WHY CONNECTICUT SB219 IS THE WRONG APPROACH

The American Suntanning Association, its members and the majority of parents in Connecticut urge you to vote “NO” on Connecticut SB 219 – as this bill will NOT accomplish what its well-meaning sponsors believe.

- **This bill would take away a parent’s right to decide** whether their teen-agers can get a suntan in a professional salon. Many families use salon sunbeds before taking sunny vacations. Many doctors encourage this practice.¹

- **Connecticut salons already require that minors 17-18 who want to tan must have their parent’s consent** in person in the salon. ASA and members in Connecticut helped author this legislation in 2013 and we support constructive measures to bolster it. Compliance with this standard is high. Phone surveys on this topic do not measure compliance of what happens in the salon. Proponents of the bill have misrepresented this.

- **This bill would have unintended consequences**: Teenagers over 16, who can drive, would turn to HOME tanning beds in unsupervised homes, basements, apartment complexes and gyms, which would INCREASE sunburn incidence, not decrease it.² Consider this: 41 percent of all tanning today occurs at these non-salon locations – an all-time high.³ This bill would increase that number and would unintentionally increase sunburns.

- **U.S. sunbed research** – when separated by location of the sunbed – clearly establishes sunburns in home sunbeds as the source of risk in the data.⁴ Bill proponents have misrepresented this critical caveat in the data.

- **A ban will hurt Connecticut businesses and will cost taxpayers money to implement.**
  - Connecticut has approximately 73 professional tanning facilities with 591 employees.
  - 70 percent of tanning facilities are female-owned small businesses.
  - 17-year-old clients represent up to 5% of salon business. In a service-based business losing 5% of top-line revenue is an even-larger net loss, which would close many of these businesses.
  - Enforcement of a UV-sunbed ban would cost taxpayers money to implement and will hurt small businesses for no reason – a ban will simply drive clients to uncontrolled home sunbeds.

- **Dermatology uses sunbeds to treat cosmetic conditions.** Many dermatologists send clients of all ages to tanning salons – particularly in rural areas – to self-treat psoriasis and other cosmetic conditions.⁶ According to a 2015 survey of American Academy of Dermatology members: (1) Fully 99 of 100 dermatologists (99%) believe UV exposure is an effective treatment option; (2) Nearly 9 out of 10 dermatologists (88%) recommend the usage of UV lamps as a form of treatment; (3) More than 1 in 4 dermatologists (28%) recommend patients use tanning salons as a convenient, cost-effective self-treatment option.¹

- **Let’s Talk About Better Solutions**: The bill is well-meaning, but would increase sunburn in Connecticut. In a legitimate stakeholder meeting we can demonstrate that our position is well-supported both scientifically and in terms of what is most effective for parents and teen-agers. Science is starting to promote a balanced message about sun care — that sunburn prevention (not sun avoidance) is what’s best.⁷,⁸ We’ve never shied away from conversation about the science — we’re happy to have that discussion.

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² Indoor tanning among NJ high school students before and after the enactment of youth access restrictions. J of Am Acad Derm. 8-2016.
⁶ Feldman et al. A Review of the Use of Tanning Beds as a Dermatological Treatment. Dermal There. 2015: 5:37-51
⁷ Weller R. Sunlight Has Cardiovascular Benefits Independently of Vitamin D. Blood Purif 2016; 41:130-134
LETTER TO THE EDITOR

Commercial tanning salons and melanoma risk

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ABSTRACT

There have been many case-control studies of melanoma and the use of indoor tanning equipment. A recent meta analysis of 8 credible studies in North America estimated an overall significant odds ratio of 1.23. Three of these 8 studies also reported separately on commercial use and home use of indoor tanning equipment. For home use the overall odds ratio was a significant 1.53 while for commercial use there was a non significant 1.05.

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Sir, In 2006, a working group of the International Agency for Research on Cancer (IARC) published a systematic review and meta analysis of epidemiological and experimental studies on the use of indoor tanning equipment and skin cancer. Indoor tanning equipment, as defined in the 2006 IARC report, included sunbeds and sunlamps, whether used in commercial tanning salons or other settings, and was referred to in the report as “sunbeds or indoor tanning equipment.” The authors did not separate data by place of use. Based on 19 informative studies, ever-use of sunbeds was positively associated with melanoma (summary relative risk, 1.15; 95% CI, 1.00–1.31).

In 2012, the 2006 IARC report was updated by 4 of its authors to include an additional 8 indoor tanning studies published since the IARC report. The term “sunbeds” was again used to refer to use of indoor tanning equipment, whether in commercial tanning salons or at home or in other settings. Based on these 27 studies of ever having used sunbeds, there was an associated summary relative risk of 1.20; (95% CI, 1.08–1.34). As in the 2006 IARC report, the authors did not separate data by place of use.

In 2014, a further systematic review and meta analysis on melanoma risk and “indoor tanning” was published. This study also combined data from home use with data from commercial tanning salon use, using the omnibus term “indoor tanning” to describe both. This study is the only meta-analysis on the subject that separated studies by geographical area. Figure 2 in their paper gives the odds ratios of melanoma for ever use versus never use of indoor tanning. For North America, the authors considered 8 studies to be credible and they calculated a meta analysis giving an overall odds ratio of melanoma of 1.23 (95% C.I. 1.03, 1.47) for ever having used indoor tanning; a statistically significant increase. As indicated, these individual studies combined data from indoor tanning at home and indoor tanning at commercial tanning salons. 3 of these 8 acceptable North American studies also provided a separate analysis of home and commercial tanning salon use. These analyses, as well as a meta analysis and the original analysis of the 8 studies are given in Table 1.

The 3 studies that considered both home and commercial indoor tanning show a considerable difference in melanoma risk between home indoor tanning and commercial tanning salon indoor tanning. The tanning salon meta analysis estimate of 1.05 essentially shows no increase melanoma effect, while the home tanning estimates a significant increase in melanoma risk. We therefore see that there is an important underlying difference between commercial tanning and “do it yourself” home tanning, which may involve
increased sun burns and their known risk for melanoma.

In 2011, a report was presented at the 3rd North American Congress of Epidemiology held in Montreal which analyzed home vs. salon use of indoor tanning based on those studies in the original IARC report of 2006. The authors also concluded in their abstract that “When professional sunbed usage is considered independent of home and medical exposures there is no association with melanoma.”

Finally, it should be said that all of the above odds ratio values may be high due to the general problem of recall bias.

Disclosure of potential conflicts of interest
The author has done consulting for the American Suntanning Association.

References

Avoiding Sun as Dangerous as Smoking
Marcia Frellick
March 23, 2016

Nonsmokers who stayed out of the sun had a life expectancy similar to smokers who soaked up the most rays, according to researchers who studied nearly 30,000 Swedish women over 20 years.

This indicates that avoiding the sun "is a risk factor for death of a similar magnitude as smoking," write the authors of the article, published March 21 in the *Journal of Internal Medicine*. Compared with those with the highest sun exposure, life expectancy for those who avoided sun dropped by 0.6 to 2.1 years.

Pelle Lindqvist, MD, of Karolinska University Hospital in Huddinge, Sweden, and colleagues found that women who seek out the sun were generally at lower risk for cardiovascular disease (CVD) and noncancer/non-CVD diseases such as diabetes, multiple sclerosis, and pulmonary diseases, than those who avoided sun exposure.

And one of the strengths of the study was that results were dose-specific — sunshine benefits went up with amount of exposure.

The researchers acknowledge that longer life expectancy for sunbathers seems paradoxical to the common thinking that sun exposure increases risk for skin cancer.

"We did find an increased risk of...skin cancer. However, the skin cancers that occurred in those exposing themselves to the sun had better prognosis," Dr Lindqvist said.

Some Daily Exposure Important for Health

Given these findings, he told *Medscape Medical News*, women should not overexpose themselves to sun, but underexposure may be even more dangerous than people think.

"We know in our population, there are three big lifestyle factors [that endanger health]: smoking, being overweight, and inactivity," he said. "Now we know there is a fourth — avoiding sun exposure."

Sweden's restrictive guidance against sun exposure over the past 4 decades may be particularly ill-advised, the study finds, in a country where the maximum UV index is low (< 3) for up to 9 months out of the year.

Use of sunscreen is also widely misunderstood in the country and elsewhere, Dr Lindqvist said.

"If you're using it to be out longer in the sun, you're using it in the wrong manner," he said. However, "If you are stuck on a boat and have to be out, it's probably better to have sunscreen than not to have it."
Women with more pigmentation would be particularly well-served to stop avoiding sunshine, he said, adding that many people in India, for instance, follow guidelines like those in Sweden to avoid sun year round.

And because melanomas are rare among women with darker skin, benefit goes up in those populations when weighing sun exposure's risk against benefits, Dr Lindqvist said.

**Age and Smoking Habits**

The researchers studied sun exposure as a risk factor for all-cause mortality for 29,518 women with no history of malignancy in a prospective 20-year follow-up of the Melanoma in Southern Sweden cohort.

The women were recruited from 1990 to 1992 when they were 25 to 64 years old. Detailed information was available at baseline on sun-exposure habits and potential confounders such as marital status, education level, smoking, alcohol consumption, and number of births.

When smoking was factored in, even smokers at approximately 60 years of age with the most active sun-exposure habits had a 2-year longer life expectancy during the study period compared with smokers who avoided sun exposure, the researchers note.

The authors do, however, acknowledge some major limitations. Among them, it was impossible to differentiate between active sun-exposure habits and a healthy lifestyle, and they did not have access to exercise data.

**Role of Vitamin D Still in Question**

The results add to the longstanding debate on the role of vitamin D in health and the amount of it people need, but this study doesn't resolve the question.

"Whether the positive effect of sun exposure demonstrated in this observational study is mediated by vitamin D, another mechanism related to ultraviolet radiation, or by unmeasured bias cannot be determined. Therefore, additional research is warranted," the authors write.

"From Irish studies we know that vitamin D deficiency makes melanomas more malignant," Dr Lindqvist said.

"This is in agreement with our results; melanomas of [those not exposed] to the sun had a worse prognosis."

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The risks and benefits of sun exposure 2016

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**ABSTRACT**

Public health authorities in the United States are recommending that men, women and children reduce their exposure to sunlight, based on concerns that this exposure will promote skin cancer. On the other hand, data show that increasing numbers of Americans suffer from vitamin D deficiencies and serious health problems caused by insufficient sun exposure. The body of science concerning the benefits of moderate sun exposure is growing rapidly, and is causing a different perception of sun/UV as it relates to human health. Melanoma and its relationship to sun exposure and sunburn is not adequately addressed in most of the scientific literature. Reports of favorable health outcomes related to adequate serum 25(OH)D concentration or vitamin D supplementation have been inappropriately merged, so that benefits of sun exposure other than production of vitamin D are not adequately described. This review of recent studies and their analyses consider the risks and benefits of sun exposure which indicate that insufficient sun exposure is an emerging public health problem. This review considers the studies that have shown a wide range health benefits from sun/UV exposure. These benefits include among others various types of cancer, cardiovascular disease, Alzheimer disease/dementia, myopia and macular degeneration, diabetes and multiple sclerosis. The message of sun avoidance must be changed to acceptance of non-burning sun exposure sufficient to achieve serum 25(OH)D concentration of 30 ng/mL or higher in the sunny season and the general benefits of UV exposure beyond those of vitamin D.

**Introduction**

Public health authorities in the United States are currently advising that human sun exposure be reduced. At the same time, NHANES data show that 32% of Americans suffer from vitamin D insufficiency.

In this paper we review the current state of the science of the risks and benefits of sun exposure and suggest that public health advice be changed to recommend that all men, women and children accumulate sufficient non-burning sun exposure to maintain their serum 25-hydroxyvitaminD [25(OH)D] levels at 30 ng/mL or more year-round.

**History**

The first scientifically-established health benefit of sun exposure was the discovery in 1919 that sunlight cured rickets. This was followed in 1924 up by the discovery that an inactive lipid in the diet and skin could be converted by UV light into an antirachitic substance. The identification of vitamin D occurred in 1931. The association between sun exposure and reduced cancer mortality in North America was identified in the 1960s. In the 1980s, it was hypothesized that vitamin D was the protective factor. For most of the intervening years, instead of pursuing further benefits of sun exposure, scientific inquiry focused on the health risks of sun exposure, especially melanoma and other types of skin cancer. Chemical sunscreens were developed in 1928. Avoidance of intentional sun exposure and use of chemical sunscreens persisted as the standard advice of physicians and public health authorities for reducing the risk of melanoma and other forms of skin cancer. The risks of inadequate sun exposure have been largely ignored. Recently, however, scientific inquiry has increasingly
turned to the benefits of moderate sun exposure and the public health risks of inadequate sun exposure.10

Risks of sun exposure

Melanoma

The mechanism of melanoma is unknown, but is believed to be linked to genetic factors.11 The principal identified non-genetic risk factor is ultraviolet radiation (UVR) exposure, and the relationship between melanoma and UVR is 2-sided: non-burning sun exposure is associated with a reduced risk of melanoma, while sunburns are associated with a doubling of the risk of melanoma.12 It has long been observed that outdoor workers have a lower incidence of melanoma than indoor workers.13–19 A 1997 meta-analysis found an OR of 0.86 (95% CI: 0.77–0.96) for occupational sun exposure.18

Biologically, UVB is known to induce DNA damage through the creation of pyrimidine dimers while UVA does so at orders of magnitude less efficiently.20 Oxidative damage through the creation of free radicals (singlet oxygen and hydrogen peroxide) occurs at all UVR frequencies.20 However, the human body has many defenses against such damage including DNA repair mechanisms, cell cycle and growth inhibitions, reduced proliferation, enhanced sensitivity to apoptosis, enhancement of cellular differentiation and anti-inflammatory effects; many of which are related to vitamin D produced by exposure to UVB.21–25

With respect to sunburns, melanocytes are not replicating cells, so once DNA damage has occurred, it is necessary for cellular replication to take place for the possibility of unrepaired or mis-repaired melanocytes to develop into malignant melanoma.20 Sunburns correspond with rare occasions of cell divisions and ensuing vulnerability to mutations in otherwise indolent melanocytes.20 With respect to chronic non-burning sun exposure, it is thought that protection against sunburn and development of melanoma derives from photo-adaptation (increased melanisation and epidermal thickening) or from the induction of higher levels of vitamin D, or possibly both.12,25–28 Vitamin D produced by UVB exposure is converted to the active form of vitamin D by its sequential metabolism in the liver to form the major circulating form of vitamin D, 25-hydroxyvitamin D [25(OH)D] which is then converted in the kidneys to 1,25-dihydroxyvitamin D [1,25(OH)2D]. Evidence suggests that vitamin D that is produced in the skin can also be converted in the skin to its active form 1,25(OH)2D25, thereby enhancing DNA repair29 and lowering cancer risk.

The incidence of melanoma in the United States has increased dramatically from 1 per 100,000 people per year in 1935 to 23 per 100,000 per year in 2012. Various explanations for this phenomenon have been suggested, including diagnostic drift,30 depletion of the ozone layer,31 the widespread use of artificial UVR devices,32 and the proliferation of large windows in office buildings.15 None of these explanations is particularly satisfactory for the reason that none explains the steady increase in melanoma incidence since 1935. While sunburns have been associated with a doubling of melanoma risk,12 chronic non-burning sun exposure and outdoor occupations have been associated with reduced risk of melanoma.12–19 Indoor occupations such as professional, managerial, clerical, sales and service workers grew from 25% to 75% of total employment between 1910 and 2000.33 25% of Americans lived on farms in 1930 whereas only 2% do so today.34 Indoor attractions such as air conditioning, television, computers and the internet probably have led to Americans spending more of their leisure time indoors, the prevalence of sunburns is high and has been increasing,16 and serum 25(OH)D levels of the American public, a likely marker for sun exposure, are low and have been declining.5 A more plausible explanation for the rise in melanoma incidence since 1935 may be the continually-increasing insufficient non-burning sun exposure and related increasing vitamin D deficiency/insufficiency, and the increasing sunburn prevalence experienced by the American public over the same time period.4 Furthermore,
epidemiological studies do not indicate any difference in melanoma risk based on the age at which UVR exposure occurs.12,17,18 Sunburns appear to be equally risky at any age.17 The public health messages of the past 50 y to avoid sun exposure and to use chemical sunscreens may have contributed to the rise in melanoma incidence.

We can find no consistent evidence that use of chemical sunscreens reduces the risk of melanoma. Green et al. 2011,42 found in a prospective study that there may be an association between sunscreen use and reduced risk of melanoma. However, since the participants were told they were participants in a skin cancer prevention trial and were questioned periodically during the trial on their use of sunscreen, the likelihood that they were significantly more diligent in applying sunscreen in accordance with manufacturers’ instructions than ordinary users of sunscreen cannot be discounted.6 In addition, this study took place in a tropical environment, differing significantly from the environments of North America and Europe. Use of a placebo sunscreen was barred by ethical concerns.

Sunscreens do, however, reduce acclimatization to UVR and vitamin D production in the skin.46 Since public health authorities recommend liberal use of sunscreens for good health, the labeling of sunscreens should contain a statement about the possibility of vitamin D deficiency that may result from excessive use of sunscreens. Labeling should also state that sunscreens have not been shown to be effective in reducing the risk of melanoma. Sunscreens have been shown in one study to be effective in reducing the risk of squamous cell, but not basal cell, skin cancer.47

**Nonmelanoma skin cancer (NMSC)**

There are no official registries for basal cell carcinoma (BCC) or squamous cell carcinoma (SCC), and estimates of the prevalence of these carcinomas vary widely. One group of investigators examined Medicare fee-for-service data, extrapolated to the entire United States population, and estimated that 2,152,500 persons were treated for 3,507,693 NMSCs in 2006.48 Several of the same investigators estimated that 3,315,554 persons were treated for 5,434,193 NMSCs in 2012 and revised the 2006 estimates to 2,463,567 persons and 4,013,890 NMSCs.49 These latter estimates indicated a 14% increase in Medicare NMSCs over the 6-year period 2006–2012 and a 54% increase in non-Medicare NMSCs over the 6-year period. It is not clear in this analysis that all treatments for NMSCs were in fact treatments for malignancies rather than for non-cancerous lesions, and these investigators found the ratio of BCC to SCC to be 1 to 1 instead of the expected 4 to 1. Another recent study50 which histologically confirmed all cases but studied only BCCs, calculated based on an analysis of a Kaiser Permanente BCC registry that approximately 2 million BCCs are treated annually in the United States in an undisclosed number of persons. Assuming a 4 to 1 ratio of BCC to SCC, this would indicate that 2.5 million NMSCs are treated annually. This study found that the incidence of BCC increased 17% during the 15-year period from 1998 to 2012.

As with melanoma, sunburns are associated with increased risk of SCC and BCC.16,17,51 Cumulative sun exposure, which is associated with decreased risk of melanoma, is apparently associated with increased risk of SCC and BCC, although the relationship between cumulative sun exposure and NMSC is not entirely clear. Armstrong and Kricker 200117 found that only SCC, not BCC, is related to total sun exposure, and Rosso et al. 199852 found no association between cumulative lifetime sun exposure and BCC. Kennedy et al. 200316 found a positive association between increasing lifetime sun exposure and the development of SCC and BCC but statistical significance was not always reached after age adjustment. English et al. 199853 found that total time spent outdoors was only weakly associated with SCC. Gallagher et al. 1995a,b54,55 found no association between cumulative lifetime sun exposure and risk of SCC or BCC, but Gallagher et al. 1995b55 found that occupational sun exposure in the 10 y prior to diagnosis was associated with increased risk of SCC. Many studies have found increased risk of SCC and to a lesser extent BCC from occupational sun exposure.17,51,56,57 Alam et al. 200158 found that the risk of SCC, but not BCC, is directly related to cumulative total dose of ionizing radiation from x-rays, that SCC may develop on sun-exposed areas in people with certain genodermatoses, such as oculocutaneous albinism, that chemical agents such as soot, arsenic and polycyclic hydrocarbons have historically been a major cause of SCC, and that

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*Sunscreens are intended to prevent sunburn when used in thickness and frequency recommended by manufacturers or used in setting SPF. However, studies have shown that the incidence of sunburn is higher or the same in people who almost always use sunscreens compared with those who rarely use sunscreens.*45,46
human papillomavirus infection has been associated with SCC. The US. Preventive Services Task Force, in its May 2012 Final Recommendation Statement on skin cancer counseling,\textsuperscript{59,60} stated that studies that measured long-term or total sun exposure had found no association between cumulative sun exposure and either SCC or BCC.

Benefits of sun exposure; Risks of inadequate sun exposure

General

Scientific inquiry into the benefits of sun exposure languished for many decades following the observation in the 1920s that farmers in Europe developed non-melanoma skin cancer on their most sun-exposed areas - their ears, face, nose and backs of their hands.\textsuperscript{61} Research on the benefits of sun exposure has accelerated in the past 15 y and particularly in the past 5 y.\textsuperscript{62}

Vitamin D

Biological plausibility

Vitamin D is a hormone and most cells and organs in the human body have a vitamin D receptor, which explains the wide variety of diseases and disorders that have been linked to vitamin D insufficiency in epidemiological studies.\textsuperscript{63} The production of vitamin D by UV B radiation, the availability of vitamin D in food and supplements, and the biological plausibility of vitamin D as a mediator for a large variety of favorable health outcomes are well described in the literature.\textsuperscript{22-25,63-65}

Recommended vitamin D status

There is considerable controversy within the scientific community regarding optimum 25(OH)D levels for human health. In 2010, the Institute of Medicine defined vitamin D deficiency as 25(OH)D of less than 12 ng/mL and vitamin D insufficiency as 25(OH)D of less than 20 ng/mL.\textsuperscript{2} In 2011, The Endocrine Society defined vitamin D deficiency as 25(OH)D below 20 ng/mL and vitamin D insufficiency as 25(OH)D of 21–29 ng/mL.\textsuperscript{66} Others have suggested even higher levels.\textsuperscript{22,67-69} A letter signed by many respected vitamin D scientists and physicians recommends 40–60 ng/mL\textsuperscript{70} which is in line with what the Endocrine Society recommended as the preferred range for health – i.e, a 25(OH)D of 40–60 ng/mL.\textsuperscript{66} Most reference laboratories have raised the lower boundary of the normal range to 30 ng/mL.\textsuperscript{68}

Prevalence of vitamin D deficiency/insufficiency

Ginde et al. 2009\textsuperscript{38} reported that NHANES data on serum 25(OH)D levels show that the prevalence of 25(OH)D of less than 10 ng/mL increased from 2% of the US population in NHANES III (1988–1994) to 6% in NHANES 2001–2004, and that over the same period the prevalence of 25(OH)D of less than 20 ng/mL increased from 22% of the US population to 36%.\textsuperscript{4} The IOM report did not offer a solution to this problem since that was not its purpose; the IOM was charged with determining the DRI of vitamin D supplements and found that there was insufficient scientific evidence on the benefits of vitamin D supplementation to support raising the DRI of vitamin D supplements to more than 600 International Units (IUs) per day.\textsuperscript{8} Using the Endocrine Society’s definition of vitamin D sufficiency of 30 ng/mL, the level of vitamin D insufficiency increased from 55% of the US population in NHANES III to 77% in NHANES 2001–2004,\textsuperscript{38} which indicates that the vast majority of Americans have an insufficient vitamin D status.

Mediators other than vitamin D

Several studies, discussed below, have found that mediators other than vitamin D are or may be involved in the beneficial effects of adequate sun exposure.

Benefits of vitamin D/sun exposure; Risks of vitamin D insufficiency/inadequate sun exposure

We next examined the health benefits associated with increasing levels of sun exposure and/or circulating serum 25(OH)D and the health risks associated with inadequate sun exposure and/or inadequate serum 25(OH)D, with particular emphasis on studies published since the 2010 IOM report.

\textsuperscript{1}The differences between NHANES III and NHANES 2001-2004 may be attenuated by approximately 4 ng/mL after adjustment for improvements in the serum 25(OH)D assay performance from NHANES III to NHANES 2001-2004.\textsuperscript{71}

\textsuperscript{2}The Endocrine Society’s 2012 review of the nonskeletal effects of vitamin D also found there was insufficient evidence to support a role of vitamin D supplementation in correcting vitamin D insufficiency.\textsuperscript{66}
**All-cause mortality**

Chowdhury et al. 2014\(^\text{72}\) performed a meta-analysis of data from 73 cohort studies with 849,000 participants and 22 randomized controlled trials with 31,000 participants. This study found an inverse association of circulating 25(OH)D with risks of death due to cardiovascular diseases, cancer and other causes (RR 1.35, 95% CI 1.22–1.49 for all cause mortality, comparing the bottom third versus top 2-thirds of baseline circulating 25(OH)D distribution), but found that, with respect to possible benefits of vitamin D supplementation, further investigation is required before any widespread supplementation occurs. The prevalence of vitamin D insufficiency (defined as 25(OH)D less than 30 ng/mL) was found to be 69.5% for the United States and 86.4% for Europe. The authors further estimate that 9.4% of all deaths in Europe and 12.8% in the United States could be attributable to vitamin D insufficiency. Other meta analyses include Garland et al. 2014\(^\text{73}\) who pooled the data from 32 studies (30 cohort studies and 2 nested case-control studies) that examined age-adjusted all-cause mortality and serum 25(OH)D levels and found that the overall age-adjusted hazard ratio for all-cause mortality comparing the lowest (0–9 ng/mL) group to the highest (greater than 50 ng/mL) was 1.9 (95% CI 1.6–2.2), indicating that individuals in the lowest group had nearly twice the age-adjusted death rate as those in the highest quantile. Schottker et al. 2014\(^\text{74}\) conducted a meta-analysis of 8 cohort studies with 26,000 participants and found a 1.6-fold higher all-cause mortality in the bottom quintile (25(OH)D approximately <12 ng/mL) compared with the top quintile (25(OH)D approximately > 24 ng/mL) (RR 1.57, 95% CI 1.36–1.81).

Lindqvist et al. 2014\(^\text{75}\) assessed the avoidance of sun exposure as a risk factor for all-cause mortality for 29,518 Swedish women in a prospective 20-year follow-up of the Melanoma In Southern Sweden cohort and found that the population attributable risk for all-cause mortality for those habitually avoiding sun exposure was 3%. As compared to the highest sun exposure group, the all-cause mortality rate was doubled (RR 2.0, 95% CI 1.6–2.5) among avoiders of sun exposure and increased by 40% (RR 1.4, 95% CI 1.1–1.7) in those with moderate exposure. The authors noted that Sweden has national guidelines providing restrictive advice on sun exposure habits in order to lower the risk of skin cancer, and stated that these guidelines may be harmful in terms of overall health of the population. Lindqvist et al. 2016\(^\text{76}\) found that women with active sun exposure habits were mainly at lower risk of cardiovascular disease mortality and other non-cancer mortality, and noted that avoidance of sun exposure is a risk factor for death of a similar magnitude as smoking. “Our finding that avoidance of sun exposure was a risk factor for all-cause death of the same magnitude as smoking is novel.”

Afzal et al. 2014\(^\text{77}\) conducted a Mendelian randomization analysis showing that genetically low 25(OH)D levels were associated with increased all-cause mortality, but not with cardiovascular mortality. These results confirm that the measured low 25(OH)D levels in the general population associated with increased mortality as indicated in the above meta-analyses are related to vitamin D rather than simply a consequence of poor health or sequestration of vitamin D in adipose tissue, but indicate that some mediator other than vitamin D may be involved in cardiovascular mortality. Afzal et al. 2014\(^\text{77}\) was the first study with sufficient sample size to investigate the association of genetically low 25(OH)D levels with increased mortality.

**Colorectal cancer**

Rebel et al. 2014\(^\text{78}\) showed for the first time the causality of the relationship between moderate UVR exposure and primary intestinal tumors in mice. The UVR-induced reduction in intestinal cancer in mice could at least in part be attributed to vitamin D. However, the investigators also found a reduced progression to malignancy as a result of UVR exposure which appeared not to be attributable to vitamin D. Three groups of hairless mice were compared: one on a low-vitamin D diet without vitamin D supplementation or UVR exposure, one on a low-vitamin D diet with vitamin D supplementation but without UVR exposure, and one on a low-vitamin D diet without vitamin D supplementation but with moderate UVR exposure. This permitted the comparison of effects of dietary vitamin D supplementation and UVR exposure. The tumor load (area) was similarly and significantly reduced in both the vitamin D supplementation group and the UVR exposure group, but only the UVR exposure group had a lower percentage of malignant adenocarcinomas. Thus the study provided the first
experimental evidence that physiologically relevant, moderate UVR exposure can reduce the load of primary intestinal tumors, which reduction can at least in part be explained by an increase in vitamin D status as a comparable reduction in tumor load was observed in the vitamin D supplementation group that had a similar increase in vitamin D status. However, a reduction in malignant progression and growth of adenocarcinomas could not be attributed to vitamin D as these effects were only observed with moderate UVR exposure and not with dietary vitamin D supplementation. Rebel et al. 2014\textsuperscript{78} noted that prior studies had long shown that low exposure to solar UVR is significantly associated with increased risk of colon cancer, and that several recent studies showed that increased risk of colon cancer was significantly associated with prediagnostic low vitamin D status. The 2010 IOM report\textsuperscript{64} acknowledged that epidemiological studies examining associations between vitamin D status and colorectal cancer incidence generally supported an inverse association, but declined to base vitamin D DRI’s on colon cancer outcomes because of the paucity and conflicting findings of prospective randomized controlled trials involving vitamin D supplementation. Notably, the most recent, and only observational, study reviewed in the IOM report found no association of vitamin D supplementation with colon cancer risk, but found that patients in the highest quintile of prediagnostic circulating 25(OH)D concentration (more than 40 ng/mL) had a 42% reduced risk of colon cancer as compared to patients with the lowest quintile (less than 10 ng/mL).\textsuperscript{79}

Breast cancer incidence and mortality

Mohr et al. 2014\textsuperscript{80} conducted a meta-analysis of data from 5 studies on the relationship between serum 25(OH)D levels at time of breast cancer diagnosis and breast cancer mortality which found that patients in the highest quintile of 25(OH)D (more than 32 ng/mL) had approximately half the death rate from breast cancer as those in the lowest quintile (less than 14 ng/mL) (HR 0.56; 95% CI: 0.4–0.7). The authors recommended that serum 25(OH)D levels in all breast cancer patients should be restored to the normal range, which the authors defined as 30–80 ng/mL.

Engel et al. 2010\textsuperscript{81} found a 27% reduced risk of breast cancer incidence in women in the highest tertile of 25(OH)D (greater than 27ng/mL) as compared to the lowest tertile (less than 19.8 ng/mL) in a nested case-control study (OR 0.73; 95% CI: 0.55–0.96). The authors noted that all 6 previous case-control studies on the subject have reported a significant inverse association between serum 25(OH)D levels and breast cancer and that an inverse effect between sun exposure and breast cancer has previously been observed. John et al. 1999\textsuperscript{82} found that women with higher solar UVB exposure in NHANES III had only about half the incidence of breast cancer as those with lower solar exposure (RR 0.50; 95% CI: 0.33–0.80) and Knight et al 2007\textsuperscript{83} found that increasing sun exposure from ages 10 to 19 reduced breast cancer risk by 35% (OR 0.65, 95% CI 0.50–0.85 for the highest quartile of outdoor activities vs. the lowest).

Non-hodgkins lymphoma, colorectal, prostate and breast cancer, and multiple sclerosis

Van der Rhee et al. 2013\textsuperscript{84} noted that the association between solar radiation and reduced cancer mortality in North America was identified more than 60 years ago\textsuperscript{15} and that in 1980 it was hypothesized that vitamin D was the protective factor.\textsuperscript{40} The authors conducted a systematic review to verify if epidemiological evidence is in line with the hypothesis that the possible preventative effect of sunlight on cancer is more than just the effect of vitamin D. Vitamin D intake studies were excluded from the review and the authors stated that their review presented the sum of epidemiological knowledge on the influence of sun exposure and circulating 25(OH)D levels on the risk of colorectal cancer, prostate cancer, breast cancer and non-Hodgkin’s lymphoma (NHL). They concluded that: 1) there is an inverse association between sun exposure and both colorectal cancer risk and colorectal cancer mortality; 2) there is an inverse association between vitamin D status and both colorectal cancer risk and colorectal cancer mortality; 3) there is a negative association between sun exposure and prostate cancer risk and prostate cancer mortality but not between vitamin D status and prostate cancer risk or mortality; 4) there is an inverse correlation between sun exposure and breast cancer risk and breast cancer mortality, and possibly between 25(OH)D and breast cancer mortality, but studies on the association between 25(OH)D and breast cancer risk are inconclusive; 5) there is a negative association between sun exposure and NHL risk and NHL mortality but not between vitamin D
status and NHL risk or mortality; 6) there is a negative association between sun exposure and lymphoma risk, but no association between lymphoma risk and vitamin D intake or 25(OH)D levels; and, 7) for multiple sclerosis, both experimental and epidemiological studies show that the preventative role of sun exposure is independent of vitamin D production. The authors concluded that for colorectal cancer and breast cancer the benefit of sun exposure is mediated by high vitamin D levels produced by sun exposure, whereas for prostate cancer, NHL and multiple sclerosis the benefit of sun exposure is independent of vitamin D.

Bladder cancer
Zhao et al. 201686 found a 30% reduced risk of bladder cancer associated with 25(OH)D concentrations above 30 ng/mL compared to less than 15 ng/mL.

Cardiovascular disease (CVD)
Liu et al. 201487 found that hypertension is reduced by UVR-induced nitric oxide independent of vitamin D. They showed that stores of nitrogen oxides in the human skin are mobilized to the systemic circulation by exposure of the body to UVA radiation, causing arterial vasodilation and a resultant decrease in blood pressure independent of vitamin D, confirming the hypothesis of Feelisch et al. 2010.88 These results correlate with the findings of Afzal et al. 201477 that genetically low 25(OH)D levels were associated with increased all-cause mortality but not with cardiovascular mortality, indicating that a mediator other than vitamin D may be involved in cardiovascular mortality, and with the results of Tunstall-Pedoe et al. 201589 challenging vitamin D’s alleged role in cardiovascular disease.

Metabolic syndrome (MetS) and type 2 diabetes
Vitezova et al. 201590 found that higher 25(OH)D levels were associated with lower prevalence of metabolic syndrome (OR 0.61, 95% CI 0.49–0.77 for more than 30 ng/mL versus less than 20 ng/mL) in the elderly in an analysis of data from 3240 people (median age 71.2 years) imbedded in the Rotterdam Study, a prospective population-based cohort study of middle-aged and elderly adults. Importantly, after adjustment for body mass index (BMI), higher 25(OH)D levels were still significantly associated with lower odds of MetS. Almost concurrent with Vitezova et al. 2015, Clemente-Postigo et al. 201591 showed that low 25(OH)D levels are associated with type 2 diabetes independently of BMI. These findings are important in light of the 2010 IOM report’s discounting of the association studies linking low 25(OH)D levels to increased risk of type 2 diabetes on the ground that they may be confounded by obesity, which not only predispose individuals to type 2 diabetes but may also cause lower 25(OH)D levels as a result of sequestration of vitamin D in adipose tissue and possibly other mechanisms. Vitezova et al. 2015 noted that other recent studies had found an inverse association between vitamin D status and MetS in younger populations, but only one other study of older persons had found the association while another study of older persons had not. Neither Vitezova et al. 2015,125 nor Clemente-Postigo et al. 201591 cited Geldenhuys et al. 2014,92 which found that UVR exposure levels, not vitamin D supplements or 25(OH)D levels, reduced the risk of obesity and type 2 diabetes, indicating that 25(OH) levels may be to some extent a marker for UVR exposure in this regard.

Afzal et al. 201393 measured 25(OH)D levels in 9841 persons of whom 810 developed type 2 diabetes during 29 y of follow-up. The investigators observed an association of low 25(OH)D with increased risk of type 2 diabetes (HR 1.35, 95% CI 1.09–1.66 for lowest (less than 5 ng/mL) vs. highest (more than 20 ng/mL) quartile of 25(OH)D. This finding was substantiated by the authors’ meta-analysis of 14 studies representing 16 cohorts with a total of 72,204 participants and 4,877 type 2 diabetes events (HR 1.50, 95% CI 1.33–1.70 for the bottom vs. top quartile of 25(OH)D). A prior 2011 meta-analysis [134 Mitri 201194] had shown that individuals with 25(OH)D levels above 25 ng/mL had a 43% lower risk of developing type 2 diabetes (95% CI, 2457%–) compared with individuals with 25(OH)D levels below 14 ng/mL, and that vitamin D supplementation had no effect.

Alzheimer disease and cognitive decline
Littlejohns et al. 201495[135] studied a group of 1,658 Americans age 65 and older who were able to walk unaided and who were free of dementia. The participants were followed for 6 y to investigate who went on to develop Alzheimer disease and other forms of dementia. The investigators found that participants
with serum 25(OH)D levels below 10 ng/mL were more than twice as likely to develop Alzheimer disease than participants with serum 25(OH)D levels greater than 20 ng/mL (HR 2.22, 95% CI 1.02–4.83) and participants with serum 25(OH)D levels of 10 ng/mL to 20 ng/mL were 69% more likely to develop Alzheimer disease than participants with serum 25(OH)D levels greater than 20 ng/mL (HR 1.69, 95% CI 1.06–2.69).

Similar results were obtained for all-cause dementia. According to the authors, this was the first large, prospective, population-based study incorporating a comprehensive adjudicated assessment of dementia and Alzheimer to examine their relationship with vitamin D concentrations. This study confirms other recent studies linking low vitamin D levels with cognitive decline.96-102

Keeney et al. 201396 manipulated vitamin D status in middle-age to old-age rats by dietary supplementation with low, moderate and high levels of vitamin D. The results suggested that dietary vitamin D deficiency contributes to significant nitrosative stress in the brain and may promote cognitive decline in middle-age and elderly humans.

Annweiler et al. 201397 was a systematic review and meta-analysis finding that 25(OH)D levels were lower in Alzheimer cases than in controls (summary random effect size 1.40, 95% CI 0.26–2.54), which means that the probability is about 140% that an individual without Alzheimer would have a higher 25(OH)D level than an individual with Alzheimer if both individuals were chosen at random from a population.

Multiple sclerosis (MS), type 1 diabetes, rheumatoid arthritis

Wang et al. 2014103 found that UVR suppressed experimental autoimmune encephalomyelitis (EAE - an animal model of MS), independent of vitamin D production, confirming the conclusions of van der Rhee et al. 201384 and the findings of Becklund et al. 2010.104 The investigators showed that UVB irradiation did not suppress immune response in the periphery, but suppressed EAE by blocking selectively the infiltration and binding of inflammatory cells into the central nervous system. These findings support the long-held view that the incidence of MS is inversely related to UVR exposure.105-109

Baarnhielm et al. 2012110 was an association study finding that persons with low UVR exposure had a significantly increased risk of MS compared with those who reported the highest exposure (OR 2.2, 95% CI 1.5–3.3), and that this association persisted after adjustment for vitamin D status. Wang et al. 2014103 and Baarnhielm et al. 2012110 confirmed the conclusions of van der Rhee et al. 201383 that sun exposure reduces the risk of MS through pathways independent of vitamin D.

Ponsonby et al. 2005108 stated that genetic factors appear to be involved in MS, but the low concordance among identical twins for MS111 and trends of increasing incidence of MS over time112 suggest environmental factors are also important determinants, and that UVR exposure may be one factor that can attenuate MS through several mechanisms and that some pathways are independent of vitamin D. Similar conclusions were made about 2 other autoimmune diseases, type 1 diabetes and rheumatoid arthritis. The authors concluded that it was critical to consider the benefits of sun exposure as well as the risks, and to provide information to the public on the minimum sun exposure required for beneficial health effects as well as the maximal sun exposure to avoid the adverse health effects associated with excessive sun exposure. Mokry et al. 2015113 was a Mendelian randomization analysis showing that genetically low 25(OH)D levels were associated with increased risk of MS. Jalkanen et al. 2015114 found a high level of vitamin D deficiency during pregnancy in MS patients.

Jacobsen et al. 2015115 found that more sun exposure in the third gestational trimester was associated with lower risk of type 1 diabetes in male children. Sawah et al. 2016116 found a high prevalence of vitamin D deficiency (25(OH)D levels less than 20 ng/mL) in children and adolescents with type 1 diabetes. Kostoglou-Athanssiou et al. 2012117 found a high prevalence vitamin D deficiency in patients with rheumatoid arthritis.

Psoriasis

Gisondi et al. 2012118 found that the prevalence of 25(OH)D of less than 20 ng/mL was 57.8% in patients with psoriasis vs. 29.7% in healthy controls, and that in a logistic regression analysis, vitamin D deficiency was associated with psoriasis independently of other factors (OR 2.50, 95% CI 1.18–4.89).
The investigators noted that topical vitamin D derivatives and UVB radiation are used in the treatment of psoriasis. Vitamin D status was found to be unrelated to levels of self-reported sun exposure, but the measure used for sun exposure, which was minutes per day of sun exposure from March to September, may not have been appropriate for vitamin D production since it apparently did not include the time of day or the area of skin exposed.

**Liver disease**

Gorman et al. 2015\(^{119}\) in a review stated that a large number of studies in recent Years\(^{92,120,121}\) have shown that exposure to UVR has the potential to curtail the development of non-alcoholic fatty liver disease (NAFLD) through vitamin D dependent and vitamin D independent mechanisms. The authors noted that most observational studies support an inverse association between serum 25(OH)D levels and NAFLD, but that vitamin D supplementation did not produce the same results. The authors further stated that circulating vitamin D levels may represent a proxy for bodily exposure to sunlight\(^{122}\) explaining the observation that mediators induced by sun exposure other than vitamin D may play important roles in curtailing NAFLD.

**Statin intolerance and muscle pain, weakness**

Khayznikov et al. 2015\(^{57}\) found that statin intolerance because of myalgia, myositis, myopathy, or myonecrosis associated with serum 25(OH)D less than 23 ng/mL can be resolved with vitamin D supplementation raising serum 25(OH)D to 53 ng/mL. Aleksic et al. 2015\(^{123}\) found that low vitamin D levels are a potentially significant and correctible risk factor for statin-related myopathy, especially in African-Americans.

**Macular degeneration**

Millen et al. 2015\(^{124}\) observed a 6.7-fold increased risk of age-related macular degeneration (AMD) among women with serum 25(OH)D levels less than 12 ng/mL who also had genetic risk for AMD, and noted that previous studies had found that decreased odds of AMD are associated with high compared to low concentrations of 25(OH)D.

**Dental caries in infants**

Schroth et al. 2014\(^{125}\) found that low prenatal 25(OH)D concentrations were associated with increased risk of dental caries among offspring in the first year of life.

**Reverse causation**

Autier et al. 2014\(^{126}\) suggested that low serum 25(OH)D levels may be the result rather than the cause of diseases associated with low serum 25(OH)D levels in observational studies (reverse causation). The authors offer little evidence to support such a hypothesis, and it is contraindicated by the prospective nature of many of the studies linking serum 25(OH)D levels with health outcomes, by Mendelian randomization studies\(^{77,113}\) and by the body of knowledge concerning the bioactivity of vitamin D, particularly its cancer-inhibiting properties.

**Obesity**

Geldenhuys et al. 2014\(^{92}\) suggests that UVR exposure may be an effective means of suppressing the development of obesity and metabolic syndrome through mechanisms that are independent of vitamin D but dependent on other UVR-induced mediators such as nitric oxide. This study investigated whether UVR and/or vitamin D supplementation had an effect on the development of obesity and type 2 diabetes in mice fed a high-fat diet, and found that UVR significantly suppressed weight gain but vitamin D supplementation did not. These results indicate that low vitamin D status in obese persons may only be a marker for low UVR exposure or a result of sequestration of vitamin D in adipose tissue, and provide a new view of previous studies showing a consistent association between increasing body mass index and lower serum 25(OH)D levels.\(^{127}\)

**Myopia**

French et al. 2015\(^{128}\) was a review stating that recent epidemiological evidence suggests that children who spend more time outdoors are less likely to be or to become myopic, irrespective of how much near work they do or whether their parents are myopic. The likely mechanism for this protective effect is visible light stimulating release of dopamine from the retina, which inhibits increased axial elongation, the structural basis of myopia.
The authors describe the effect of time outdoors on the risk of myopia as robust. The prevalence of myopia in the US in persons 12 to 54 y old increased 66% between 1971–1972 and 1999–2004, from 25.0% to 41.6%, according to the National Eye Institute of the National Institutes of Health. For African Americans, the increase was 157.7%. This high prevalence of myopia presents a major public health problem since, in addition to requiring corrective lenses, myopia poses substantially increased risk of retinal detachment, glaucoma, macular degeneration, amblyopia and cataracts.

Other benefits of sun exposure

Lambert et al. 2002 suggested that the prevailing amount of sunlight affects brain serotonergic activity. Deficiencies in serotonin and brain serotonergic activity have been linked to sudden infant death syndrome, seasonal affective disorder, depression, schizophrenia, Alzheimer disease, and migraine headaches. Beta-endorphin, a neurohormone that acts as an analgesic, has been known for many years to be released in the human body by exercise, producing a feeling of wellbeing similar to the feeling of wellbeing induced by sun exposure. A recent study showed that UVR exposure significantly raised circulating plasma β-endorphin levels in a UV-exposure mouse model, leading to suggestions that UVR exposure is addictive. Alternatively, the release of β-endorphins by sun exposure could be a natural reward mechanism encouraging sun exposure.

The benefits of serotonin and β-endorphin, as well as the effects of sun exposure on melatonin, photodegradation of folic acid, immunomodulation, photoadaptation, and circadian clocks, are reviewed in van der Rhee et al. 2016.

Vitamin D supplements vs. sun exposure

In light of the studies discussed in this review that found health outcomes related to sun exposure independent of vitamin D, health outcomes dependent on serum 25(OH)D levels but not vitamin D supplementation, and health outcomes dependent on mediators other than vitamin D, it is apparent that vitamin D supplements are not an effective substitute for adequate sun exposure.

Balancing the risks of moderate non-burning sun exposure against the risks of inadequate sun exposure

The only identified risk associated with the amount of non-burning sun exposure needed to achieve serum 25(OH)D levels of 30 ng/mL is some possible increased risk of nonmelanoma skin cancer. The amount of sun exposure required to produce this level of vitamin D varies among individuals and according to time of year, time of day and latitude. White people with Type II skins at 40 degrees latitude can obtain their annual requirements of vitamin D by spending about 15 minutes in the sun with face, arms and legs exposed (half that time if in a bathing suit) 2 to 3 times a week between 11 a.m. and 3 p.m. during the months of May through October. In comparison, nonmelanoma skin cancer is associated with many thousands or tens of thousands of cumulated hours of lifetime sun exposure. Moreover, inadequate acclimatization to UVR in daily life carries the risk of sunburn and corresponding increased risk of both nonmelanoma skin cancer and melanoma.

The risks of inadequate non-burning sun exposure include increased risks of all-cause mortality, colorectal cancer, breast cancer, non-Hodgkins lymphoma, prostate cancer, pancreatic cancer, hypertension, cardiovascular disease, metabolic syndrome, type 2 diabetes, obesity, Alzheimer disease, multiple sclerosis, type 1 diabetes, rheumatoid arthritis, psoriasis, non-alcoholic fatty liver disease, statin intolerance, macular degeneration and myopia.

People with darker skins require more time in the sun to produce their requirements of vitamin D but also have lower risks of nonmelanoma skin cancer, and people with Type I skins, who are unable to tan, require less time in the sun but have higher risks of nonmelanoma skin cancer. All persons should avoid sunburns, which are associated with substantial increased risk of melanoma and nonmelanoma skin cancer.

There are 6 categories of skin on the Fitzpatrick Scale: Type I Very Fair White - always burns, never tans; Type II Fair White - usually burns, tans minimally; Type III Cream White – sometimes mild burn, gradually tans; Type IV Brown – rarely burns, tans with ease; Type V Dark Brown – very rarely burns, tans very easily; Type VI Black – never burns, tans very easily.
Conclusions

Insufficient sun exposure has become a major public health problem, demanding an immediate change in the current sun-avoidance public health advice. The degree of change needed is small but critically important. The public must be advised to obtain enough sun exposure and vitamin D supplementation to maintain a serum 25(OH)D level of at least 30 ng/mL. The skin has a large capacity to produce vitamin D and a single whole body exposure to an amount of sunlight that is equal to 1 minimal erythemal dose is equivalent to ingesting approximately 15,000–20,000 IUs of vitamin D. Therefore to produce an equivalent of 4000 IUs of vitamin D a day would require that 50% of the body surface be exposed to 0.5 MEDs. To achieve a blood level of at least 30 ng/mL would require ingesting 2000 IUs of vitamin D daily which would be equivalent to 25% of the body surface exposed to 0.5 MEDs 2–3 times a week. The amount of sun exposure required to achieve an MED depends on skin pigmentation, latitude, time of day and time of year. Warnings on the dangers of sunburn at any age should be emphasized. Periodic testing of serum 25(OH)D levels is also reasonable especially at the end of the summer which is when the blood level of 25(OH)D is at its highest level.  

Abbreviations

5(OH)D 25-hydroxyvitamin D  
BCC basil cell carcinoma  
CI confidence interval  
CVD cardiovascular disease  
HR hazard ratio  
IU international units  
MS multiple sclerosis  
NMSC non-melanoma skin cancer  
ng/mL nanograms per milliliter  
NHL non-Hodgkin’s lymphoma  
OR odds ratio  
RR relative risk  
SCC squamous cell carcinoma  
UVR Ultraviolet Radiation (290–400 nm)  
UVA Ultraviolet-A (316–400 nm)  
UVB Ultraviolet-B (290–315 nm)

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Sunlight Has Cardiovascular Benefits Independently of Vitamin D

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Key Words
Ultraviolet · Skin · Nitric oxide · Blood pressure · Nitrate · Vitamin D · Sunlight · Cardiovascular

Abstract

Background: High blood pressure (BP) is the leading risk factor for disability adjusted life years lost globally. Epidemiological data show a correlation between increased sun exposure and reduced population BP and cardiovascular mortality. Individuals with high serum vitamin D levels are at reduced risk of hypertension, cardiovascular disease and metabolic syndrome, yet multiple trial data show that oral vitamin D supplementation has no effect on these endpoints. Sunlight is a risk factor for skin cancers, but no link has been shown with increased all-cause mortality. Cohort studies from Scandinavia show a dose-dependent fall in mortality with increased sun-seeking behaviour. Skin contains significant stores of nitrogen oxides, which can be converted to NO by UV radiation and exported to the systemic circulation. Human studies show that this pathway can cause arterial vasodilatation and reduced BP. Murine studies suggest the same mechanism may reduce metabolic syndrome. Summary: Sunlight has beneficial effects on cardiovascular risk factors independently of vitamin D. Key Messages: All-cause mortality should be the primary determinant of public health messages. Sunlight is a risk factor for skin cancer, but sun avoidance may carry more of a cost than benefit for overall good health.

The most recent data from the World Health Organisation’s survey of the global burden of disease show that high blood pressure (BP) is the leading cause of premature death and disease worldwide [1]. This risk factor underlies stroke and coronary heart disease, which in combination have an age-standardised mortality of 237 per 100,000 in the United States [2]. Measures to control hypertension are thus of the greatest importance.

Epidemiology

Active management of hypertension with effective modern drugs has led to a fall in population BP within western economies. Plotting population BP in 1980 – before the availability and widespread use of effective pharmacological agents – against latitude, a clear correlation exists with around a quarter of variation in BP attributable for by latitude (fig. 1). This relationship persists when the data are stratified by country income level. Seasonal changes in BP are also well described, with individual BP being lower in summer than winter in temperate latitudes [3]. Around a quarter of cardiovascular mortality within Europe can be accounted for by latitude [4], and in a multicentre observational study of risk factors correlating with atherosclerosis, latitude was found to be the strongest predictor of carotid artery atheroma [5].

Biologically active vitamin D (1,25 di-hydroxy cholecalciferol) in man can be derived from the diet or syn-

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thesised endogenously in a pathway dependent on UVB irradiation of the skin. Inadequate sun exposure with insufficient dietary intake can thus lead to deficiency (25(OH)D <20 ng/ml) and insufficiency (25(OH)D 20–29 ng/ml). Vitamin D receptors are expressed on most cell types, and they play a well-established role in skeletal metabolism. Additionally, in vitro mechanistic studies show vitamin D to have effects on cell differentiation and immune function [6]. Observational data from numerous large cohort studies, now summarised in several meta-analyses show that individuals with measured vitamin D levels in the lowest quartile have around twice the all-cause mortality of those in the upper quartile, and are more likely to have hypertension, cardiovascular disease, metabolic syndrome, and solid organ cancers [7–9]. Clinical trials of vitamin D supplementation have however shown that vitamin D is of no benefit in the prevention or treatment of hypertension, cardiovascular disease, cerebrovascular disease or metabolic syndrome, although it is important for bone health [8]. This is further supported by a recent Mendelian randomisation study, which showed that patients with genetic polymorphisms leading to lifelong reduced vita-

For the general white-skinned population, sunlight is the major preventable risk factor for skin cancers, but the pattern of sun exposure varies with cancer type. Intermittent sun exposure and sunburn, particularly in childhood, increase the risk of melanoma, whereas chronic occupational exposure may be protective [13]. Squamous cell skin cancer by contrast is predisposed in a dose-dependent fashion by chronic sun exposure. Immunosuppression particularly increases the risk of developing SCC, a link first made in patients who had undergone renal transplantation, with subsequent immunosuppression. SCCs in the immunosuppressed are clinically harder to diagnose than in the immunocompetent and are more likely to metastasise. Advice on sun avoidance is thus particularly important to renal allograft recipients, and these patients require regular screening, and a high index of suspicion from their dermatologist [14].

Skin cancers can be used as a proxy measure for lifetime sun exposure. A case–control study of 4.4 million Danish patients over the age of 40, showed that NMSC patients had a multi-factorially corrected OR of 0.97 (0.96–0.99) for all-cause mortality compared to age- and sex-matched ‘healthy’ controls. The reduction in cardio-

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**Fig. 1.** Population BP correlates with latitude. Each point represents a country. Male systolic population BP is plotted against the latitude of the geographical mid-point of each country. BP values are from the MRC-HPA data in 1980.
vascular disease was greater, with an OR of 0.90 (0.88–0.92) for incident myocardial infarction [15, 16].

Prospective cohort studies are less prone to confounding and bias than case–control studies. Two Scandinavian studies, initiated in the early 1990s, have provided valuable information on sun exposure and all-cause mortality. In the Swedish Women’s Lifestyle and Health cohort study, increased sun exposure, as recorded by the number of weeks spent on sun-bathing holidays, predicted reduced all-cause mortality 25 years later [17] even at the expense of increased melanoma [18]. Subjects in the Melanoma in Southern Sweden study were asked about sun-bathing, sun-seeking holidays in summer, sun-seeking holidays in winter, and use of sunbeds to give a sun-exposure score of 0–4. Extensive adjustment for possible confounders was made, and subjects were re-poll 25 years after enrolment. Dose dependently, the higher the sun-seeking behaviour, the lower the all-cause mortality, with those scoring 4 having half the mortality of sun-avoiders. Extrapolating from these data, the authors calculate that 3% of deaths in Sweden can be accounted for by inadequate sun.

Scandinavian data on sunlight and all-cause mortality may not be generally applicable. A similar prospective design of study in the United States, the NIH-AARP Diet and Health Study, showed a small increase in mortality in those who had lived in the most insolated areas [19], although it showed no increase in the number of skin cancer deaths. The study did not measure individual sun exposure, but instead calculated environmental sun exposure based on the residence of the individual at the time of enrolment. It may be that higher levels of sun exposure than those experienced by north Europeans are unhealthy, or alternatively that individuals living in the sunniest areas adopt lifestyles that avoid the sun [20].

The balance of epidemiological and observational data thus suggests that sunlight exposure can reduce all-cause mortality, and has particular benefits on hypertension and cardiovascular disease. These benefits are at the cost of increasing the risk of skin cancer incidence, although the overall benefits outweigh the risks as demonstrated by dose-dependent reductions in all-cause mortality with increased sun exposure. Importantly, vitamin D is not solely responsible for these proposed health benefits of sunshine. Supplementation with oral vitamin D is not adequate to reduce cardiovascular disease. Alternative mechanisms must exist to account for these benefits of sunlight.

Nitric oxide has a wide range of roles, but the first described was as a vasodilator, synthesised by the actions of one of the family of 3 nitric oxide synthase (NOS) enzymes on L-arginine. NO has a half-life of a few seconds before being oxidised to nitrite (NO$_2^-$), which itself has biological actions, particularly in conditions of hypoxia and low pH, where it can be reduced to NO. Nitrite is further oxidised to nitrate (NO$_3^-$) and this was considered the inert end product of NO until recently. The dermis and epidermis contain significant stores of nitrogen oxides particularly nitrate, the quantity of which is about 10 times as much as in the total vascular space [21].

Although nitrate has been considered to be biologically inactive, it is now apparent that an alternative mechanism of NO synthesis involves sequential reduction of nitrate to nitrite and then NO [22]. This occurs on the skin surface, where nitrate-reducing bacteria generate nitrite from sweat nitrite. The nitrite in turn is reduced to NO in the slightly acidic conditions of the skin surface [23]. Bacterial nitrate reductases allow the use of nitrate as an electron acceptor in respiration in the absence of oxygen. Nitrate reductase enzymes have also been described in mammalian tissues [24]. Photochemical reduction of nitrate also occurs with ultraviolet wavelengths, and is enhanced in the presence of thiols [25]. Thiol-rich cysteine is a major component of keratins, the key structural components of skin.

Human skin brings together nitrate, thiols, environmental ultraviolet radiation, and a rich dermal vascular plexus giving access to the systemic circulation. Irradiation of healthy human volunteers with physiologically relevant doses of ultraviolet A radiation (which does not synthesise vitamin D) produces a fall in systemic BP and rise in heart rate, independently of temperature change, and concurrent with a rise in circulating nitrite (a marker for NO levels) and fall in nitrate [26, 27]. Forearm plethysmography studies in which UVA irradiation of the arm occurs simultaneously with intra-brachial artery infusion of a NOS antagonist, show arterial vasodilatation, confirming that this effect is independent of NOS [26].

While these human in vivo studies are recent, the observation that sunlight and ultraviolet could directly dilate the arterial vasculature was made by Robert Furchgott almost 40 years before his Nobel prize for the discovery that ‘endothelium derived relaxant factor’ was NO. Following a chance observation in the laboratory where organ baths were intermittently exposed to daylight on a cloudy day, he showed that isolated arterial smooth muscle from which the endothelium had been removed dilated in response to ultraviolet radiation [28]. The absence of endothelium in these experiments differentiated these results from his later classic Nobel Prize–winning work, where he demonstrated an acetyl choline–driven
release of a diffusible vasodilator from endothelial cells. The mechanism of NO synthesis differs in these 2 experimental set ups, but NO is the active mediator in both [29].

UV-induced release of NO from the skin may have more widespread cardiovascular actions than BP reduction. Oral nitrate reduces oxygen cost during exercise [30] due to an improvement in mitochondrial efficiency [31]. We have shown that the combination of UVA irradiation and oral nitrate supplementation produces an additive improvement in exercise performance with reduced oxygen demand in elite cyclists [32].

Metabolic syndrome and type 2 diabetes have a lower prevalence in summer than in winter. In a mouse model of diabetes, mice fed with a high-fat diet developed weight gain, impaired glucose and insulin tolerance, fatty livers, and gonadal fat deposition [33]. Irradiation of the mouse with a sub-erythemal dose of UV twice weekly reduced weight gain and development of markers of metabolic syndrome, but addition of oral vitamin D supplementation had no effect. Applying a topical NO donor to the dorsal skin of the mice reproduced the effects of UV, and treating the mice with an NO scavenger on the back blocked the beneficial effects of the UV [33].

Ultraviolet therapy might well have a therapeutic role beyond the treatment of skin disease. It should be avoided in those with particular risk factors, such as the immunosuppressed transplant patient, but as a non-pharmacological intervention it has several potential benefits. Hypertension, metabolic syndrome and diabetes are three of the major morbidities of our age. The mechanistic and early trial data I have outlined suggest that these may be amenable to a form of phototherapy. Hypertension is clearly a risk factor that must be treated. In patients with impaired renal function, pharmacological choices are reduced and phototherapy offers potential as an adjunctive therapy. The reduced oxygen demand demonstrated in athletes treated with UVA and nitrate supplementation suggests benefit in patients with heart failure and other conditions where oxygen delivery is compromised.

Public health advice on sunlight exposure is at the crossroads. Almost a century of data has confirmed the carcinogenic effects of UV radiation on the skin, and delineated the mechanisms by which this occurs. There is however a remarkable absence of any evidence that UV reduces lifespan, in sharp contrast to other risk factors (e.g. hypertension, smoking, alcohol) on which we advise. A substantial body of evidence shows that sunlight has health benefits and that these are independent of vitamin D and thus cannot be reproduced by oral supplementation. The UV-induced reduction of cutaneous nitrate and its export to the systemic vasculature, which I have helped delineate, is an additional mechanism by which sunlight may exert beneficial effects on health, but other mechanisms surely exist. All-cause mortality and its reduction should be the primary aim of physicians, not the narrow avoidance of skin cancer.

Disclosure Statement

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References


A Review of the Use of Tanning Beds as a Dermatological Treatment

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ABSTRACT

Introduction: In-office phototherapy is an effective treatment for many dermatologic conditions, however, many patients are unable to adhere to the rigorous travel and time commitments sometimes needed. Tanning bed facilities are nearly ubiquitous in modern society and could represent a more convenient means to obtain ultraviolet (UV) exposure when office phototherapy is not feasible. The purpose of this study was to review available evidence on the use of tanning facilities as a treatment for dermatologic conditions.

Methods: PubMed was searched on February 2015 for “tanning beds” and “phototherapy”, and with some dermatologic conditions sensitive to UV light, including “psoriasis”, “mycosis fungoides”, “acne”, “atopic dermatitis” and “eczema”. From there, further articles were found using the reference sections of the initial papers. A similar methodology was used with the Google Scholar search engine. Only articles in English and prospective studies were included in this review.

Results: We found studies validating the use of tanning facilities for psoriasis treatment. Use as a treatment option for atopic dermatitis, mycosis fungoides, acne, scleroderma, vitiligo, and pruritus, as well as other UV sensitive dermatoses, may also be beneficial. This study is limited by the lack of double-blind, placebo-controlled trials, long-term follow-up studies, and meta-analyses for tanning facility use in dermatologic phototherapy, and by the lack of standardization of both tanning facilities and exposure dosing.

Conclusion: Unsupervised sun exposure is a standard recommendation for some patients to obtain phototherapy. Selected use of commercial tanning beds in the treatment of...
dermatologic conditions may be another useful and effective treatment for those patients with an inability to access office-based or home-based phototherapy.

**Keywords:** Acne; Dermatitis; Eczema; Mycosis fungoides; Phototherapy; Pruritus; Psoriasis; Tanning beds

**INTRODUCTION**

Ultraviolet (UV) phototherapy is used for a myriad of dermatologic conditions such as psoriasis and mycosis fungoides (MF). UV phototherapy is most commonly administered in an office setting, with ideal treatment typically consisting of several sessions per week.

While phototherapy is effective for many conditions, the time and expense of this treatment can be a burden and an obstacle [1]. Many patients live over one hundred miles from a dermatologist or have other time and resource limitations that make in-office phototherapy inaccessible. Therefore, in-office phototherapy may not be a pragmatic treatment option for many patients who could potentially benefit from it.

Unsupervised sun exposure is a standard recommendation when in-office phototherapy is not feasible [2]. Commercial tanning facilities may offer another potential alternative means to access phototherapy, being both conveniently located and economically feasible. This can provide access to phototherapy to many patients who currently find treatment with in-office phototherapy to be cumbersome or impracticable. We examined available evidence for the use of commercial tanning facilities as a dermatologic treatment modality in diseases such as atopic dermatitis, acne, hand eczema, MF, vitiligo, and pruritus.

**METHODS**

Literature searches were done in PubMed in February 2015 combining therapy descriptor keywords, such as “tanning beds” and “phototherapy”, with dermatologic conditions known or believed to be sensitive to UV light, including “psoriasis”, “mycosis fungoides”, “acne”, and “atopic dermatitis”/“eczema”. No inclusion or exclusion dates were defined. From there, further articles were found using the reference sections of the initial papers. A similar methodology was used with the Google Scholar search engine. Additional information was sought with targeted searches in both PubMed and Google Scholar. In conditions that did not have studies using commercial tanning beds, we investigated the efficacy of UV radiation overlapping with the emission spectrum of tanning beds. Only articles in English and prospective studies were included in this review. This article is based on previously conducted studies and does not involve any new studies of human or animal subjects performed by any of the authors.

**RESULTS**

**Characteristics of Indoor Tanning Light**

The light used during indoor tanning is poorly defined. The US Food and Drug Administration does not specify limits on the power of UV light emissions, instead defining “irradiance ratio limits”, where the ratio of irradiance between wavelengths of 200 and 260 nm to the irradiance between wavelengths 260 and 320 nm should not exceed 0.003 at any distance and direction from the source [3]. While in the US there are state and federal regulations, according to a study performed in
North Carolina, the extent to which commercial tanning facilities comply is poor, with only 1 out of 32 commercial tanning establishments within complete compliance of state and federal guidelines [4].

The wavelengths of UVA and UVB irradiation from tanning beds are highly variable; however, tanning beds as a whole tend to emit primarily UVA irradiation. Rates of UVB emissions range from 0.5% to 5.0% in North Carolina tanning beds [4]. Another study of North Carolina tanning beds found a wide range of UVA irradiance, 17.7–674.0 W/m² and a UVB range of 0.12–0.82 W/m² (2.11–14.00 minimal erythemal dose/h) [5].

Tanning beds analyzed in the UK between 2004 and 2005 showed tremendous variability in spectral distribution of UV output, resulting in the average erythemal irradiance ranging from 0.02–0.93 W/m², with an average of 0.41 W/m² [6]. In a study conducted in 2008, 78 indoor tanning facilities from 6 regions throughout Norway were characterized [7]. The average UVB irradiance was 0.194 W/m² erythema-weighted dose (range 0.059–0.489 W/m²), and the average UVA irradiance was 0.156 W/m² erythema-weighted dose (range 0.079–0.568 W/m²). Norway regulates indoor tanning facilities, with both short-wave and long-wave UV irradiance limits set at 0.15 W/m². Only 23.3% of tanning facilities were in compliance with maximal irradiances for both UVA and UVB spectra. Ninety-six percent of tanning bed devices were approved models, but only 74% of lamps in these tanning beds were an approved type. The maximum erythema-weighted UV irradiance varied by up to a factor of 2 for the same tanning bed devices in different facilities, due to the difference in lamps used. Additionally, within each facility, irradiance measures varied by up to a factor of two, due to the different tanning bed devices [7]. The variety of tanning bed devices and lack of standardization of lamps within these devices present a therapeutic hurdle to recommending their use as a treatment for skin disease.

**Efficacy of Tanning Beds**

While different tanning beds emit variable amounts of UVB and UVA (varying in both the absolute flux and the ratio of UVB to UVA), there is extensive in vitro evidence that both UVA and UVB have anti-inflammatory effects (Tables 1, 2).

**Risks of Tanning**

As with any UV light-based therapies, there are potential risks of using tanning beds as treatment (Table 3). There is a link between artificial UV light exposure and an increased risk of developing skin cancer. In 2006, a meta-analysis showed an increased risk of developing melanoma, squamous cell carcinoma (SCC), and basal cell carcinoma (BCC) in patients who have ever used a tanning bed compared with those who have never tanned with artificial UV light [8]. A particularly large increase in melanoma risk was found when comparing those who ever tanned before age 35 years to those who had never used an indoor tanning device. A subsequent study found a dose/response relationship between artificial UV light exposure and increasing risk of melanoma, with those having tanned 10 times or fewer having only a 34% increased risk of developing a melanoma, compared to 272% in those patients who have used indoor tanning beds over 100 times [9]. In a more recent study, an association was found between age of first tanning bed exposure and increased risk of melanoma in patients with more than 10 tanning bed exposures [10]. A large
prospective study found no association between age range of most frequent tanning bed use and risk of melanoma or SCC, but did find an even greater risk of BCC in women who visited tanning beds most frequently during their high school and college years compared to those who visited most frequently during age 25–35 years, both of which were greater than the risk in women who had never used a tanning bed [11]. This was further supported by findings that a dose/response relationship can be found between the risk of developing a BCC and increasing numbers of tanning sessions, hours spent indoor tanning, years spent indoor tanning, number of burns at the biopsy site, and number of burns associated with indoor tanning [12]. This study also found a strong relationship with artificial UV light exposure and truncal BCCs, as compared to the head and neck, indicating a possible increases susceptibility of bodily areas that receive less incidental solar irradiation [12]. Furthermore,

**Table 1** Summary of the known anti-inflammatory mechanisms of UV light

<table>
<thead>
<tr>
<th>Type of UV</th>
<th>Anti-inflammatory mechanisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>UVA</td>
<td>Induces expression of HO-1, which catalyzes the degradation of heme to biliverdin and bilirubin, themselves potent antioxidants, and to carbon monoxide, which suppresses proinflammatory cytokines. HO-1 activation may play a immunoprotective role in humans from increased IFN-γ as well. Langerhans cell counts are decreased in human epidermis after 4 weeks of UVA tanning bed exposure [60] Blood CD₃⁺ and CD₄⁺ counts are reduced in patients after exposure to UVA dominant tanning bed treatments [61]</td>
</tr>
<tr>
<td>UVB</td>
<td>UVB depletes of LC, the major antigen-presenting cell of the skin, through migration of damaged LCs to regional lymph nodes and through direct apoptosis. UVB exposed LCs preferential present antigens to Th2 and do not stimulate Th1. UVB irradiation induces T-suppressor and immunotolerant macrophages in the epidermis [62] Suppression of ICAM-1 expression by keratinocytes associated with a significant increase in intracellular thymine dimers in vivo with restoration of ICAM-1 expression via topical DNA repair enzyme [63]</td>
</tr>
<tr>
<td>Both</td>
<td>CGRP is released from cutaneous nerves after exposure to UVR, increasing cAMP levels in T cells, inhibiting T cell proliferation and inhibiting the production of IL-2 and expression of TNF-α, TNF-β and IFN-γ. CGRP also causes mast cells to degranulate and release TNF-α, which can interfere with APC’s ability to initiate the inflammatory cascade [64] The UV-induced mast cell degranulation releases the anti-inflammatory cytokine IL-10. UV irradiation damages keratinocyte DNA, activating p53 and subsequently increasing the transcription of POMC, which itself induces further production of IL-10 [65] Stimulates HDMEC to produce α-melanocyte-stimulating hormone, inhibiting expression of the adhesion molecules VCAM-1 and E-selectin, inhibiting the extravasation of leukocytes during inflammation [64]</td>
</tr>
<tr>
<td>PUVA</td>
<td>Induces cell death by inducing DNA damage, initiating a delayed apoptotic cascade [66]</td>
</tr>
</tbody>
</table>

**APC** antigen-presenting cell, **CGRP** calcitonin gene-related peptide, **HDMEC** human dermal microvascular endothelial cells, **HO-1** heme oxygenase, **ICAM-1** intracellular adhesion molecule 1, **IFN** Interferon, **IL** interleukin, **LC** langerhans cells, **POMC** proopiomelanocortin, **PUVA** psoralen ultraviolet A, **Th1** type 1 T cells, **Th2** Type 2 T cells, **TNF** tumor necrosis factor, **UV** ultraviolet, **UVR** ultraviolet radiation, **VCAM-1** vascular cell adhesion molecule 1
**Table 2** Summary of evidence supporting commercial tanning beds or UV light in the treatment of selected dermatologic conditions graded on the basis of level of evidence by using the Scottish Intercollegiate Guidelines Networks grading recommendations

<table>
<thead>
<tr>
<th>Dermatologic condition</th>
<th>Description of evidence</th>
<th>Level of evidence supporting UV light</th>
<th>Level of evidence supporting commercial tanning beds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psoriasis</td>
<td>Within-patient control supports both high and lower percentage UVB output tanning bed light [18]</td>
<td>Ib</td>
<td>Ia</td>
</tr>
<tr>
<td></td>
<td>Clinical trial demonstrates more improvement in PASI with increased UV light exposure [19]</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Increased reduction in PASI score of unilateral side of patients treated with UVA dominant light vs. the contralateral side treated with dominantly visible light [22]</td>
<td>Ia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Randomized controlled trial noted a 74% reduction in PASI 75 scores in patients using home UVB vs. 70% reduction in outpatient UVB [25]</td>
<td>Ia</td>
<td></td>
</tr>
<tr>
<td>Acne</td>
<td>Experimental trial for blue light [67] and red–blue light [68], and photodynamic therapy [27, 28] but no direct evidence for ultraviolet light</td>
<td>Ia</td>
<td></td>
</tr>
<tr>
<td>Atopic dermatitis</td>
<td>NB-UVA1, medium-dose UVA1, NB-UVB, and combination UVA/UVB irradiation have demonstrated efficacy [21, 30–32, 35]</td>
<td>Ia</td>
<td>Ia</td>
</tr>
<tr>
<td>Hand eczema</td>
<td>Oral methoxsalen UVA treatments three times per week at home with a portable facial tanning unit was found to be as effective as inpatient, biweekly trioxsalen bath UVA treatments [38]</td>
<td>Ia</td>
<td>Ia</td>
</tr>
<tr>
<td>CTCL</td>
<td>4/4 Stage I/II CTCL plaques cleared with 120 J/cm² max dose UVA1 and 3/4 cleared with 80 J/cm² max dose [40]</td>
<td>Ia</td>
<td>Ia</td>
</tr>
<tr>
<td></td>
<td>Treatment NB-UVB ranging from led to complete remission in 76.4% of patients [39]</td>
<td>Ia</td>
<td>Ia</td>
</tr>
<tr>
<td></td>
<td>NB-UVB found to be effective in 6/8 patients with Stage I CTCL [69]</td>
<td>Ia</td>
<td>Ia</td>
</tr>
</tbody>
</table>
the World Health Organization characterizes tanning beds as carcinogenic to humans, therefore, caution should be exercised in recommending tanning beds for treatment, especially in those who are at risk for developing melanoma or other skin cancers [13]. While there is strong evidence supporting association of tanning bed use and the increased risk of skin cancer, some of this association may not be causal in nature.

While there is strong evidence supporting association of tanning bed use and the increased risk of skin cancer, some of this association may not be causal in nature.

Table 2 continued

<table>
<thead>
<tr>
<th>Dermatologic condition</th>
<th>Description of evidence</th>
<th>Level of evidence supporting UV light</th>
<th>Level of evidence supporting commercial tanning beds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitiligo</td>
<td>PUVA [70], broadband and NB-UVB [42–45, 70, 71], and excimer laser [72] with/without adjuvant therapies, employed in the treatment of vitiligo [41]</td>
<td>Ib</td>
<td>Ib</td>
</tr>
<tr>
<td>Uremic pruritus</td>
<td>UVB light effective in 80–90% of patients with uremic pruritus [54] and NB-UVB was also effective in decreasing symptoms of pruritus in patients on dialysis [51]</td>
<td>IIa</td>
<td>IIb</td>
</tr>
</tbody>
</table>

CTLC cutaneous T cell lymphoma, NB narrow band, PASI Psoriasis Area Severity Index, PUVA psoralen ultraviolet A, UV ultraviolet

Table 3 Risks and side effects associated with excess ultraviolet light exposure [73]

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Description of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythema</td>
<td>Epidermal hyperplasia</td>
</tr>
<tr>
<td>Pruritus</td>
<td>Dermal edema</td>
</tr>
<tr>
<td>Polymorphic light eruption</td>
<td>Perivascular inflammation</td>
</tr>
<tr>
<td>Immune system modulation</td>
<td>Tanning</td>
</tr>
<tr>
<td>Cutaneous malignancy</td>
<td>Photoaging</td>
</tr>
</tbody>
</table>

Tanning and Conditions Treated by Phototherapy

Psoriasis

Assessing the evidence for commercial tanning facilities as a treatment for psoriasis is important as indoor tanning is already commonly used by people as a psoriasis treatment, perhaps the most frequently used form of phototherapy for psoriasis. One center reported that more than 50% of patients presenting to their clinic had tried or were currently treating their psoriasis with commercial tanning sessions [14]. Another survey found that 36% of patients reported having tried commercial tanning beds as a psoriasis treatment [15].

There may be concern that tanning beds that emit primarily UVA would not be effective for the treatment of psoriasis. While one study
found that UVA doses up to 30 J/cm² were ineffective for psoriasis, Parrish [16] found that psoriatic plaques are responsive to erythemogenic doses of either UVA or UVB light [16, 17]. The ability of tanning beds to treat psoriasis was compared on the basis of their UVB output, one with a UVB output of 4.6% was compared to another with a lower UVB output (0.7%) in a within-patient comparison technique [18]. There were marked and equivalent improvements in Psoriasis Area Severity Index (PASI) scores from baseline in patients treated unilaterally with either lamp with 12 exposures to an equal erythemal dose over a 4-week period. While exposure to either UVA or UVB light can induce clearance of psoriatic plaques, UVA requires more energy (time × power) to reach erythemogenic dosing [16].

The ability of a specific tanning bed using the Bellarium S lamp (a commonly used tanning bulb) to clear psoriatic plaques was tested in a clinical trial [19]. Twenty patients with psoriasis vulgaris were treated with three to five tanning bed sessions per week for a 6-week period. Sixteen patients had improvement in their disease as measured by PASI and 17 patients as measured by the self-administered PASI (SAPASI). The average reduction in the PASI and SAPASI was 35.4% and 36.2%, respectively, for all enrolled patients and 39.4% and 52.3%, respectively, in those completing the 6-week study. A clear dose response was observed, with greater cumulative UV exposure associated with greater disease improvement. The magnitude of PASI reduction was modest compared to recent studies of biologics, but the authors commented that the improvement was comparable to PASI reductions reported in patients treated with betamethasone valerate, calcipotriol, dithranol, and etretinate [20, 21].

Short-term side effects were minimal, including mild phototoxic reactions in seven patients and itching in three patients [15]. Long-term risks, however, were not assessed. Overall, this study demonstrated the efficacy and feasibility of using commercial tanning beds in the treatment of psoriasis, but as the tanning bed treatments were administered in a well-monitored medical setting, the findings may not fully extrapolate to tanning in the community setting.

A study assessing the effectiveness of a UVA light-dominant commercial tanning unit compared to visible light using each patient as their own control demonstrated a slight, but significant improvement in the PASI score, with the difference coming from an improvement in the erythema component of the PASI score [22].

One of the most effective treatments for psoriasis is the combination of phototherapy and oral retinoids [23]. Acitretin and tanning bed UV exposure combination therapy has been studied and is more effective than tanning alone, with 83% of patients achieving clearance or near clearance in a retrospective review, and PASI scores demonstrating an average reduction of 79% from baseline in a prospective open-label trial of 17 patients [24]. Not only did many patients clear or experience near clearing of the psoriasis, but in both the retrospective review and prospective trial, several patients were able to remain clear after stopping acitretin and only using two maintenance tanning bed light treatments per week. This illustrates the potential for tanning bed treatments as the only maintenance therapy for patients who are currently clear of their psoriasis [24].

Home UVB therapy is also a convenient option for patients with psoriasis, although not all patients have access to it. One randomized, controlled study comparing
home UVB to outpatient administered UVB treatment demonstrated similar efficacy to that of outpatient UVB therapy [25]. In this study, median PASI scores decreased for patients receiving home phototherapy 74%, respectively, compared to a 70% decrease in the outpatient phototherapy group.

Acne
Various light source therapies are either currently used or under investigation for the treatment of acne vulgaris, mainly pulsed dye laser or photodynamic therapy [26–28]. While the evidence for the use of tanning beds to treat acne is limited, in a study of Swedish tanning bed users, 34% believed that sunbathing in natural light improved acne versus only 11% of non-users, which suggests a potential use of tanning beds as a possible adjuvant treatment for acne [29]. However, we did not identify any clinical trial supporting the use of tanning bed UV light in the treatment of acne vulgaris.

Atopic Dermatitis
The prevalence of therapeutic use of tanning beds in patients with atopic dermatitis has been reported to be 66% [29]. This is not unexpected as narrow band (NB) UVA1, medium-dose UVA1, and combination UVA/UVB irradiation have been successfully employed as treatments for atopic dermatitis [30–32].

Daily exposure to high-dose UVA1 (130 J/cm²) resulted in significant improvement of study subjects' atopic dermatitis [21]. UVA1 (60 J/cm²) is equally effective compared to topical tacrolimus in treating atopic dermatitis [33]. UVA/UVB treatment was also effective at reducing clinical score [34]. NB-UVB as monotherapy is also effective in treating atopic dermatitis [35]. To our knowledge, no studies have been done investigating the use of tanning beds in atopic dermatitis, however, the range of UV light sources demonstrated to be effective in the treatment of atopic dermatitis suggests that the use of tanning beds as a treatment for atopic dermatitis may be efficacious.

Hand Eczema
Psoralen UVA (PUVA) is highly effective in the treatment of hand eczema [36, 37]. In an open-label randomized controlled trial comparing two established protocols, oral methoxsalen UVA treatments three times per week at home with a portable facial tanning unit were found to be as effective as inpatient, biweekly trioxsalen bath UVA treatments [38]. A 9 mW/cm² (90 W/m²) UVA facial tanning unit was used; the power output of this device is far below the average of 192.1 W/m² found in the North Carolina tanning bed study. Due to commercial tanning beds having primarily UVA irradiation, use of tanning beds with psoralen may have a place in the out of office treatment of chronic hand eczema, however, care must be taken because of the risks of severe burns. Concurrent use of tanning beds and psoralen may be potentially used in hand eczema due to the low body surface area involved, as patients would only need to expose their hands to the tanning bed radiation. The application of psoralen to extensive areas or systemic psoralen should not be used with tanning beds, as the risks of burns may be life threatening in these patients.

Cutaneous T Cell Lymphoma
Various phototherapeutic modalities are currently used for MF. Treatment with NB-UVB is effective for MF, leading to complete remission in the majority of patients [39]. The efficacy of five times weekly UVA1 phototherapy for the treatment of MF was also investigated [40]. After 3 initial treatment
sessions with standardized doses of 10, 20, and 40 J/cm², symptoms were used to determine future dosing, with all 4 patients clearing with maximum doses of 120 J/cm² UVA1 and 3 out of 4 clearing with maximum doses of 80 J/cm². With minimal erythemal dosing of UVA light noted to be 10–100 J/cm² [16] commercial tanning beds could be used to deliver therapeutic doses of UVA light in the treatment of cutaneous T cell lymphoma, though we found no reported cases of this therapeutic approach.

**Vitiligo**

Many UV-based therapies are employed when treating vitiligo, including PUVA, NB-UVB (both in office and home units) and excimer laser, along with adjuvant treatments such as topical calcineurin inhibitors and topical corticosteroids [41–44]. One study found that broadband UVB phototherapy was superior to NB-UVB in treating vitiligo, which suggests that tanning beds would also be effective [45]. Sun exposure induces repigmentation of vitiligo lesions during the summer in many patients [46]. While there is a possibility of using commercial tanning beds to deliver therapeutic doses of UV light to patients with vitiligo, we did not find clinical trials assessing this potential use.

**Pruritus**

The pathophysiology of itch is still being elucidated, and the mechanism by which UV light reduces pruritus is not well defined. Given the relative lack of penetration of UVB through the epidermis, the effect of UVB is thought to be through its action on epidermal keratinocytes and Langerhans cells. The effects of UVA light are generally believed to be dermal in origin, affecting lymphocytes, mast cells, and fibroblasts [47]. Dermal Schwann cells and perineural cells degenerate after exposure to UVA light as well [48].

UVB light has been successfully employed in the treatment of uremic pruritus for decades. Early studies demonstrated the efficacy of broadband UVB, with 9 out of 10 patients experiencing a significant reduction in pruritus [49]. NB-UVB is also effective [50, 51]. There are several theories on the mechanism of UVB light in the treatment of uremic pruritus, including UVB-induced reduction in skin phosphorus, leading to decreased microprecipitation of divalent cations with phosphorous in the skin and UVB-induced mast cell apoptosis [52, 53]. There may be a systemic effect of UV on uremic itch, as patients treated unilaterally with UVB light report a reduction in pruritus on both sides of their body [54].

HIV pruritus can be treated with either UVB or PUVA [55, 56]. And while in vitro and animal studies on the safety of UV light therapy raise concerns about induction of viral replication, these safety concerns have not shown up in vivo, and reviews of the literature have endorsed UV light therapy as safe in this setting [57, 58]. However, we found no data on the potential use of commercial tanning beds in the treatment of HIV-associated pruritus.

**DISCUSSION**

Many skin conditions are responsive to office phototherapy, however, office phototherapy can be expensive and inconvenient. Home UVB therapy is a potential alternative. When phototherapy is desired and office and home UVB treatments are not feasible, indoor tanning may be of benefit. There are certainly limitations to this approach—imprecise outputs of the lamps and beds, imprecise spectral targeting of commercial tanning beds,
administration by the patient or non-medical staff, acute and long-term side effects—but there are limitations to all treatment options. Due to the significant risks of tanning beds and the potential variability in dosing, practitioners should exercise their clinical judgment in recommending it to their patients. While some patients may benefit, others may have significant risk factors, such as a predisposition to skin cancer, that would need to be taken into account (along with the risks of other treatments and the risk of suffering with no treatment) when recommending treatment options.

A significant concern for use of commercial tanning facilities in phototherapy is their considerable variability in emission make up and dosing. Variability in exposure can be reduced by selecting a single bed, with additional caution/dose reduction when bulbs are changed; doing so may provide more predictable dosimetry than is obtainable with sun exposure. For psoriasis treatment, 3–5 sessions per week for 6 weeks with 4.6% UVB tanning lamps was effective (Table 4) [19]. The length of the sessions was based upon self-reported skin type and the manufacturer's suggestions for the particular bulb used in that study. For patients on an oral retinoid, a starting dose of 2–3 min with 1 min incremental increases (30 min maximum), 5–7 times a week was safe in a single study that used a 4.7% UVB output commercial tanning unit (Table 5) [24]. Because of the variability between different tanning beds, these data can give only a limited reference point for dosing; starting with a low dose and increasing slowly as tolerated would be prudent.

Given the variability demonstrated in the UV output of indoor tanning devices, we recommend some practical safety tips (Table 5). Patients should keep treatment time the same if they have asymptomatic pinkness or erythema of the skin and should be aware side effects such as pain and/or blisters. Patients with lighter skin types should exercise more care as they are more susceptible to burns from tanning compared to darker skinned individuals. After about six times per week for 1 month, reassess for response to treatment. This approach maximizes safety and allows for increasing doses as tolerated.

This study is limited by the lack of double-blind, placebo-controlled trials, long-term follow-up studies and meta-analyses for tanning facility use in dermatologic phototherapy, and by the lack of standardization of both tanning facilities and exposure dosing. Furthermore, much of what is extrapolated for the efficacy of tanning beds is through methods which emit UV therapy that overlaps with the UV emissions of tanning beds. Commercial tanning beds have been successfully used as a treatment modality for patients with psoriasis, and show promise for the treatment of many other dermatoses.

Table 4 Fleischer et al. [19] exposure schedule for the use of tanning beds for psoriasis treatment

<table>
<thead>
<tr>
<th>Skin type</th>
<th>Exposure, min</th>
<th>Sessions per week</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Week 1</td>
<td>Week 2</td>
</tr>
<tr>
<td>I</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>II</td>
<td>3</td>
<td>7</td>
</tr>
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<td>III</td>
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The evidence for the use of commercial tanning, with its clear dose–response effect [18], is as strong as or stronger than for sun exposure, which lacks demonstration of a dose–response effect [59]. Moreover, dosimetry can be better controlled with the use of indoor tanning when compared to exposure to natural sunlight, which can vary greatly based on geographical location, weather conditions, and the time of day and year [59]. The National Psoriasis Foundation [2] recommends natural sunlight as a potential treatment for psoriasis. Considering this, recommending the use of tanning beds as a potential treatment may be just as reasonable.

### CONCLUSIONS

While the use of tanning beds may not be right for every patient, in some patients the benefits of tanning beds as a source of UV therapy for their dermatological disease may be beneficial. Whether physicians recommend commercial tanning bed use or not, patients are likely to try it. In one study, nearly a third of male patients with psoriasis and nearly half of female patients with psoriasis reported having tried tanning as a treatment [15]. Withholding information on how to best use tanning may not be in our patients’ best interest. While tanning beds carry the possibility for significant side effects, their benefits and risks should be weighted just as with any treatment or medication. Furthermore, the risks of treatments that would be used as an alternative to tanning beds should also be considered, as many medications, such as methotrexate, carry the risk of severe side effects. Although there are significant risks associated with tanning beds, completely discounting its use may be a disservice to patients who have poor access to in-office and home phototherapy.

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Compliance with ethics guidelines. This article is based on previously conducted studies and does not involve any new studies of human or animal subjects performed by any of the authors.

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Melanoma is uncommon in non-white populations in the United States, with incidence rates in African Americans around 1 per 100,000. According to the National Cancer Institute, the largest increases in melanoma incidence and mortality are in white men over age 60 – a group that is not the focus of any major public health campaigns on melanoma prevention.

"During the 1970's, the incidence rate of melanoma increased rapidly by about 6% per year. However, from 1981-2000, the rate of increase slowed to 3% per year and since 2000 melanoma incidence has been stable...The death rate for melanoma has been decreasing rapidly in whites younger than 50, by 3% per year since 1991 in men and by 2.3% per year since 1985 in women."

- The American Cancer Society “Cancer Facts & Figures, 2008”

Source for this chart: National Cancer Institute SEER data registry.
MELANOMA INCIDENCE: INCREASING IN MEN

The National Cancer Institute shows that melanoma incidence is increasing much faster in men than in women since the early 1970s. For women under age 50, incidence rates have actually leveled off and are declining. But dermatology industry lobbying groups continue to promote the opposite -- leading the press to believe that melanoma is increasing fastest in young women. The best data suggest otherwise.
This report also provides updated statistics on trends in cancer incidence and mortality rates, the probability of developing cancer, and 5-year relative-survival rates for selected cancer sites based on data from 1975 through 2005. All age-adjusted incidence and death rates are standardized to the 2000 US standard population and expressed per 100,000 population. The long-term incidence rates and trends (1975 to 2005) are adjusted for delays in reporting where possible. Delayed reporting primarily affects the most recent 1-3 years of incidence data (in this case, 2003-2005), especially for cancers such as melanoma, leukemia, and prostate that are frequently diagnosed in outpatient settings. The NCI has developed a method to account for expected reporting delays in SEER registries for all cancer sites combined and many specific cancer sites. Delay-adjusted rates provide a more accurate assessment of trends in the most recent years for which data are available. Long-term incidence and mortality trends (1975-2005) for selected cancer sites were previously published in the 2008 Annual Report to the Nation on the Status of Cancer.

We also provide the contribution of individual cancer sites to the total decrease in overall cancer death rates since 1990 in men and since 1991 in women and estimates of the total number of cancer deaths avoided because of the reduction in overall age-standardized cancer death rates over these time intervals. The total number of cancer deaths avoided was calculated by applying the age-specific cancer death rates in the peak year for the age-standardized cancer death rates (1990 for males and 1991 for females) to the corresponding age-specific popula-

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