervals (CI)] for the higher categories of 25(OH)D (30–45, 45–60, 60–75 and ‡75 nM) were 0.57 (0.45–0.73), 0.49 (0.38–0.64), 0.43 (0.32–0.57) and 0.31 (0.24–0.42), respectively (Ptrend < 0.0001).

12. **John EM, Schwartz GG, Koo J, Wang W, Ingles SA. Sun exposure, Vitamin D Receptor Gene Polymorphisms, and Breast Cancer Risk in a Multiethnic Population. Am J Epidemiol. 2007 Dec 15;166(12):1409-19.**

This study supports the hypothesis that sunlight exposure reduces risk of advanced breast cancer among women with light skin pigmentation.

B. UV exposure and health effects

1. **Oskar Franco et all. 2014**

Department of epidemiology Erasmus university M.C. Rotterdam, The Netherlands

Title: Vitamin D and risk of cause specific death: systematic review and meta-analysis of observational cohort and randomised intervention studies

BMJ 2014; 348 doi: http://dx.doi.org/10.1136/bmj.g1903 (Published 1 April 2014)
Conclusion: "The sun vitamin", Vitamin D3 reduced all cause mortality significantly by 11%.

2. **Ling Yang and Marit B. Veierød et all. 2011**

Karolinska Institutet, Stockholm, Sweden, Department of Medical Epidemiology and Biostatistics,

Title: Prospective Study of UV Exposure and Cancer Incidence Among Swedish Women in Cancer Epidemiol Biomarkers Prev; 20(7) July 2011

Conclusion: in this cohort of Swedish women we found no evidence of an association between any cumulative measure of UV exposure at ages 10 to 39 years and subsequent incidence of overall cancer, or cancers of the breast, ovary, lung, colon-rectum, and brain. However, a reduced overall cancer risk and breast cancer risk was observed among women who spent one week or more per year on sunbathing vacations between ages 10 and 29 years, and a reduced breast cancer risk among women UV Exposure and Cancer Incidence in Swedish Women who used solarium between ages 10 and 39 years.

3. **Sharif Mohr and Cedric Garland et all. 2014**

Scientific Programs Office, Code 01A, Naval Health Research Center, San Diego, CA, U.S.A. Published 2014 International Institute of Anticancer Research (Dr. John G. Delinassios)

Title: Meta-analysis of Vitamin D Sufficiency for Improving Survival of Patients with Breast Cancer

Conclusion: A high Vitamin D level was associated with lower mortality from breast cancer.

4. **Pelle Lindqvist et all. 2010**

Karolinska University Hospital, Stockholm, Sweden
Diabetes Res Clin Pract. 2010 Oct;90(1):109-14. doi: 10.1016/j.diabres.2010.06.007.

Title: Are active sun exposure habits related to lowering risk of type 2 diabetes mellitus for women, a prospective cohort study?

Conclusion: Our findings indicated that women with active sun exposure habits were at a 30% lower risk of having Diabetes, as compared to those with non-active sun habits.

Note ESA: This effect is caused by UV induced (no supplements possible) Nitric Oxide

5. **D Liu et all. 2013**

MRC Centre for Inflammation Research & Department of Dermatology, University of Edinburgh, UK.
Published at university medical illustration unit

Title: UVA lowers blood pressure and vasodilates the systemic arterial vasculature by mobilisation of cutaneous nitric oxide stores

Conclusion: UV exposure lowers blood pressure and cardiac vascular disease by UV induced Nitric Oxide. Vitamin D supplements had no result, so here it is not vitamin D but NO what creates the health benefit. Quote: We hypothesized that the benefits of sunlight on cardiovascular health are mediated by mobilization of skin stores of nitrogen oxides to the systemic circulation

Note ESA: This effect is caused by UV induced (no supplements possible) Nitric Oxide

6. **Seeta Durvasula et all. 2014**

Sydney Medical School Northern, University of Sydney, Australia
Arch Osteoporos (2014) 9:197 DOI 10.1007/s11657-014-0197-9

Title: Vitamin D response of older people in residential aged care to sunlight-derived ultraviolet radiation.

Conclusion: Natural UVR exposure can increase vitamin D levels in older people in residential care, but depends on the season of exposure. However, due to inadequate sun exposure, Vitamin D did not reach optimal levels. Nevertheless, where sun exposure is encouraged in this group, the focus for the start of exposure should be in the months of spring or autumn, as this timing was associated with a vitamin D response.

7. **Fredrick Garland et all, 1990**

US Navy Institute of Medicine
Scientific Programs Office, Naval Health Research Center, San Diego, CA, U.S.A.
Arch Environ Health. 1990 Sep-Oct;45(5):261-7.

Title: Occupational sunlight exposure and melanoma in the U.S. Navy.

Conclusion: Findings on the anatomical site of melanoma from this study suggest a protective role for brief, regular exposure to sunlight and fit with recent laboratory studies that have shown vitamin D to suppress growth of malignant melanoma cells in tissue culture. A mechanism is proposed in which vitamin D inhibits previously initiated melanomas from becoming clinically apparent.

8. **William Grant et all, 2009**

Sunlight, Nutrition, and Health Research Center, San Francisco
Progress in Biophysics and Molecular Biology, 2009 Mar 3.
10.1016/j.pbiomolbio.2009.02.003

Title: Estimated benefit of increased vitamin D status in reducing the economic burden of disease in Western Europe.

Conclusion: The reduction in direct plus indirect economic burden of disease was based on increasing the mean serum 25(OH)D level to 40 ng/mL, which could be achieved by a daily intake of 2000–3000 IU of vitamin D. For 2007, the reduction is estimated at €187,000 million/year.

9. **Grant WB, Garland CF. The Association of Solar Ultraviolet B UVB with Reducing Risk of Cancer: Multifactorial Ecologic Analysis of Geographic Variation in Age-adjusted Cancer Mortality Rates. Anticancer Res. 2006 Jul-Aug;26(4A):2687-99.**

Fifteen types of cancer were inversely-associated with UVB.

10. **Lombardi C, Heck JE, Cockburn M, Ritz B. Solar UV Radiation and Cancer in Young Children. Cancer Epidemiol Biomarkers Prev; 22(6); 1118-28, 2013**

Conclusions: Our findings suggest that UVR during pregnancy may decrease the odds of some childhood cancers.

Impact: This study shows protective associations of UVR with some childhood cancers.

11. **Tran et al,. Association between ultraviolet radiation, skin sun sensitivity and risk of pancreatic cancer. Cancer Epidemiol. 2013 Dec;37(6):886-92**

Results: Being born in or living in areas of higher ambient UVR (compared to lower ambient UVR) was associated with about 30–40% lower risk of pancreatic cancer.

12. **John EM, Koo J, Schwartz GG. Sun Exposure and Prostate Cancer Risk: Evidence for a Protective Effect of Early-Life Exposure. Cancer Epidemiol Biomarkers Prev. 2007 Jun;16(6):1283-6.**

Significant inverse associations were found for men born in a region of high solar radiation (relative risk, 0.49, 95% confidence interval, 0.27-0.90 for high versus low solar radiation), with a slightly greater reduction for fatal than for nonfatal prostate cancer. Frequent recreational sun exposure in adulthood was associated with a significantly reduced risk of fatal prostate cancer only (relative risk, 0.47; 95% confidence interval, 0.23-0.99). These findings suggest that, in addition to sun exposure in adulthood, sun exposure in early life protects against prostate cancer.

13. **Yang L, Lof M, Veierod MB, Sandin S, Adami HO, Weiderpass E. Ultraviolet Exposure and Mortality among Women in Sweden. Cancer Epidemiol Biomarkers Prev. 2011 Apr;20(4):683-90.**

Results: During 15 years of follow-up, among the 38,472 women included in the present study, 754 deaths occurred: 457 due to cancer and 100 due to CVD. When combining the information on sun exposure from age 10 to 39 years, women who got sunburned twice or more per year during adolescence had a reduced all-cause mortality, compared with women who had been sunburned once or less.Areduced risk for all-cause and CVD mortality was observed in women who went on sunbathing vacations more than once a year over three decades. Solarium use once or more per month for at least one decade increased the risk of all-cause mortality, when compared with women who never used a solarium.

Conclusions: Solar UV exposure was associated with reduced overall and CVD mortality, whereas artificial UV exposure was associated with increased overall and cancer mortality among Swedish women.

Impact: Moderate sun exposure may protect against cause-specific mortality.

14. **Feelish M, Kolb-Bachofen V, Liu D, Lundberg JO, Revelo LP, Suschek CV, Weller RB. Is sunlight good for our heart? Eur Heart J. 2010 May;31(9):1041-5.**

We propose here that many of the beneficial effects of sunlight, particularly those related to cardiovascular health, are mediated by mechanisms that are independent of melatonin, vitamin D, and exposure to UVB alone. Specifically, we suggest that the skin is a significant store of nitric oxide (NO)-related species that can be mobilized by sunlight and delivered to the systemic circulation to exert coronary vasodilator and cardioprotective as well as antihypertensive effects (Figure 1). We further hypothesize that this dermal NO reservoir is a product of local production and dietary supply with nitrate-rich foods.

15. **Lindqvist PG, Olsson H, Landin-Olsson M. Are active sun exposure habits related to lowering risk of type 2 diabetes mellitus in women, a prospective cohort study? Diabetes Res Clin Pract. 2010 Oct;90(1):109-14.**

Results: Our findings indicated that women with active sun exposure habits were at a 30% lower risk of having DM, as compared to those with non-active habits.

16. **Lucas RM et al. Sun exposure and vitamin D are independent risk factors for CNS demyelination. Neurology. 2011 Feb 8;76(6):540-8.**

Higher levels of past, recent, and accumulated leisure-time sun exposure were each associated with reduced risk of FDE, e.g., accumulated leisure-time sun exposure (age 6 years to current), adjusted odds ratio (AOR) _0.70

17. **Becklund BR, Severson KS, Vang SV, DeLuca HF. UV radiation suppresses experimental autoimmune encephalomyelitis independent of vitamin D production. Proc Natl Acad Sci U S A. Apr 6, 2010; 107(14): 6418–6423.**

These results suggest that UVR is likely suppressing disease independent of vitamin D production, and that vitamin D supplementation alone may not replace the ability of sunlight to reduce MS susceptibility.

18. **Hollingworth S, Walker K, Page A, Eadie M. Pharmacoepidemiology and the Australian regional prevalence of multiple sclerosis. Mult Scler. 2013 Nov;19(13):1712-6.**

Results: In the 2005–2008 period, the calculated mean treated RRMS prevalence in Australia ranged from 7.5 per 100,000 in the far north to 53.2 per 100,000 in the extreme south and was linearly related to increasing southerly latitude. Public domain Australian data suggested that multiplying this prevalence by a factor of 2.2 (to account for untreated RRMS and other types of MS) may provide a measure of the prevalence of all varieties of the disease.

Conclusion: These findings provide contemporary and more comprehensive evidence for the gradient of MS prevalence with latitude in Australia than has previously been available.

19. **Bjornevik K et al. Sun exposure and multiple sclerosis risk in Norway and Italy: The EnvIMS study. Multiple Sclerosis Journal Jan 10, 2014**

Results: A significant association between infrequent summer outdoor activity and increased MS risk was found in Norway and in Italy. The association was strongest between the ages of 16 and 18 years in Norway (odds ratio (OR) 1.83, 95% confidence interval (CI) 1.30–2.59), and between birth and age 5 years in Italy (OR 1.56, 95% CI 1.16–2.10). In Italy a significant association was also found during winter (OR 1.42, 95% CI 1.03–1.97). Frequent sunscreen use between birth and the age of 6 years was associated with MS in Norway (OR 1.44, 95% CI 1.08–1.93) after adjusting for outdoor activity during the same period.

Conclusion: Converging evidence from different measures underlines the beneficial effect of sun exposure on MS risk.

20. **Islam T, Gauderman WJ, Cozen W, Mack TM. Childhood sun exposure influences risk of multiple sclerosis in monozygotic twins. Neurology. 2007 Jul 24;69(4):381-8.**

Results: Each of the nine sun exposure– related activities during childhood seemed to convey a strong protection against MS within MZ twin pairs. Depending on the activity, the odds ratio (OR) ranged from 0.25 to 0.57. For example, the risk of subsequent MS was substantially lower (OR 0.40, 95% CI 0.19 to 0.83) for the twin who spent more time suntanning in comparison with the co-twin. For each unit increase in SI, the relative risk of MS decreased by 25%.

Conclusion: Early sun avoidance seems to precede the diagnosis of multiple sclerosis (MS). This protective effect is independent of genetic susceptibility to MS.

21. **Effect of sunlight exposure on cognitive function among depressed and non-depressed participants: a REGARDS cross-sectional study, Shia T Kent*, Leslie A McClure, William L Crosson, Donna K Arnett, Virginia G Wadley and Nalini Sathiakumar**

Results: Among depressed participants, a dose-response relationship was found between sunlight exposure and cognitive function, with lower levels of sunlight associated with impaired cognitive status (odds ratio = 2.58; 95% CI 1.43–6.69). While both season and sunlight were correlated with cognitive function, a significant relation remained between each of them and cognitive impairment after controlling for their joint effects.

22. **Grant W. A review of the role of solar ultraviolet-B irradiance and vitamin D in reducing risk of dental caries. Dermato-Endocrinology 3:3, 193-198; July/August/September 2011; c 2011 Landes Bioscience**

There was a significant inverse correlation for dental health rank with respect to solar UVB from doses of 4.0 to 6.5 kJ/m2 with little change thereafter.

23. **UK – Consensus Vitamin D Position Statement**
http://www.nhs.uk/livewell/summerhealth/documents/concensus_statement%20_vitd_dec_2010.pdf

This consensus statement represents the unified views of the British Association of Dermatologists, Cancer Research UK, Diabetes UK, the Multiple Sclerosis Society, the National Heart Forum, the National Osteoporosis Society and the Primary Care Dermatology Society. Vitamin D is essential for good bone health and for most people sunlight is the most important source of vitamin D. The time required to make sufficient vitamin D varies according to a number of environmental, physical and personal factors, but is typically short and less than the amount of time needed for skin to redden and burn. Enjoying the sun safely, while taking care not to burn, can help to provide the benefits of vitamin D without unduly raising the risk of skin cancer. Vitamin D supplements and specific foods can help to maintain sufficient levels of vitamin D, particularly in people at risk of deficiency.
However, there is still a lot of uncertainty around what levels qualify as “optimal” or “sufficient”, how much sunlight different people need to achieve a given level of vitamin D, whether vitamin D protects against chronic diseases such as cancer, heart disease and diabetes, and the benefits and risks of widespread supplementation.

24. GrassrootsHealth – Scientists Call to D*action. The Vitamin D Deficiency Epidemic
http://www.grassrootshealth.net/epidemic

The Scientists "Call to D*action," an international consensus published by 42 prominent vitamin D doctors, researchers and scientists, recommends that people of all ages achieve optimal vitamin D blood serum levels between 100-150 nmol/L for best overall health and disease prevention. The consensus was organized by GrassrootsHealth, a non-profit public health promotion organization dedicated to moving the vitamin D research into practice.

25. CIE 201:2011 Recommendations on Minimum Levels of Solar UV Exposure. ISBN 978 3 902842 39 8
http://www.cie.co.at/index.php/Publications/index.php?i_ca_id=837

A large technical report was undertaken by the International Commission on Illumination (CIE) in 2011 to address the issue of sensible exposure to solar (UV) radiation. The CIE report concluded: *"Based on a review of the evidence of both the beneficial and the harmful effects of solar exposures it is concluded that people should not shun the sun, even not at noon."*

26. World Health Organization website – Ultraviolet radiation and the INTERSUN Programme. The known health effects of UV.
http://who.int/uv/faq/uvhealtfac/en/index1.html#

World Health Organization on their website report that "*there is no doubt that a little sunlight is good for you*" and that '*5 to 15 minutes of casual sun exposure of hands, face and arms two or three times per week during summer months is sufficient to keep your vitamin D levels high.*"

27. 2014 Ultraviolet Radiation Suppresses Obesity and Symptoms of Metabolic Syndrome Independently of Vitamin D in Mice Fed a High-Fat Diet Diabetes 2014;63:3759–3769 | DOI: 10.2337/db13-1675

Sian Geldenhuys, Prue H. Hart, Raelene Endersby, Peter Jacoby, Martin Feelisch, Richard B. Weller, Vance Matthews, and Shelley Gorman

Many of the benefits of UVR were not reproduced by vitamin D supplementation. In further mechanistic studies, skin induction of the UVR-induced mediator nitric oxide (NO) reproduced many of the effects of UVR. These studies suggest that UVR (sunlight exposure) may be an effective means of suppressing the development of obesity and MetS, through

mechanisms that are independent of vitamin D but dependent on other UVR-induced mediators such as NO.

28. **Lindqvist PG et al., Does an active sun exposure habit lower the risk of venous thrombotic events? A D-lightful hypothesis. J Thromb Haemost 2009; 7: 605-10**

In 2010, researchers from Lund University in Sweden found that the health benefits of sun exposure far outweighed the risks – as long as you sunbathe sensibly. Oncologist Hakan Olsson told a Swedish newspaper *'Our studies show that women with active sunbathing habits live longer.'* They reported their controversial finding after studying the effect of sun exposure on 40,000 Swedish women.

29. **Moan J. et al,. Addressing the health benefits and risks, involving vitamin D or skin cancer, of increased sun exposure www.pnas.org/cgi/doi/10.1073/pnas.0710615105**

In 2008, Johan Moan from the University of Oslo in Norway published a paper – to try and answer the question – *"will increased sun exposure lead to net health benefits or risks?"* The study concluded *"These data indicate that increased sun exposure may lead to improved cancer prognosis and, possibly, give more positive than adverse health effects."*

30. **Goring H, and Koshuchowa S. Vitamin D – the Sun Hormone. Life in Environmental Mismatch. Biochemistry (Moscow) January 2015, Volume 80, Issue 1, pp 8-20**

"No life can exist on the Earth without the Sun. Everything on the Earth, from favorable temperature conditions to creation of bioorganic mass and free oxygen in the atmosphere is created only due to the rays of the Sun. For formation of vitamin D, only two additional factors are needed: UV radiation for photoisomerization of 7_dehydroxycholesterol to previtamin D, and temperature above 25°C for thermoisomerization of previtamin D to vitamin D. There is clear evidence that for the majority of animals living under conditions of the atmosphere, from amphibians to primates, a vitally indispensable photo-dependent mechanism of vitamin D synthesis has been elaborated."

31. **Van Leeuwen et al,. Latitude Gradients for Lymphoid Neoplasm Subtypes in Australia Support an Association with Ultraviolet Radiation Exposure. International Journal of Cacncer doi: 10.1002/ijc.28081**

In this national, population-based study of all incident lymphoid neoplasms diagnosed in Australia between 2002 and 2006; increasing incidence with increasing distance from the equator was observed for several types of non-Hodgkin and Hodgkin lymphoma. The study

concluded "*Our findings support a possible protective effect of UVR exposure on the risk of several neoplasms, possibly through vitamin d-related immune modulation critical in lymphomagenesis*."

32. Zivadinov et al,. Interdependence and contributions of sun exposure and vitamin D to MRI measures in multiple sclerosis. J Neurol Neurosurg Psychiatry doi: 10.1136/jnnp-2012-304661

A study evaluating the associations between sun exposure to MRI measures of brain injury in MS found that increased sun exposure was associated with increased whole brain volume and grey matter volume after adjusting for disability and vitamin D levels. The study concluded "*Sun exposure may have direct effects on MRI measures of neurodegeneration in MS, independently of vitamin D*."

33. Grant WB. Scientific and social controversies regarding UV and pigmentation: the beneficial effects of UV irradiance outweigh the risks. Pigment Cell Melanoma Res. 22; 137-138 doi: 10.1111/j.1755-148X2008.00523.x

A letter published in 2008, supported that the beneficial effects of UV irradiance outweigh the risks. Solar UVB has always been the primary source for vitamin D for life on earth. It concluded: "*Solar UVB is the natural way to obtain vitamin D but, of course, care should be taken to limit irradiance in order to reduce the risk of adverse effects*."

34. Lucas RM, McMichael AJ, Armstrong BK, Smith WT. Estimating the global disease burden due to ultraviolet radiation exposure. International Journal of Epidemiology 2008;1-14 doi:10.1093/ije/dyn017

Notably, UVR is one of few environmental exposures that may both cause and protect against disease. A study funded by the World Health Organization (WHO) set out to assess the overall disease burden attributable to ultraviolet radiation (UVR) at global and regional levels. The disease burden would be measured in DALYs – disability-adjusted life years consistent with WHO's global burden of disease studies. The burden of disease that might result from reduction of global UVR exposure to very low levels was estimated for the three vitamin D-deficiency bone diseases – rickets, osteomalacia and osteoporosis. The positive role vitamin D could play in reducing cancers, autoimmune diseases, cardiovascular diseases and infectious diseases was not considered due to insufficient evidence. The study reported "*UVR exposure is a minor contributor to the world's disease burden, causing an estimated annual lose of 1.6 million DALYs; i.e. 0.1% of the total global disease burden. A markedly*

larger annual disease burden, 3.3 billion DALYs, might result from reduction in global UVR exposure to very low levels." So if UVR exposure was reduced to very low levels the disease burden due to vitamin D insufficiency would be over 2000 times (1.6m to 3.3b) the current disease burden for UVR diseases such as skin cancers.

35. Mason RS, Reichrath J. Sunlight Vitamin D and Skin Cancer. Anti-Cancer Agents in Medicinal Chemistry, 2013 Jan. 1;13(1):83-97

A study published in Anti-Cancer Agents in Medical Chemistry in 2012 reviewed how much sunlight is appropriate to balance between the positive and negative effects of solar UV-exposure. Statements made in the research paper include:

- **Pale skin increases the risk of all types of skin cancer, while ability to tan lessens the risk, with decreases greatest in risk of squamous cell carcinoma followed by basal cell carcinoma and then melanoma**

- An increasing body of evidence now indicates that the vitamin D endocrine system is of relevance for carcinogenesis and progression of non-melanoma skin cancer and that vitamin D compounds may hold promise as effective agents for the prevention and treatment of these malignancies.

- It has been speculated that the beneficial (protective) effect of less intense solar radiation outweighs its negative (mutagenic) effect. In agreement with this assumption, some authors concluded that many lives could be prolonged through careful exposure to sunlight or possibly more safely, vitamin D supplementation, especially in non-summer months.

- **To summarize, it is important that recommendations of health campaigns on sun protection represent a balanced view of positive and negative effects of solar UV-exposure.**

- The important take home message for dermatologists and other clinicians is that health campaigns promoting strict sun protection procedures to prevent skin cancer may increase the substantial health risk of vitamin D-deficiency.

The study concluded "*If we follow the recommendations discussed above carefully, they will help to ensure an adequate vitamin D-status, thereby protecting us against adverse effects of strict solar UV-protection. Most importantly, these measures will protect us sufficiently against the multiple negative effects of vitamin D-deficiency on health without greatly increasing our risk of developing UV-radiation-induced skin cancer. To reach this goal it is*

important that health campaigns transfer this information to the general population, and to every clinician, especially dermatologists."

36. Van der Rhee H, Coebergh JW, de Vries E. Is prevention of cancer by sun exposure more than just the effect of vitamin D ? A systematic review of epidemiological studies.Eur J Cancer. 2013 Apr;49(6):1422-36. doi: 10.1016/j.ejca.2012.11.001. Epub 2012 Dec 10

In a systematic review, researchers investigated evidence that the possible preventive effect of sunlight on cancer might be mediated not only by vitamin D but also other pathways. They found that for sustained vitamin D production chronic (continuous) sun exposure is probably more effective than intermittent bouts of intense exposure, particularly when it is considered that vitamin D production is self-limiting. The study concluded "*The evidence that chronic (not intermittent) sun exposure decreases the risk of colorectal, breast, prostate cancer and NHL is accumulating and gradually getting stronger. We therefore think that, particularly in countries with a moderate climate, intermittent sun exposure (and sunburn) should on the one hand be discouraged, because of skin cancer prevention, while on the other hand (moderate) chronic exposure possibly should be advised*."

37. Taksler et al., Ultraviolet Index and Racial Differences in Prostate Cancer Incidence and Mortality. Cancer 2013 Sep 1;119(17):3195-203 doi: 10.1002/cncr.28127

A large U.S. study analyzed prostate cancer incidence cases (906,381) and deaths (288,874) by county over a 10 year period. These data were linked with the average monthly solar ultraviolet (UV) radiation index by county. The study reported "Compared with counties in the lowest UV index decile, prostate cancer incidence rates for white and black men were lower in counties with a higher UV index. These results suggest that even moderate doses of sunlight may help to reduce the incidence of prostate cancer, although they should be confirmed by future research."

38. Mohr SB, Garland CF, Gorham ED, Garland FC. The association between ultraviolet B irradiance, vitamin D status and incidence rates of type 1 diabetes in 51 regions worldwide. Diabetologia. 2008 Aug;51(8):1391-8. doi: 10.1007/s00125-008-1061-5. Epub 2008 Jun 12.

A study from the University of California in San Diego analyzed the relationship between ultraviolet B (UVB) irradiance, the primary source of circulating vitamin D in humans, and age-standardised incidence rates of type 1 diabetes mellitus in children, according to region

of the world. The study concluded " Incidence rates of type 1 diabetes approached zero in regions worldwide with high UVB irradiance, adding new support to the concept of a role of vitamin D in reducing the risk of disease."

39. **NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE, DRAFT GUIDELINE - Sunlight exposure: communicating the benefits and risks to the general public**

    http://www.nice.org.uk/guidance/gid-phg77/resources/sunlight-exposure-benefits-and-risks-draft-guideline2
    https://www.nice.org.uk/news/press-and-media/weighing-the-benefits-and-risks-of-sunlight-exposure

The National Institute for Health and Care Excellence (NICE), an independent body responsible for driving improvement and excellence in health in the UK, published a draft guideline on January 20, 2015 – Sunlight exposure: communicating the benefits and risks to the general public. The goal of the document is to give people a better understanding of the various risks and benefits of exposure to sunlight so they know how to modify their behavior. A balance needs to be struck. Risks can be reduced if people never expose their skin long enough for it to redden or burn. Balanced policy can reduce disease from vitamin D deficiency caused by lack of UV exposure. Public health managers were warned that UV policies should "adopt a balanced approach and avoid scaremongering." And that "Skin cancer prevention campaigns should also mention the risk of under-exposure."

40. **Michael F. Holick. Sunlight, Ultraviolet Radiation, Vitamin D and Skin Cancer – How Much Sunlight Do We Need? Chapter 1 – Sunlight, Vitamin D and Skin Cancer, Second Edition, edited by Jorg Reichrath 2014 Landes Bioscience**

Sunlight, Vitamin D and the Skin Cancer Conundrum

Humans evolved in sunlight and their skin pigment gene has evolved in order to protect the skin from the damaging effects from excessive exposure to sunlight, but permitting enough UVB radiation to enter the skin to produce an adequate amount of vitamin D to sustain health. The pigment gene has rapidly mutated to decrease skin pigmentation in order to permit humans to survive in environments where there is markedly reduced UVB irradiation and, thus, vitamin D synthesis.

As skin pigment devolved in order to permit humans to produce an adequate amount of vitamin D, the skin was perfectly designed to take advantage of the beneficial effect of sun exposure while minimizing the damaging effects. A study in people who frequent a tanning bed at least once a week at the end of the winter had robust levels of 25(OH)D of

approximately 100-125 nmol/L which was comparable to people of colour being exposed to sunlight on almost a daily basis living near the equator. Elders exposed to either sunlight, a tanning bed or other UVB emitting devices are able to raise their blood levels of 25(OH)D often above 75 nmol/L.

The fact that most melanomas occur on the least sun exposed areas at least raises the question whether moderate sun exposure is at all related to an increase risk of this deadly disease. It's unfortunate that the sun has been demonized for more than 30 years by those who have been poorly informed or lack knowledge about the beneficial effect of sunlight that our forefathers had appreciated more than 100 years ago. There needs to be moderation in the recommendation regarding sensible sun exposure and increasing the awareness of the vitamin D pandemic.

41. **Bikle DD. The Vitamin D Receptor: A Tumor Suppressor in Skin. Chapter 16 – Sunlight, Vitamin D and Skin Cancer, Second Edition, edited by Jorg Reichrath 2014 Landes Bioscience**

In early 2014 Dr. Bikle released a new paper – The Vitamin D Receptor: A Tumor Suppressor in skin. He reported: "Based on our own data and that reported in the literature we hypothesize that vitamin D signaling in the skin suppresses UVR induced epidermal tumor formation." He proposed three mechanisms: inhibition of proliferation and stimulation of differentiation, immune regulation and stimulation of DNA damage repair (DDR). The study concluded: "Epidemiologic data suggest that there may be a threshold below which UVR is not carcinogenic, a threshold that would suffice for adequate vitamin D production. Conceivably, vitamin D production at such levels of UVB exposure might even be protective. On teleologic grounds one might anticipate that the skin has developed mechanisms to protect itself from the harmful effects of UVR. Vitamin D production, metabolism, and regulation of the processes described in this chapter may play a key role in this protection."

42. **Dixon et al,. Vitamin D and death by Sunshine. Int. J. Mol. Sci. 2013, 14, 1964-1977; doi:10.3390/ijms14011964**

A 2013 study from Australia examined the various signaling pathways involved in the vitamin D-induced protection of skin cells from UV. Past studies have shown that vitamin D receptor knock-out mice show increased susceptibility to photocarcinogenesis. Vitamin D protects skin and reduces DNA damage and skin carcinogenesis through increased p53 which facilitates DNA repair, a reduction in CPDs, a reduction in nitric oxide products, and the inhibiting of UV-induced immunosuppresion. The study concluded "*Taken together, the*

studies reviewed here indicate that the inhibition of UV-induced cell death by vitamin D compounds is indeed a protective effect."

43. Ann R. Webb and Ola Engelsen. Ultraviolet Exposure Scenarios – Risks of Erythema from Recommendations on Cutaneous Vitamin D Synthesis. Chapter 23 – Sunlight, Vitamin D and Skin Cancer, Second Edition, edited by Jorg Reichrath 2014 Landes Bioscience

Exposure to sunlight is a major source of vitamin D for most people yet public health advice focuses overwhelmingly on avoiding exposure of unprotected skin because of the risks of erythema and skin cancer. Existing recommendations to the public are contradictory: one assumes that UV exposure will, for a normal adult, provide necessary vitamin D, while the other advises minimizing exposure to UV. Two sub-erythemal doses gained a week apart are not additive for erythema, while the same two exposures either side of lunch on the same day could produce an erythemal response since there is inadequate time for repair processes to function. "Thus the best way to increase vitamin D status while minimizing the risk of erythema is to expose a large area of skin for a short period of time, rather than a small area of skin for a longer time. The most effective UV exposure regime for acquiring and maintaining a sufficient vitamin D status is "little and often", that is small (sub-erythemal) doses on a regular basis- every day or two."

44. Grober U, Spitz J, Reichrath J, Kisters K, Holick MF. Vitamin D: Update 2013. From rickets prophylaxis to general preventive healthcare. Dermatoendocrinol. 2013 Jun 1;5(3):331-347. Epub 2013 Nov 5

"Sensible sun exposure is the least expensive and most efficient way of obtaining an adequate amount of vitamin D. It has been estimated that a healthy adult in a bathing suit exposed to one minimal erythemal dose (MED) of sunlight is equivalent to ingesting about 20,000 IUs of vitamin D. Thus the skin has a large capacity to produce vitamin D." The study concluded: "Closer attention should be paid to vitamin D deficiency in medical and pharmaceutical practice than has been the case hitherto."

45. http://www.cancer.org.au/preventing-cancer/sun-protection/vitamin-d/

Cancer Council Australia on their website under Vitamin D state "The best source of vitamin D is UV-B radiation from the sun. UV radiation levels vary depending on location, time of year, time of day, cloud coverage and the environment." Further advice included "In winter

in the southern parts of Australia, where UV radiation levels are less intense, people may need about two to three hours of sunlight to the face, arms and hands, or equivalent area of skin, spread over a week to maintain adequate vitamin D levels."

46. **http://www.cancerresearchuk.org/cancer-help/about-cancer/cancer-questions/vitamin-d-sunlight-and-cancer**

Cancer Research UK on their website under 'Vitamin D, sunlight and cancer' recommended the following: "The good news is that you can enjoy the sun safely and not burn while getting enough vitamin D. The amount of time you need to be out in the sun varies depending on - your skin type and colour, the time of day, the time of year, and where you are in the world."

47. **Monlezun DJ, Bittner EA, Christopher KB, Camargo CA, and Quraishi SA. Vitamin D Status and Acute Respiratory Infection: Cross Sectional Results from the United States National Health and Nutrition Examination Survey, 2001-2006. Nutrients 2015, 7, 1933-1944; doi:10.3390/nu7031933**

A study on vitamin D and acute respiratory infection found that participants with the highest ambient ultraviolet B radiation exposure had less than half the risk of having an acute respiratory infection (OR 2.19) .

48. **Gordon-Thompson C, Tongkao-on W, Song EJ, Carter SE, Dixon KM, Mason RS. Protection Frrom Ultraviolet Damage and Photocarcinogenesis by Vitamin D Compounds. Chapter 17 – Sunlight, Vitamin D and Skin Cancer, Second Edition, edited by Jorg Reichrath 2014 Landes Bioscience**

"Skin has a number of adaptive responses to increasing sunlight exposure – these include the development of pigmentation (tan), an increase in the thickness of the epidermal layer, which reduces UV penetration, and an upregulation of DNA repair processes. These adaptive responses protect against future exposures to UV. The vitamin D system in skin reduces DNA damage, inflammation and photocarcinogenesis. Because vitamin D is made in skin, sun damage is less than it would be otherwise."

49. **Egan KM. Vitamin D and Melanoma. Ann Epidemiol. 2009 Jul;19(7):455-61. doi: 10.1016/j.annepidem.2009.01.005. Epub 2009 Mar 17**

"Sufficient levels of vitamin D can be obtained from relatively minimal exposure to sunlight so skin cancer avoidance and vitamin D 'nutrition' from moderate, safe levels of sun exposure need not be at odds."

50. **Gillie, O. The Scots' Paradox: can sun exposure, or lack of it, explain major paradoxes in epidemiology? Anticancer Res. 2012 Jan;32(1):237-48.**

A review study sought to explain the 'Scots' Paradox' and why the mortality of Scots is higher than that of the English across all social classes even though many aspects of culture, environment and health provision are the same through the UVB – vitamin D hypothesis. The study found that Scotland's northern location and climate provide little sunshine and so Scots have low vitamin D levels compared with England. The study recommended: "The importance of open sunny spaces and clean air that allows full penetration of UVB needs to be recognized by city planners and politicians. New advice and new fashions are needed to encourage maximum exposure of skin to summer sun without burning. Use of sunlamps to boost vitamin D synthesis could be useful."

C. Indoor UV exposure and vitamin D3

1. **Johan Moan et all. 2009**

University of Oslo,Department of Radiation Biology, Rikshospitalet - Radiumhospitalet HF, Oslo, Norway

Title: Sun beds as vitamin D sources in Photochemistry and Photobiology

Conclusion: The sun bed sessions raised the vitamin D levels from typical winter values to typical summer values. For the purpose of maintaining a summer level through the winter, when no vitamin D is produced by the sun in Northern countries, one should consider a significant increase of the recommended intake of vitamin D intake, or to encourage the population to get moderate, non erythemal sun bed exposures.

2. **Morten Bogh et all. 2012**

Department of Dermatology, Copenhagen University Hospital, Bispebjerg, Bispebjerg Bakke 23, 2400 Copenhagen, NV, Denmark
DOI: 10.1111/j.1365-2133.2011.10697.x

Title: A small suberythemal ultraviolet B dose every second week is sufficient to maintain summer vitamin D levels: a randomized controlled trial

Conclusion: "Exposure to a UVB dose of 1 SED every second week to ~88% body area is sufficient for maintaining summer 25(OH)D"

3. **Zoya Lagunova et all. 2013**

University of Oslo, Norway
British Journal of Dermatology, June 2013, DOI 10.1111/bjd.12349

Title: Effect of vitamin D supplementation and ultraviolet B exposure on serum 25-hydroxyvitamin D concentrations in healthy volunteers: a randomized, crossover clinical trial

Conclusion: Twice-weekly whole-body sunbed exposure to a dose of 4_8 SED is equal to 2000 IU daily of oral vitamin D supplementation for 30 days and enough to achieve and maintain serum 25(OH)D concentrations > 75 nmol L_1 in ~55% of cases. Based on our calculations, this dose corresponds to a cumulative weekly whole-body exposure of 3_4 SED (~ 40 min around midday during the summer at the latitude of Oslo).

4. **Frank R. de Gruijl ett all, 2012**

Dept. of Dermatology, Leiden Univ. Med. Ctr./LUMC, The Netherlands
Page 1 of 30 Photochemical & Photobiological Sciences, 2012

Title: The effects of a mid-winter 8-weeks course of sub-sunburn sunbed exposures on tanning, vitamin D status and colds

Conclusion: Overall, our study showed sub-sunburn sunbed treatment to be effective in tanning and increasing the 25(OH)D serum level, more so than oral vitamin D supplementation by 1000 IU/d.

5. **Oplander C et al. Whole Body UVA Irradiation Lowers Systemic Blood Pressure by Release of Nitric Oxide From Intracutaneous Photolabile Nitric Oxide Derivates. Circ Res. 2009 Nov 6;105(10):1031-40.**

Conclusions: UVA irradiation of human skin caused a significant drop in blood pressure even at moderate UVA doses. The effects were attributed to UVA induced release of NO from cutaneous photolabile NO derivates.

6. **Mohr SB, Garland CF, Gorham ED, Garland FC. The association between ultraviolet B irradiance, vitamin D status and incidence rates of type 1 diabetes in 51 regions worldwide. Diabetologia. 2008 Aug;51(8):1391-8.**

Conclusions: An association was found between low UVB irradiance and high incidence rates of type 1 childhood diabetes after controlling for per capita health expenditure. Incidence rates of type 1 diabetes approached zero in regions worldwide with high UVB irradiance, adding new support to the concept of a role of vitamin D in reducing the risk of the disease.

7. **Arkema EV, Hart JE, Bertrand KA, Laden F, Grodstein F, Rosner BA, Karlson EW, Costenbader KH. Exposure to ultraviolet-B and risk of developing rheumatoid arthritis among women in the Nurses' Health Study. Ann Rheum Dis. 2013 Apr;72(4):506-11**

1314 incident RA cases were identified in total. Among NHS participants, higher cumulative average UV-B exposure was associated with decreased RA risk; those in the highest versus lowest category had a 21% decreased RA risk (HR (95% CI); 0.79 (0.66 to 0.94)).

8. **Datta P, Bogh MK, Olsen P, Eriksen P, Schmedes AV, Grage MML, Philipsen PA, Wulf HC. Increase in serum 25-hydroxyvitamin-D3 in humans after solare exposure under natural conditions compared to artificial UVB exposure of hands and face. Photochem. Photobiol. Sci., 2012, 11, 1817 doi: 10.1039/c2pp25093d**

"Artificial UVB was thus at least 8 times more efficient in increasing 25(OH)D than solar UVR at a UV-exposed area consisting of approximately hands and face."

9. **Bogh MKB, Schmedes AV, Philipsen PA, Thieden E, and Wulf HC. A small suberythemal ultraviolet B dose every second week is sufficient to maintain summer vitamin D levels: a randomized controlled trial. Br J Dermatol. 2012 Feb;166(2):430-3. doi: 10.1111/j.1365-2133.2011.10697.x.**

An RCT study was completed in Denmark to define the frequency of UVB exposure necessary for maintaining summer vitamin D levels during the winter. The study had 4 groups, and were randomized to receive 1 standard erythema dose (SED) to ~88% of the body area, of

UVB exposure, either, once a week, every second week, every fourth week, or not at all. The study found that those receiving exposure once a week had their vitamin D level go up slightly, once every 2 weeks maintained vitamin D levels, those exposed once evry 4 weeks had their vitamin D levels go down and the control group vitamin D levels dropped the most. The study concluded: "Exposure to a UVB dose of 1 SED every second week to ~88% body area is sufficient for maintaining summer 25(OH)D levels during the winter."

10. **Gruijl FR, Pavel S. The effects of a mid-winter 8-week course of sub-sunburn sunbed exposures on tanning, vitamin D status and colds. Photochem Photobiol Sci. 2012 Dec;11(12):1848-54. doi: 10.1039/c2pp25179e**

A European study investigating the effects of sunbed sessions and vitamin D supplements on colds found that three non-burning sunbed sessions weekly was more effective at raising vitamin D blood levels than 1,000 IU of daily vitamin D supplement. The study involved 105 young adults (18-30 years old) most of whom were female. The sunbed users rose from an insufficient level of 62 nmol/L to 109 nmol/L. The group taking 1000 IU of vitamin D supplement had levels 15% less than the sunbed users at 93 nmol/L. The control group dropped 7 nmol/L to 55 nmol/L over the course of the study in the winter. The study concluded "*The sub-sunburn sunbed treatment was effective in tanning and increasing the 25(OH)D serum level,...*"

11. **Fears et al,. Sunbeds and sunlamps: who used them and their risk for melanoma. Pigment Cell Melanoma 2011 Jun;24(3):574-81. doi: 10.1111/j.1755-148X.2011.00842.x. Epub 2011 Mar 29**

A recent study in the US reports that sunbed use actually lowers the melanoma risk. A large case-control study conducted in the US and completed in 2011 looked at sunbeds and sunlamps and their risk of melanoma. They found for females, use before age 20 yr, current use and years of use were not significant after adjustments. The estimated relative odds of melanoma was 0.8 for occasional users (<10 sessions) and 1.1 for more frequent users (10+ sessions). For males, the melanoma risk from sunbeds was 0.90 with no significant difference between occasional and frequent users.

12. **Canadian Health Measures Survey, 2012 to 2013**
    http://www.statcan.gc.ca/pub/82-625-x/2014001/article/14125-eng.htm

The Government of Canada, Statistics Canada, released the latest report on vitamin D levels for Canadians from 2012 to 2013. It reported that 35% of Canadians do not meet the 25(OH)D level recommended by Health Canada of 50 nmol/L. In fact the rate of deficiency is increasing quickly and increased by 9% from the last report and now adversely affects the health of 12.25M Canadians. Those who reported recent sun exposure were more likely to have sufficient vitamin D levels. The study when recommending vitamin D sources reported: "Exposure to sunlight and to artificial ultraviolet B radiation (tanning beds) is another source of vitamin D."

13. **Cicarma E, Porojnicu AC, Lagunova Z, Dahlback A, Juzeniene A, Moan J. Sun and Sun Beds: Inducers of Vitamin D and Skin Cancer. Anticancer Research 29:3495-3500 (2009)**

"Sun and sunbeds act similarly: one quantum of radiation at a given wavelength has the same biological effect, irrespective of the source from which it comes." "Populations living at high latitudes would probably benefit from moderately increasing their exposure to UVB to provide a good vitamin D status."

"The UVB component of the radiation emitted by tanning beds used for artificial tanning induces vitamin D synthesis in the skin, and actually increases serum levels of 25(OH)D and it has been suggested that exposure to tanning bed could compensate a vitamin D insufficiency."

14. **Jean-Francois Dore and Marie-Christine Chignol. Vitamin D and Cancer. OCL 2014, 21(3) D306. DOI: 10.1051/ocl/2013058**

15. **Schwalfenberg et al,. Addressing vitamin D deficiency in Canada: A public health innovation whose time has come. Public Health (2010), doi:10.1016/j.puhe.2010.03.003**

A study in Alberta found that regular indoor tanners had the highest vitamin D levels compared to supplement users and people who got lots of sun exposure.

16. **Wallingford et al,. UV and dietary predictors of serum 25-hydroxyvitamin D concentrations among young shift-working nurses and implications for bone density and skin cancer. Public Health Nutr. 2014 Apr;17(4):772-9. doi: 10.1017/S1368980013001754. Epub 2013 Jul 9**

Sunbeds are a great source of Vitamin D. In a Court Affidavit, Dr. Reinhold Vieth, Mount Sinai Hospital, Toronto, foremost researcher on Vitamin D in Canada stated the following:

". . . sunbeds and summer sunshine are effective means by which to increase our serum 25(OH)D levels. The advantage of a tanning bed is that exposure to UV light can be controlled more precisely than casual sun exposure and thus can be safer than advising the public to guess at their own sun exposure from sunlight,"

A study of young, shift-working, female nurses in Kingston, Ontario found that 30% of study participants used a tanning bed. This was double the national average of 15% from the 2006 National Sun Survey. The study found that tanning bed use was the strongest modifiable predictor that was identified to increase serum 25(OH)D concentration. In fact tanning bed use increased serum 25(OH)D by 23-24 nmol/L on average. The study concluded: "As health promotion campaigns and legal restrictions are successful in reducing tanning bed use among women, our data suggests that increased prevalence of vitamin D inadequacy and deficiency may be a consequence, and that low vitamin D status will need to be countered with supplementation."

17. **Jenab et al,. Association between pre-diagnostic circulating vitamin D concentration and risk of colorectal cancer in European populations: a nested case-control study. BMJ 2010;340:b5500**

The study was conducted within the EPIC study, a cohort of more than 520 000 participants from 10 western European countries. In analyses by quintile of 25-(OH)D concentration, patients in the highest quintile had a 40% lower risk of colorectal cancer than did those in the lowest quintile ($P<0.001$).

D. UV exposure and melanoma

1. **Phillipe Autier et all, 2015**

WHO-IARC-IPRI
Eur J Cancer. 2015 Mar 12. pii: S0959-8049(15)00100-8.

Title: The forthcoming inexorable decline of cutaneous melanoma mortality in light-skinned populations.

Result: Cohort effects better explained changes in melanoma mortality over time than period effects. Lifetime risk to die from melanoma increased in successive generations from 1875 until a peak year. Peak years were for subjects born in 1936-1940 in Oceania, 1937-1943 in North America, 1941-1942 in Northern Europe, 1945-1953 in the United Kingdom (UK) and Ireland, 1948 in Western Europe and 1957 in Central Europe. After peak years, lifetime risk of melanoma death gradually decreased in successive generations and risks of subjects born in 1990-1995 were back to risk levels observed for subjects born before 1900-1905. In Southern Europe, birth years with highest lifetime risk of melanoma death have not yet been attained. As time passes, melanoma deaths will steadily rarefy in younger age groups and concentrate in older age groups, for ultimately fade away after 2040-2050.

Conclusion: Independently from screening or treatment, over next decades, death from melanoma is likely to become an increasingly rare event. The temporary epidemic of fatal melanoma was most probably due to excessive UV-exposure of children that prevailed in 1900-1960, and mortality decreases would be due to progressive reductions in UV-exposure of children over the last decades.

2. **Relationship between Sunbed Use and Melanoma Risk in a Large Case-Control Study in the United Kingdom, Faye Elliott, Mariano Suppa, May Chan, Susan Leake, Birute Karpavicius, Sue Haynes, Jennifer H Barrett, D Timothy Bishop and Julia A Newton-Bishop**

In summary, we have found no evidence for sunbed use as a risk factor for melanoma in the UK; although we cannot exclude a small effect of ever sunbed use, nor risk associated with use early in life, we can exclude a large effect.

3. **2005 A multicentre epidemiological study on sunbed use and cutaneous melanoma in Europe Véronique Bataille a,b,*, Mathieu Boniol c, Esther De Vries d, Gianluca Severi e,f, Yvonne Brandberg g, Peter Sasieni a, Jack Cuzick a, Alexander Eggermont h, Ulrik Ringborg g, Andre´-Robert Grivegne´e i, Jan Willem Coebergh d,j, Marie Christine Chignol c, Jean-Franc¸ois Dore´ c, Philippe Autier e,i**

In conclusion, sunbed and sun exposure were not found to be significant risk factors for melanoma in this case–control study performed in five European countries.

4. **2013 Sun Exposure, Sunbeds and Sunscreens and Melanoma. What Are the Controversies? Veronique Bataille**

As UV exposure is the only environmental factor ever linked to melanoma, it is still prudent to avoid excessive sun exposure and sunburn especially in poor tanners. However, the impact of strict sun avoidance, which should not be recommended, may take years to be apparent as vitamin D deficiency is a now a common health issue in Caucasian populations, with a significant impact on health in general.

Conclusion: Lighter skin pigmentation with increasing latitude has been an adaptive process in evolution to maximize vitamin D production with migration to more temperate climates, and this highlights the risk of altering this adaptive response too rapidly [72]. There is an urgent need to assess the long-term impacts of recommending strict sun avoidance and widespread use of sunscreens in Caucasian populations.

5. **Papas – Differential risk of malignant melanoma by sunbed exposure type (2011) Abstract and poster presented at the 3rd North American Congress of Epidemiology in Montreal June 21-24, 2011**

The cited increased risk for people under 35 from professional, commercial sunbathing equipment is only 6% and this included exposure to a Skin Type 1 person

6. **Grant, Critique of the International Agency for Research on Cancers meta-analyses of the association of sunbed use with risk of cutaneous malignant melanoma. Dermato-Endocrinology 1:6, 1-7; November/December 2009ndoor tanning facilities and melanoma exists"**

"Removing skin type 1, those who are genetically predisposed to cutaneous malignant melanoma (CMM), showed no statistically significant link between ever use of indoor tanning facilities and melanoma exists"

7. **Moan J, Baturaite Z, Juzeniene A, Porojnicu AC. Vitamin D, sun, sunbeds and health. Public Health Nutr. 2012 Apr;15(4):711-5. doi: 10.1017/S1368980011002801. Epub 2011 Oct 24**

In a 2012 review of sunbeds, vitamin D and health, researchers determined that tanning bed use would decrease 10 times as many cancers than they might contribute to. They reported "*Due to the fear of skin cancer, health authorities warn against sun and sunbed exposure. This policy, as well as the recommended vitamin D doses, may need revision.*" They elaborated further "*Tanning is thought to protect DNA and reduce carcinogenesis as indicated by the low skin cancer risk of dark-skinned people. 10 min of exposure to sunbeds, twice weekly, give similar vitamin D levels as a daily intake of 2000 IU of vitamin D and can bring a winter level of vitamin D up to a summer level (70-90 nmol/L), which may be optimal.*" Other points made; occupational exposure (farmers, fisherman) and regular weekend sun exposure are associated with decreased risk of CMM. UV exposure earlier in life is related to reduced overall and breast cancer. The study concluded "*The overall health benefit of an improved vitamin D status may be more important than the possibly increased CMM risk resulting from carefully increasing UV exposure.*"

8. **Iannacone et al., Patterns and timing of sunlight exposure and risk of basal cell and squamous cell carcinomas of the skin – a case-control study. BMC Cancer 2012, 12:417 doi:10.1186/1471-2407-12-417**

A study just released examined the relationship between sunlight exposure and risk of NMSC. Researchers found that lifetime tanning bed use, >10 times, provided a 36% reduced risk of BCC (OR 0.64). The study concluded "*A history of blistering sunburn (a measure of intermittent sunlight exposure) was associated with both BCC (OR = 1.96) and SCC (OR = 2.02).*

9. **Surdu et al,. Occupational Exposure to Ultraviolet Radiation and Risk of Non-Melanoma Skin Cancer in a Multinational European Study. PLOS ONE April 2013, Volume 8, Issue 4 e62359**

This study investigated the relationship between exposure to occupational UV radiation and NMSC in a large multicenter case-control study conducted in Central and Eastern Europe. Significantly lower adjusted odds ratios of NMSC were observed for ever exposure to occupational natural UV radiation compared to never exposure OR 0.47 (53% reduced risk) and for lifetime cumulative exposure in the lower tertile OR 0.34 (66% reduced risk) compared to the never exposed group. Conclusion "The study results do not provide support

for an increased risk of NMSC in association with workplace exposure to natural or artificial UV radiation. These results add to the evidence that moderate sunlight exposure might decrease the risk of some types of cancer, likely in association with sun-protection behaviors."

10. **Lewis and Weinstock. Trends in Nonmelanoma Skin Cancer Mortality Rates in the United States, 1969 through 2000. Journal of Investigative Dermatology (2007) 127, 2323-2327**

A study published in 2007 looked at non-melanoma skin cancer mortality rates in the United States from 1969 to 2000. It found that 40% of deaths were due to NMSC arising on genital skin. The study concluded *"These data suggest that greater emphasis could be placed on the risk of mortality from genital skin cancer".* It went on to say "*The magnitude of the public health burden is great; nevertheless, efforts on the part of the dermatology community to prevent human papilloma virus infection in the United States have been slight compared to similar effort to reduce excess exposure to UV light."*

11. **http://www.who.int/uv/faq/uvhealtfac/en/index2.html**

The World Health Organization (WHO) has acknowledged that indoor workers — who get 3-9 times less UV exposure than their outdoor counterparts – get more melanomas.

The World Health Organization's web site in a statement on melanoma it states "*Tumour development may be linked to occasional exposure to short periods of intense sunlight, such as at weekends or on holiday. The higher incidence of malignant melanoma in indoor workers compared to outdoor workers support that notion."*

12. **Jorg Reichrath and Sandra Reichrath. Sunlight, Vitamin D and Malignant Melanoma Chapter 22 – Sunlight, Vitamin D and Skin Cancer, Second Edition, edited by Jorg Reichrath 2014 Landes Bioscience**

Solar radiation represents an essential requirement for life and facilitates the cutaneous synthesis of vitamin D in vertebrates and many other organisms. It exerts multiple positive and negative effects on life on earth and on human health. It has to be concluded that melanoma risk is strongly genetically determined (Pale skin, number of nevi), and the most important environmental risk factor for melanoma is intermittent high-dose solar UV exposure. "It has to be emphasized that, in contrast to intermittent, short-term high-dose solar UV-exposure, more chronic less intense exposure (which is recommended by many

experts in the field to obtain a sufficient vitamin D status) has not been found to be a risk factor for the development of melanoma and in fact has been found in several studies to be protective."

13. **Vuong et al., Occupational sun exposure and risk of melanoma according to anatomical site. Int J Cancer 2013 Nov 13. Doi: 10.1002/ijc.28603**

"Although sunburn and intermittent sun exposures are associated with increased melanoma risk, most studies have found null or inverse associations between occupational (more continuous pattern) sun exposure and melanoma risk." This

Australian study from 2013 examined the association between occupational sun exposure and melanoma risk according to anatomical site. They combined data from two existing studies. The study found that occupational sun exposure was not positively associated with melanoma risk overall or at different body sites in both studies. For the highest vs lowest sun exposure they reported a 44% reduced risk of melanoma. They accounted for the reduction in melanoma risk due to the melanin role as an antioxidant in absorbing ultraviolet radiation and scavenges free radicals. In addition, more continuous sun exposure increases melanin production and epidermal thickness and thus may confer protection against melanoma through photoadaptation. The researchers concluded: "Our results suggest that occupational sun exposure does not increase risk of melanoma, even of melanoma situated on the head and neck."

14. **Levell NJ, Beattie CC, Shuster S, Greenberg DC. Melanoma epidemic: a midsummer night's dream? British Journal of Dermatology 2009 161, pp630-634 DOI 10.1111/j.1365-2133.2009.09299.x**

There is a widespread belief that excessive ultraviolet (UV) exposure has led to an increased incidence of melanoma, and this has been passed on to the public in an alarmist way. A study analyzed histological diagnosis, mortality and incidence of melanoma in East Anglia, UK between 1991 and 2004. Melanoma incidence increased from 9.39 cases per 100,000 to 13.91 (48%). Stage 1 melanoma accounted for the total increase in melanoma incidence. Survival with stage 1 melanoma was effectively 100% and remained at that level throughout the period. The increase in stage 1 lesions came from less UV exposed skin sites not predominantly that of solar exposure. The study reported "This increase was due to changes in the incidence of stage 1 disease, the combined incidence of more advanced stages being unchanged, and despite this appreciable increase, there was only a slight increase in disease mortality, the ratio of the increase in incidence and mortality being 11.9 : 1."

"Dermatologists, pathologists and other medical practitioners have become more cautious in the last two decades, as the consequences of a wrong diagnosis have become more pervasive. Lesions previously diagnosed as simple, or dysplastic naevi, were considered benign, because they were observed not to progress if left (as they were in the past, when pigmented lesion removal was less enthusiastically pursued than now), are now being diagnosed as stage 1 melanoma. It is not surprising, therefore, that the incidence of 'melanoma' has increased, but not its mortality."

"It would be even more remarkable for an epidemic of a cancer known for its variability, to present only with the most minimal form of the disease, without any of the more serious forms, which regularly occur at the first presentation of the disease, as our findings of outcome in the first years of presentation have confirmed. Thus, we deduce that encouragement of patients to present early for treatment does not explain our findings. We must conclude that the present findings make it extremely unlikely that the reported large increase in the incidence of melanoma is real. These findings inevitably challenge the validity of epidemiology studies linking increasing melanoma incidence with UV radiation, and suggest the need for a search for other ways in which the disease may be caused."

15. **van Schanke A, Jongsma MJ, Bisschop R, van Venrooij GMCA, Rebel H, and de Gruijl FR. Single UVB overexposure stimulates melanocyte proliferation in murine skin, in contrast to fractionated or UVA-1 exposure. J Invest Dermatol. 2005 Jan;124(1):241-7.**

Melanocytes (like nerve cells) are unusual in that they are normally indolent (which means they do not commonly undergo cell division); it takes a trauma such as a sunburn to trigger proliferation; even if the DNA is damaged by UV, there is no chance of melanoma if the cells containing the defective DNA do not subdivide and produce daughter cells. This was confirmed in a study published in the Journal of Investigative Dermatology which found that melanocytes proliferate in response to erythemagenic (producing erythema or sun burn) UVB radiation. The study stated "These results show that an erythemagenic dose is required to effectively induce melanocyte proliferation in hairless mice." The study concluded "Hence, melanocyte proliferation appears to be most efficiently induced by a single UVB overexposure."

16. **World Health Organization (WHO) – Ultraviolet radiation and human health. Fact sheet No. 305, December 2009**

The WHO in its "Ultraviolet radiation and human health – Fact Sheet No. 305, December 2009" reported – *"Between 50% and 90% of skin cancers are due to UV radiation",* indicating the high degree of uncertainty which exists around the interrelationship between UV radiation and skin cancer. Research indicates that it's the type of exposure that is the risk; intermittent and sun burning exposure.

17. **Skin Cancer Foundation. The Melanoma Letter Summer 2010 Volume 28 No. 2 – Carcinogenic to Humans: Why the International Agency for Research on Cancer Added Indoor Ultraviolet (UV) Tanning to Group I by Philippe Autier**

According to the Skin Cancer Foundation and Dr. Phillipe Autier, melanoma is caused mainly by intense, occasional UV exposure that most frequently leads to sunburn. Dr Autier states "Systematic reviews of epidemiological studies provide strong evidence that intermittent, intense sun exposure – the type of exposure often sustained on weekends or sunny vacations, leading to sunburn – is the main environmental risk factor for melanoma" Tanning equipment if used properly in the manner it was designed to be used does not burn people. The UV dose is controlled for the clients skin type and current tanned condition of their skin.

http://www.skincancer.org/publications/the-melanoma-letter/summer-2010-vol-28-no-2/carcinogenic-to-humans-why-the-international-agency-for-research-on-cancer-added-indoor-ultraviolet-uv-tanning-to-group-i

18. **Bataille V. Melanoma. Shall we move away from the sun and focus more on embryogenesis, body weight and longevity? Medical Hypotheses 81 (2013) 846-850**

A new study by Dr. Veronique Bataille has further cast doubt on sun and UV as the primary cause of melanoma. Here is a brief summary:

There are many observations regarding the behavior of melanoma, which points away from sunshine as the main cause of this tumor. The avoidance of sun exposure has not been proven to reduce melanoma incidence and mortality and may be harmful. The incidence of melanoma has risen dramatically in all countries where access to dermatologists is relatively easy and public health campaigns have been quite active. However, mortality has remained relatively stable. These screening campaigns have led to a rapid rise in the number of very thin and borderline melanomas, which in turn inflates overall incidence.

Gender – Melanomas in males tend to occur more commonly on the trunk whilst melanomas in females are mostly seen on the legs. This observation is again somehow attributed to differences in sun exposure habits between males and females but the data does not support this as the difference in body sites according to gender is constant across all Caucasian populations irrespective of sun exposure. This difference is most likely to be explained by differences in melanocyte differentiation between males and females. Boys and girls already differ in their naevus distribution with more naevi on the limbs especially arms and legs in girls and more naevi on the trunk in boys which reflects the distribution of melanoma in adults. Males also show consistently higher number of naevi than females and this is also seen in different parts of the world irrespective of sun exposure.

Naevi – The number and types of naevi is the strongest risk factor for melanoma in all Caucasian populations and the magnitude of the odds ratios (5-20) is much greater than any odds ratios ever reported for sun exposure and skin color (1.5-2). Naevi confer the same magnitude of risk for melanoma at all altitudes showing again that sunlight is not that important for this association. BRAF somatic mutations are also very common in naevi and melanoma. BRAF mutated melanomas are more common on the trunk and limbs compared to the head and neck.

Photoageing – As sunshine is thought to be the main cause of melanoma one would expect that the deleterious effects of UV light would be visible with significant photo ageing in melanoma patients. In fact, it is often the reverse as melanoma patients often have less photo ageing with a lower prevalence of solar keratosis and solar lentigines compared to subjects susceptible to squamous cell and basal cell carcinomas.

Skin Pigmentation – The risk associated with sunburns and fair skin is small with risk factors in the order of 1.5-2 compared to relative risks of 5-30 for multiple atypical naevi. Once adjusted for skin type, many sun exposure measures do no longer confer a risk for melanoma so it is not a fixed amount of sun exposure that matters but the host response.

The arguments used to support sunshine as the main cause of melanoma do not always stack up. Genome sequencing of melanoma tumors have shown that the number of all types of genetic alterations exceed 70,000 and that many of the point mutations are C-T pyrimidine dimmers, which in principle supports sun exposure in melanoma. C-T mutations are, however, also found in genome sequencing of other tumors which have no link to sun exposure.

It should be recognized that drastically reducing sun exposure in Caucasians may have deleterious effects which may take many years to unravel and has not been successful in reducing melanoma incidence. Vitamin D is linked to so many melanoma risk factors and

appears to be protective for melanoma so more research is needed especially as vitamin D deficiency is now becoming very prevalent an all Caucasian populations.

19. **Olsen CM, Carroll HJ, Whiteman DC. Estimating the attributable fraction for cancer: A meta-analysis of nevi and melanoma. Cancer Prev Res (Phila). 2010 Feb;3(2):233-45. doi: 10.1158/1940-6207.CAPR-09-0108. Epub 2010 Jan 19.**

Epidemiologic research has shown convincingly that certain phenotypic attributes are associated with increased relative risks of melanoma. This Australian study quantified the risk of common nevi and melanoma. They reported: "We estimated that 42% of melanomas were attributable to having > or = 25 common nevi. The highest melanoma burden was always among those with high nevus counts. Patients with > or = 25 common nevi and/or > or = 1 atypical nevi are a high risk group, which might be targeted for identification, screening, and education."

20. **http://www.skincancer.org/prevention/sunburn/facts-about-sunburn-and-skin-cancer**

On the webpage of skincancer.org, Facts about Sunburn and Skin Cancer, stated: "The sun exposure pattern believed to result in melanoma is that of brief, intense exposure – a blistering sunburn – rather than years of tanning. (Some studies now indicate that basal cell carcinoma also may be triggered by this exposure pattern.) Other risk factors are also associated with melanoma, such as a family history, skin type and having a large number of sizeable moles on the body. Like non-melanoma skin cancer, melanoma can arise on any area of the body, regardless of whether or not sunburn occurred in that location. The lesson? Simple: do not burn"

21. **Mason et al,. Photoprotection by 1,25-dihydroxyvitamin D and analogs: Further studies on mechanisms and implications for UV-damage. Journal of Steroid Biochemistry & Molecular Biology 121 (2010) 164-168**

A tan protects against UV-induced DNA damage in 3 ways. Increased pigmentation and cornification (skin thickening) guard against UV skin penetration. In addition, increased concentrations of vitamin D compound in skin resulting from UV exposure act to protect against DNA damage through the reduction of nitric oxide products and increase p53 expression, which facilitates DNA repair.

22. **Gandini S, et al., Meta-analysis of risk factors for cutaneous melanoma: I. Common and atypical naevi doi:10.1016/j.ejca.2004.10.015**

Gandini S, et al., Meta-analysis of risk factors for cutaneous melanoma: II. Sun exposure doi:10.1016/j.ejca.2004.10.016

Gandini S, et al., Meta-analysis of risk factors for cutaneous melanoma: III. Family history, actinic damage and phenotypic factors doi:10.1016/j.ejca.2005.03.034

Melanoma is a very complicated disease. A true meta-analysis of melanoma risks was completed by Dr. Sara Gandini in 2005. Her team reviewed over 60 studies and summarized the data. They found the following risk factors for melanoma: large number of moles +589%, freckles +110%, red hair +264%, Skin Type 1 +109%, Family history +74%, sunburns +103%, and intermittent UV exposure +61%. The study found that "Chronic" (defined as regular, continuous) sun exposure REDUCED the risk of melanoma by 5%. This is consistent with scientific studies of outdoor workers which show a higher, continuous, regular UV exposure results in a lower melanoma rate than indoor workers who get less UV.

23. **Gandini S, et al., Meta-analysis of risk factors for cutaneous melanoma: II. Sun exposure doi:10.1016/j.ejca.2004.10.016**

If you look at the Gandini study and look at four population-based case-control studies of a "well conducted" design which stated that controls with dermatological diseases had been excluded the results for chronic UV exposure were even better and statistically significant with a 36% reduced risk of melanoma (RR = 0.64, 95% CI: 0.51, 0.81)

24. **Herzfeld PM, Fitzgerald EF, Hwang SA, et al. A case-control study of malignant melanoma of the trunk among white males in upstate New York. Cancer Detect Prev 1993, 17, 601–608.**

25. **Holly EA, Aston DA, Cress RD, et al. Cutaneous melanoma in women. I. Exposure to sunlight, ability to tan, and other risk factors related to ultraviolet light. Am J Epidemiol 1995, 141, 923–933.**

26. **Holman CD, Armstrong BK, Heenan PJ. Relationship of cutaneous malignant melanoma to individual sunlight-exposure habits. J Natl Cancer Inst 1986, 76, 403–414.**

27. **White E, Kirkpatrick CS, Lee JA. Case-control study of malignant melanoma in Washington State. I. Constitutional factors and sun exposure. Am J Epidemiol 1994, 139, 857–868.**

28. **Dr. A. Bernard Ackerman MD, book – The Sun and the Epidemic of Melanoma: Myth on Myth published in 2008, Second Edition, page 154**

"Factors genetic, alone, unrelated entirely to sunlight, could be solely responsible for melanoma."

Dr. A. Bernard Ackerman MD, recognized by the American Academy of Dermatology in 2004 as Master Dermatologist, wrote a book entitled – The Sun and the Epidemic of Melanoma: Myth on Myth, published in 2008. When reviewing the evidence on the role genetics plays in melanoma, Ackerman stated that *"in my opinion, those who spawn one or more melanomas have a disposition genetic to that malignant neoplasm and without it no amount of sunlight and no length of time of exposure to it is sufficient to galvanize proliferation of the abnormal melanocytes constituent of it*". He went on to say *"the majority of melanomas in Caucasians occur in skin that is free of solar elastosis, that is a sign of unquestionable damage by virtue of exposure excessive and for very long to sunlight"*.

29. **Ang KC, et al. Skin Color Variation in Orang Asli Tribes of Peninsular Malaysia. PLoS One. 2012;7(8):e42752. doi: 10.1371/journal.pone.0042752. Epub 2012 Aug 13.**

Why do Europeans have a higher rate of melanoma than East Asians? Both lighter skins can tan. Convergent human evolution from the ancestral state, darker skin, towards lighter skin colors involved divergent genetic mechanisms in people of European vs east Asian ancestry. It is striking that the European mechanisms result in a 10-20-fold increase in skin cancer susceptibility while East Asian mechanisms do not. A research team studied ancient tribes in Malaysia to map genes that contribute to pigmentation. They found "the lighter skin colors of East Asian population are associated with almost no increase in melanoma; their incidences are comparable with those of Africans. A molecular understanding of this disparity can only be gained after the alleles involved in skin lightening for both groups are identified."

30. **Demenais et al,. Association of MC1R Variants and Host Phenotypes With Melanoma Risk in CDKN2A mutation Carriers: A GenoMEL Study. J Natl Cancer Inst 2010;102:1-16**

MC1R Variants – partial loss of function mutation are associated not only with red hair, fair skin, and poor tanning, but also with increased skin cancer risk independent of cutaneous pigmentation. A study by Demenais found that carrying any one of the four most frequent MC1R variants was associated with an increased risk of melanoma. One variant increased the risk twofold, but having two or more variants increased melanoma risk nearly six fold.

31. **David C. Whiteman, Adele C Green. Correspondence Re: A prospective Study of Pigmentation, Sun Exposure, and Risk of Cutaneous Malignant Melanoma in Women. Journal of the National Cancer Institute, Vol. 96, No. 4, February 18, 2004**

In a correspondence to the Journal of the National Cancer Institute in 2004 these notable Australian authors reinforced the importance of individual susceptibility for melanoma: "Although the importance of UV exposure in the development of melanoma is well documented, the majority of Australians never develop melanoma despite considerable (and, in many cases, extraordinary) exposure to intense UV radiation, which underscores the importance of individual susceptibility."

32. **Shipman et al. Sunnier European countries have lower melanoma mortality. Clinical and Experimental Dermatology doi:10.1111/j. 1365-2230.2011.04024.x**

Doubt has been cast on sunlight as the major causative factor for malignant melanoma. A study by Shipman in 2010 found that sunnier European countries have lower melanoma mortality. *"It is possible that the major factor affecting MM mortality is therefore the difference in skin colour between northern and southern Europe." "In conclusion, this study supports the notion that research in MM epidemiology should focus on identifying genetic, phenotypic and other environmental triggers for fatal MM."*

33. **Krauthammer et al,. Exome sequencing identifies recurrent somatic RAC1 mutations in melanoma. Nat Genet. 2012 September ; 44(9): 1006-1014. doi:10.1038/ng.2359**

A study analyzing somatic mutations in 147 melanomas did not detect UV damage signature mutations in acral, mucosal or ocular melanomas. In addition, BRAF mutations which are found in ~50% of cutaneous melanomas also were not UV induced and does not have the UV signature.

34. **Landi et al,. MC1R Germline Variants Confer Risk for BRAF-Mutant Melanoma. Science Vol 313 28 July 2006**

"We found that BRAF mutations were 6 to 13 times as frequent in those with at least one MC1R variant compared to those with no MC1R variants. The odds ratio increased from 7.2 for individuals with one MC1R variant to 17.0 for those with multiple variants compared to individuals with no MC1R variants. Moreover most BRAF mutations do not show the standard C > T signature of direct UVR induction."

35. **Cui et al., Central role of p53 in the suntan response and pathologic hyperpigmentation. Cell 128, 853-864, March 9, 2007**

We're also discovering that skin tanning has a function in preventing the development of skin cancer. Researchers found that the protein p53, which plays a role in causing the skin to tan after sun exposure, also reduces the risk of melanoma. The ability to tan seems to be a protective factor against skin cancer. *"The number one risk factor for melanoma is an inability to tan,"* said Dr. David E. Fisher, director of the Melanoma Program at Dana-Farber. The study showed that p53, which is a tumor-suppressor protein in the skin, *"has a powerful role in protecting us against sun damage in the skin"* according to Fisher."

36. **Mitra et al,. An ultraviolet-radiation-independent pathway to melanoma carcinogenesis in the red hair/fair skin background. Doi:10.1038/nature11624**

A study published in the peer-reviewed journal Nature in 2012 found that people with pale skin, red hair, freckles and an inability to tan – the red hair/fair skin phenotype (MC1R variant) – are at the highest risk of developing melanoma, compared to all other pigmentation types. Minimal receptor activity, as in red hair/fair skin polymorphisms, produces the red/yellow pheomelanin pigment, whereas increasing MC1R activity stimulates the production of black/brown eumelanin. Pheomelanin has weak shielding capacity against ultraviolet radiation relative to eumelanin, and has been shown to amplify ultraviolet-A-

induced reactive oxygen species. Unlike non-melanoma skin cancers, melanoma is not restricted to sun-exposed skin and ultraviolet radiation signature mutations are infrequently oncogenic drivers. Ultraviolet-radiation-independent events are likely to have a significant role.

The study introduced a conditional, melanocyte-targeted allele of the most common melanoma on coprotein, BRAF V600E, into mice carrying an inactivating mutation in the MC1R gene. They observed a high incidence of invasive melanomas without providing additional gene aberrations or ultraviolet radiation exposure. Selective absence of pheomelanin synthesis was protective against melanoma development. The study concluded "*These data suggest that the pheomelanin pigment pathway produces ultraviolet-radiation-independent carcinogenic contributions to melanomagenesis by a mechanism of oxidative damage.*" This explains why red hair/fair skin (Skin Type 1) people have a higher risk of melanoma. They don't have the type of melanin to protect a person from overexposure.

37. **Morgan AM, Lo J, and Fisher DE. How does pheomelanin synthesis contribute to melanomagenesis? Bioessays. 2013 Aug;35(8):672-6. doi: 10.1002/bies.201300020. Epub 2013 May 7.**

Recent studies suggest that the very pigment that gives red hair its fiery color may be carcinogenic itself, independent of UV radiation. This new study discusses two distinct mechanisms that could explain the carcinogenicity of pheomelanin synthesis. On the one hand, pheomelanin might generate reactive oxygen species (ROS) that lead indirectly to DNA damage. On the other hand, pheomelanin synthesis might tax melanocytes' antioxidant capacities by consuming glutathione stores. The study concluded "Uncovering the mechanistic pathway between pheomelanin and oxidative DNA damage will be an important step in developing strategies to lower melanoma risk in redheads."

38. **Hacker et al,. NRAS and BRAF Mutations in Cutaneous Melanoma and the Association with MC1R Genotype: Findings from Spanish and Austrian Populations. J Invest Dermatol. 2013 Apr;133(4):1027-33. doi: 10.1038/jid.2012.385. Epub 2012 Oct 25**

"MC1R variants are associated with increased risk of melanoma and nonmelanoma skin Cancer. Persons carrying MC1R variants produce more red/yellow pheomelanin than brown/black eumelanin. Pheomelanin is more likely than eumelanin to generate potentially damaging reactive oxygen species following UVR exposure. In tissue culture experiments melanocytes harboring MC1R variants have less effective repair of both UVR-induced pyrimidine dimers and oxidative damage than wild-type melanocytes, and are more sensitive to UVR-induced cell death. The level of UVR exposure sufficient to induce DNA damage to

melanocytes harboring MC1R variants and drive subsequent melanoma formation is unknown."

39. **Marzuka-Alcala A, Gabree MJ, Tsao H. Melanoma susceptibility genes and risk assessment. Methods Mol Biol. 2014;1102:381-93. doi: 10.1007/978-1-62703-727-3_20.**

"MC1R variants were traditionally thought to increase risk for melanoma secondary to intensified UV-mediated DNA damage in the setting of absent photoprotective eumelanin. Accumulation of pheomelanin, which appears to have a carcinogenic effect regardless of UV exposure, may be a more likely mechanism."

40. **Zanetti et al,. Comparison of risk patterns in carcinoma and melanoma of the skin in men: a multi-centre case-case-control study. British Journal of Cancer (2006) 94, 743-751. doi: 10.1038/sj.bjc.6602982**

A study reviewing risk patterns in carcinoma and melanoma of the skin in men found that subjects with an elevated number of naevi had a high and consistent risk increase for CMM of OR 8.4. Other key factors for melanoma included blonde hair, green eyes; however, high hours of outdoor work did not show an increased risk. SCC risk was found in people with blonde/red hair and green eyes who were poor tanners and those with high sun exposure. BCC risk resulted from people with blonde/red hair, green eyes and medium to high sun exposure. The study concluded "*our direct case-case comparison to mitigate a possible bias in comparing results from different studies confirmed previous findings on the association between pale eyes, naevi and CMM, compared to other skin cancers, and the increased risk of BCC for intermittent sun exposure when compared to the risk of SCC."* This study confirms moles and red hair/pale eyes are risk factors for skin cancer and that the protective tan that would be found on outdoor workers prevents melanoma risk.

41. **Kudchadkar et al,. Targeting Mutant BRAF in Melanoma. Current Status and Future Development of Combination Therapy Strategies. Cancer J 2012;18: 124-131**

BRAF mutations are in over 50% of all melanomas and are not a result of UV exposure. New drugs have been developed to help treat BRAF melanoma.

42. **Newton-Bishop et al,. Melanocytic nevi, nevus genes and melanoma risk in a large case-control study in the United Kingdom. Cancer Epidemiol Biomarkers Prev. 2010 Aug;19(8):2043-54. doi: 10.1158/1055-9965.EPI-10-0233. Epub 2010 Jul 20**

A study looked at melanocytic nevi, nevus genes and melanoma risk in the UK. Twin studies have provided strong evidence that the number of nevi is predominantly genetically determined, with a smaller effect of sun exposure. The study reported "There was no convincing relationship between either average daily exposure or sunburn and nevus number." The analysis confirmed the strong relationship between nevus number and melanoma risk, with a crude odds ratio (OR) for melanoma of 10.02 when comparing the top quartile with the lowest quartile of nevus count. The study concluded "*This paper confirms the importance of nevi in melanoma pathogenesis and increases understanding of their genetic determinants*."

43. Cust et al,. Melanoma risk for CDKN2A mutation carriers who are relatives of population-based case carriers in Australia and the UK. J Med Genet. 2011 Apr;48(4):266-72. doi: 10.1136/jmg.2010.086538

A study looked at melanoma risk for CDKN2A mutation carriers and compared Australia with the UK. The estimated HR for melanoma carriers relative to the general population decreased with regions of increasing ambient ultraviolet (UV) irradiance being higher for the UK – 87 than Australia – 31. The study concluded "*Contrary to the strong association between UV radiation exposure and melanoma risk for the general population, CDKN2A mutation carriers appear to have the same cumulative risk of melanoma irrespective of the ambient UV irradiance of the region in which they live.*"

44. Tsao et al., Melanoma: from mutations to medicine. Genes & Development 26:1131-1155 2012

One can argue that melanoma is fundamentally a genetic disease, since the range of heritable risk factors – from physical characteristics such as light complexion, an inability to tan, red hair, and blue eyes to the familial atypical mole/melanoma (FAMM) syndrome – are all determined by distinct genetic elements. Germline variants of MC1R disrupt the signaling for the production of eumelanin and are present in ~80% o individuals with red hair color, <20% of people with brown or black hair, and <4% of persons with a robust tanning response. "Although it is tempting to speculate that the BRAF (V600E) mutation is induced by UV damage, the T→A transversion that converts the valine to glutamic acid at amino acid 600 (V600E) is not part of the 'classic' UV-induced mutational signature."

45. **Hacker E, Hayward NK, Dumenil T, James MR, Whiteman DC. The association between MC1R genotype and BRAF mutation status in cutaneous melanoma: findings from an Australian population. J Invest Dermatol. 2010 Jan;130(1):241-8. doi: 10.1038/jid.2009.182**

There is increasing epidemiological and molecular evidence that cutaneous melanomas arise through multiple causal pathways. The purpose of this study was to explore the relationship between germline and somatic mutations in a population-based series of melanoma patients to reshape and refine the divergent pathway model for melanoma. "We found that melanomas harboring BRAF V600 mutations were more likely among younger patients and those with high nevus counts, and were more likely to occur in melanomas with adjacent neval remnants. Compared with patients who had 1-15 nevi, those with 16-60 nevi were 10-fold more likely to have BRAF V600 mutant melanoma and patients with > 60 nevi had similarly increased risks of harboring a mutation. We found that BRAF V600 mutant melanomas were statistically significantly less likely to occur in people in the highest groups of cumulative sun exposure or actinic keratosis counts. Similarly, BRAF V600 mutant melanomas were less common among people who reported large numbers of sunburns as adults, although this was not statistically significant. BRAF-mutant melanomas have different origins from other cutaneous melanomas. These data support the divergent pathways hypothesis for melanoma, which may require a reappraisal of targeted cancer prevention activities."

46. **Thomas NE, Berwick M, Cordeiro-Stone M. Could BRAF mutations in melanocytic lesions arise from DNA damage induced by ultraviolet radiation? J Invest Dermatol. 2006 Aug;126(8):1693-6.**

"The most common BRAF mutation found in melanocytic nevi and melanomas, the t1799a substitution – that is, the V600E mutation – is not at a dipyrimidine site, and, thus, it is not generally viewed as resulting from error-prone replication of UVB-damaged DNA."

47. **Shekar et al,. A population based study of Australian twins with melanoma suggests a strong genetic contribution to liability. J Invest Dermatol. 2009 September ; 129(9): 2211–2219. doi:10.1038/jid.2009.48**

An Australian study using twins ascertained through QFMP and NSW Central Cancer Registry, performed a classical twin analysis to determine the proportion of genetic and environmental effects of variation in liability to melanoma. Identical twins share all their genes, and non-identical twins share approximately half their genes. A conditional logistic

regression found that those unaffected with melanoma reported a greater time spent outdoors than affected twins. A paired t-test showed that affected individuals had a greater number of moles on their arms and legs than their unaffected, non-identical, co-twins and their unaffected, identical , co-twins. In pairs of identical twins, affected twins had, on average, 71 moles on their arms and legs compared to 46 for their identical, unaffected, co-twins. In twin pairs where both individuals are affected, they had a similar number of moles on their arms and legs. The study concluded "Using these data and population prevalences, it was estimated that 55% of variation in liability to melanoma is due to genetic influences."

48. Hodis et al,. A Landscape of Driver Mutations in Melanoma. Cell 150,251-263, July 20, 2012

"It has been perplexing that the most prevalent UVB-radiation-induced genetic change – the transition of a cytosine to a thymidine, accounting for >70% of nucleotide substitutions – has not been shown to be the molecular basis for known oncogenic mutations in melanoma, including BRAF V600E and NRAS Q61L/R."

49. Gallagher et al – Plasma levels of polychlorinated biphenyls and risk of cutaneous malignant melanoma: a preliminary study. Int. J. Cancer: 000, 000-000 (2010)

Do factors other than UV radiation play a role in CMM? Richard Gallagher of BC Cancer, recently (2010) investigated the role of PCB's and cutaneous malignant melanoma (CMM). He found strong associations between risk of CMM and plasma levels of non-dioxin-like PCB's – OR 7.02 or a 700% increase in risk. He concluded that his study results *"suggest that environmental factors other than UV radiation may play a role in genesis of CMM, and indicate that it may be productive to search for further agents which might increase risk".*

50. Asta Juzeniene, Zivile Baturaite, and Johan Moan. Sun Exposure and Melanomas on Sun-Shielded and Sun-Exposed Body Areas Chapter 21 – Sunlight, Vitamin D and Skin Cancer, Second Edition, edited by Jorg Reichrath 2014 Landes Bioscience

"Reviews of the scientific literature reveals many significant correlations between chemical exposure (polycyclicaromatichydrocarbon (PAHs), benzene, and polychlorinated biphenyls (PCBs), pesticides, trichloroethylene, dioxin) in the workplace and the occurrence of malignant melanoma, particularly in cutaneous areas that have never been exposed to sunlight. More studies are needed to define the role of chemical exposure as a co-factor in the pathogenesis of melanoma. The type of occupation may also be a risk factor of melanoma."

51. Fortes C, deVries E. Nonsolar occupational risk factors for cutaneous melanoma. Int J Dermatol. 2008 Apr;47(4):319-28. doi: 10.1111/j.1365-4632.2008.03653.x.

"Overall and notwithstanding the different types of epidemiological studies, we found strong evidence of an increased cutaneous melanoma risk for workers in the petroleum (1.4-8.0), printing (1.23-8.7), and electrical and electronics (1.23-4.0) industries, which may be associated with exposure to polychlorinated polycyclic aromatic hydrocarbons (PAHs), such as 7,12-dimethylbenz-(a)-anthracene (DMBA), benzene, and polychlorinated biphenyls (PCBs)."

"In conclusion, and based on the risk estimates and a thorough evaluation of the quality of the studies, there is a possible relationship between PAH, benzene, and/or PCB exposure of workers in the petroleum and automobile industry, engine-men, and printers and an increased risk for melanoma. Likewise workers exposed to ionizing radiation, such as radiation workers, dentists, and cockpit personnel, seem to have an increased melanoma risk. We hope these results will be used to generate new hypothesis and to suggest new areas for case-control studies with careful exposure assessment."

52. Rota et al,. Alcohol drinking and cutaneous melanoma risk – A systematic review and dose-risk meta-analysis. Br J Dermatol. 2014 Feb 3. doi: 10.1111/bjd.12856.

A meta-analysis of 16 studies with a total of 6,251 melanoma cases found that the pooled relative risk (RR) for any alcohol drinking compared with non/occasional drinking was 1.20 or a 20% increased risk. And or those who drink more than four glasses a day, the risk jumped to 55%. The researchers believe that ethanol is converted to a chemical compound called acetaldehyde soon after it is ingested. It is thought that acetaldehyde may act as a 'photosensitizer' making skin more sensitive to light, which in turn generates molecules called 'reactive oxygen species' that damage cells in a way that can cause skin cancers. The study concluded "This meta-analysis of published data revealed that alcohol consumption is positively associated to the risk of cutaneous melanoma."

53. Yamaguchi Y. et al., Cyclobutane pyrimidine dimmer formation and p53 production in human skin after repeated UV irradiation Experimental Dermatology 2008; 17: 916-924

Yuji Yamaguchi in 2008 initiated a study to assess whether facultative pigmentation (tanning) induced by repeated UV irradiation is photoprotective. The study concluded *"These results suggest that pigmentation induced in skin by repeated UV irradiation protects against*

subsequent UV-induced DNA damage." The report went on to say *"it may reflect development of a mature, efficient defense system."*

54. **Newton-Bishop JA et al., Relationship between sun exposure and melanoma risk for tumours in different body sites in a large case-control study in a temperate climate, Eur J Cancer (2010), doi:10.1016/j.ejca.2010.10.008**

Professor Julia Newton-Bishop, an epidemiologist who led the research at Leeds University, UK, said "it seems regular exposure helps the skin adapt and protect itself against the harmful affects of sunshine". "Increased levels of vitamin D made in the skin while exposed to sunlight may also be protective." They found that those who spent between four to five hours in the sun each day over the weekend were less likely to develop tumours.

55. **Guido Bens. Sunscreens. Chapter 25 – Sunlight, Vitamin D and Skin Cancer, Second Edition, edited by Jorg Reichrath 2014 Landes Bioscience**

"The suppression of natural photoprotection mechanisms by the currently marketed sunscreens: Melanine synthesis, release of melanosomes, and thickening of stratum corneum are mainly triggered by UVBR that is effectively blocked by modern sunscreens. The sunscreen user is thus more submitted to the harmful epidermal and dermal effects of UVAR than an unprotected individual who will undergo natural adaptation that protects against both UVBR and UVAR. This is consistent with the observation that people with important chronic UV exposure by occupational outdoor activity, e.g., agricultural workers, who typically have tan and skin thickening in sun-exposed sites, are at a significantly reduced risk of melanoma compared with indoor workers with intermittent UV exposure."

56. **Gandini et al,. Sunny Holidays before and after Melanoma Diagnosis Are Respectively Associated with Lower Breslow Thickness and Lower Relapse Rates in Italy. Plos One November 2013 Volume 8 Issue 11 e78820**

Dr. Sara Gandini investigated if different indicators of UV exposure, collected before and after melanoma diagnosis are associated with Breslow thickness and melanoma recurrence in Italy. The study found that sun exposure during hot hours and residence in tropical countries in youth, that are proxy for sunbathing and sunburns more than sunny holidays, were not found to be associated with melanoma prognosis. No association was found with sunbed exposure. The 5-year cumulative incidence of melanoma recurrences was 8% for those having a sunny holiday after diagnosis compared to 17% for those without. A HR of

0.30. The study concluded "Holidays in the sun were associated with thinner melanomas in women and reduced rates of relapse in both sexes."

57. Gambichler T, Bindsteiner M, Hoxtermann S, Kreuter A. Serum 25-hydroxyvitamin D serum levels in a large German cohort of patients with melanoma. Br J Dermatol 2013 Mar;168(3):625-8 doi: 10.1111/j.1365-2133.2012.11212.x

A study from Germany looked at vitamin D levels in patients with melanoma. We know that increased UVB exposure will increase your vitamin D level. Therefore you would expect that if increased UV exposure caused melanoma than these patients would have higher vitamin D levels. The study reported the opposite – "*we observed considerably decreased median 25(OH)D serum levels in patients with MM.*" In addition the study found "*that decreased 25(OH)D serum levels are associated with increased tumour thickness and advanced tumour stage*." The study concluded "*there is increasing evidence that patients with MM who strictly avoid sun exposure might benefit from 25(OH)D supplements that are sufficient to maintain serum levels above 30 ng/ml*."

58. Asta Juzeniene, Zivile Baturaite, and Johan Moan. Sun Exposure and Melanomas on Sun-Shielded and Sun-Exposed Body Areas Chapter 21 – Sunlight, Vitamin D and Skin Cancer, Second Edition, edited by Jorg Reichrath 2014 Landes Bioscience

"Inconsistent with the idea that the primary cause of cutaneous melanoma is the sun, is the observation that melanoma is much more frequent in those who work indoor (dentists, physicians, journalists) than outdoor (fisherman, farmers, gardeners). It has been demonstrated that sun exposure prior to diagnosis is associated with improved survival in melanoma patients, and that sunnier European countries have lower melanoma mortality. This means that solar UV radiation, probably through its role in vitamin D photosynthesis, may protect against melanoma. Several other studies have found that decreased 25(OH)D serum levels in melanoma patients were associated with larger tumor thickness and advanced tumor stage."

59. Wong JR, Harris JK, Rodriguez-Galindo C, Johnson KJ. Incidence of Childhood and Adolescent Melanoma in the United States: 1973-2009. Pediatrics. 2013 Apr 15. DOI: 10.1542/peds.2012-2520

A study of childhood and adolescent melanoma in the United States from 1973-2009 had some baffling results. Overall, pediatric melanoma increased by an average of 2% per year. But this increase was solely from the low UVB exposure area or the North part of the USA. The study reported "*there was an unexpected increased trend in low UV-B exposure registries, with a negative trend in high UV-B registries for 15-19 year olds starting in 1985*." The study went on to say "*recent data has indicated stable UV measurements since the 1990's. This is consistent with our results suggesting UV-B exposure is not the primary factor in increased melanoma incidence.*"

60. **Bleyer A, O'Leary M, Barr R, Ries LAG (eds): Cancer Epidemiology in Older Adolescents and Young Adults 15 to 29 Years of Age, Including SEER Incidence and Survival: 1975-2000. Chapter 5. National Cancer Institute, NIH Pub. No. 06-5767. Bethesda, MD 2006.**

A study from the National Cancer Institute, U.S. Department of Health and Human Services published in 2007 studied cancer in young adults age 15-29 and found that melanoma was the 2nd most common type of cancer in this age group. It went on to say *"the etiology of melanoma in 15-29 year old individuals is not known. Solar/ultraviolet irradiation does not appear to be as important a causative factor in this age group as it is in older individuals"*. It concluded *"most of the melanomas that occur in young persons arise in dysplastic nevi or in parts of the body that are likely to have been protected from ultraviolet light exposure"*.

61. **Cust AE, Jenkins MA, Goumas C, Armstrong BK, Schmid H, Aitken JF, Giles GG, Kefford RF, Hopper JL, Mann GJ. Early-life sun exposure and risk of melanoma before age 40 years. Cancer Causes Control. 2011 Jun;22(6):885-97. doi: 10.1007/s10552-011-9762-3. Epub 2011 Apr 7.**

Sun exposure during childhood is of particular etiological interest because it is considered a key life period for initiation and promotion of melanomagenesis. This Australian study examined associations between early-life sun exposure and risk of invasive cutaneous melanoma diagnosed between ages 18 and 39 years. The study reported: "Melanoma risk overall was not associated with self-reported lifetime total sun exposure (from age 5 years onwards) or childhood total sun exposure (exposure from 5 to 17 years of age), nor with sun exposure during weekdays or weekends (as cumulative time and as a proportion of total time), warmer months, summer holidays or leisure-time activities, or severe sunburn." The study concluded "The association of early-life sun exposure with early-onset melanoma is influenced by host factors."

62. **Radespiel-Troger M, Meyer M, Pfahlberg A, Lausen B, Uter W, Gefeller O. Outdoor work and skin cancer incidence: a registry-based study in Bavaria. Int Arch Occup environ Health (2009) 82:357-363 doi: 10.1007/s00420-008-0342-0**

An outdoor work and skin cancer study from Bavaria concluded "*CMM risk was not significantly associated with outdoor work.*"

63. **Elliott F, et al, Relationship between sunbed use and melanoma risk in a large case-control study in the United Kingdom. Int. J. Cancer: 000, 000-000 (2011)**

This evidence was further supported in a 2011 study by Faye Elliott, University of Leeds, UK. Elliott studied the relationship between sunbed use and melanoma risk in a large case-control study in the United Kingdom. They found no evidence for sunbed use as a risk factor for melanoma in the UK – OR 1.06. They also stated *"Age at first use of sunbeds showed a small non-significant increased risk for use < 25 years – OR 1.16"* [14].

64. **Rhodes AR. Cutaneous melanoma and intervention strategies to reduce tumor-related mortality: what we know, what we don't know, and what we think we know that isn't so. Dermatologic Therapy, Vol. 19, 2006, 50-69**

In fact, we do not know the case fraction of CM directly attributable to UVR, and the unintended consequences of current messages directly linking UVR exposure and CM development may be thwarting the primary intervention goal of reducing tumor-related mortality."

65. **Zhang M, Qureshi AA, Geller AC, Frazier L, Hunter DJ, Han J. Use of Tanning Bed and Incidence of Skin Cancer. J Clin Oncol. 2012 May 10;30(14):1588-93. doi: 10.1200/JCO.2011.39.3652. Epub 2012 Feb 27**

A study evaluating tanning beds and the incidence of skin cancer analyzed a large US cohort of nurses (NHSII). The study provided subset analysis for both high and low skin pigmentation. This was based on hair colour and reaction to sun exposure during childhood or adolescence. The study reported for women who used a sunbed > 3 times per year during their ages of 25 to 35 years, high pigmentation had a 12% reduced risk of melanoma (OR 0.88).

E. Other published peer reviewed studies stressing the importance of sun/UV exposure for maintaining good health.

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