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The Netherlands

## **Vitamin D: ultraviolet light and well-being of older people**

Veleva, B.I.

### **Citation**

Veleva, B. I. (2021, November 23). *Vitamin D: ultraviolet light and well-being of older people*. Retrieved from <https://hdl.handle.net/1887/3244001>

Version: Publisher's Version

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**Note:** To cite this publication please use the final published version (if applicable).

# Chapter 8

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**Summary**

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Vitamin D is a regulating hormone that modulates multifactorial processes, helping to ensure the balance and maintenance of human health. Just a few of these processes include sustaining bone mineral homeostasis, body balance, anticancer activity, blood pressure and the regulation of immunity. Most cells and organs in the human body express vitamin D receptors, but below a certain threshold (25(OH)D<sub>3</sub> - the vitamin D metabolite that best reflects vitamin D serum concentration) vitamin D is unable to exert its effects. In general, a serum concentration of 50 nmol/l is accepted as vitamin D sufficiency, although it is unclear whether this figure can be generalized to all clinical outcomes. Factors such as age, liver and kidney function, medication and body mass index (BMI) all influence vitamin D serum concentrations in the human body.

Vitamin D deficiency (serum 25(OH)D<sub>3</sub> < 30 nmol/l) and insufficiency (serum 25(OH)D<sub>3</sub> > 30 nmol/l < 50 nmol/l) are both common in older people and are mediated by factors such as a reduction in mobility, more time spent indoors, a lower intrinsic skin response to UV radiation and a reduced dietary vitamin D intake. Almost all nursing home residents are vitamin D insufficient if vitamin D is not supplemented.

In addition to being a risk factor for dermatologic malignancies, observational and epidemiological studies suggest that sunlight may have positive effects on human health via mechanisms other than vitamin D synthesis alone. These effects may include prevention of some types of cancers, cardiovascular disease, autoimmune diseases and the improvement of mood disorders.

The aims of this thesis were to examine whether recommended vitamin D supplementation strategies are applicable to the most vulnerable population of people aged 70 years and over, and whether ultraviolet light has additional benefits (other than vitamin D synthesis alone) for the well-being, quality of life and blood pressure of vitamin D sufficient but particularly sun-deprived nursing home residents with dementia.

In **chapter 2**, we present a cross-sectional study designed to evaluate the efficacy of vitamin D supplementation in achieving vitamin D sufficiency. As advised by the Dutch Health Council, vitamin D sufficiency was defined as serum 25(OH)D  $\geq$  50 nmol/l in vulnerable people 70 years and over, and the supplementation regime consisted of cholecalciferol capsules 5600 IE once a week or cholecalciferol drops, 3 drops (7500 IU) once a week.

The mean serum 25(OH)D concentration of capsule users was 90 nmol/l, and while no one in this group was vitamin D deficient (serum 25(OH)D < 30 nmol/l), 6% was vitamin insufficient (serum 25(OH)D < 50 nmol/l > 30 nmol/l). The mean serum 25(OH)D concentration of those receiving drops was 41 nmol/l, 32% of whom were vitamin D deficient and 37% were vitamin D insufficient. Analysis of the baseline characteristics of those receiving capsules versus drops showed a significant difference in BMI between the two groups, with a higher number

of persons with overweight amongst those receiving drops. To search for predictors of low vitamin D concentrations (lower than 50nmol/l) we applied logistic regression analysis to the whole group of nursing home residents, but could not identify a significant trend for possible predictors of vitamin D insufficiency and deficiency apart from the use of vitamin D drops.

This study showed that weekly vitamin D supplementation with 5600 IU cholecalciferol capsules (equal to 800 IU daily) results in vitamin D sufficiency, regardless of gender, age, BMI, renal function, sun exposure, comorbidity, medication or mobility status.

In **Chapter 3**, we looked at the vitamin D prescribing behaviour of general practitioners (GPs) and elderly care physicians (ECPs) caring for people 70 years old and over, encompassing both community dwelling older persons and nursing home residents in the Netherlands.

Today, international guidelines and expert societies recognize the vitamin D deficiency pandemic in older people and the consequent health risks. However, their recommendations concerning vitamin D supplementation differ due to a lack of consensus in the scientific literature regarding the optimal serum vitamin D concentration and the most efficient approach to vitamin D supplementation: population-based or individual-based. In the Netherlands, the Dutch Health Council has chosen an unambiguous, population-based approach to vitamin D supplementation for people 70 years and older: daily supplementation with vitamin D 800 IU for everyone in this group.

We carried out a Netherlands-based survey using either the Survey Monkey Platform or a general information letter sent to 1685 ECPs. In addition, we approached 310 GPs with the same questions during a vocational training day. To identify a possible trend in vitamin D prescription we compared these results to a survey carried out in 2010. Analysis showed that 79% of ECPs and 71% of GPs had a good understanding of the vitamin D guidelines. In comparison to the earlier survey, there was an increasing awareness of the importance of vitamin D supplementation in older people, with 94% of ECPs and 34% of GPs systematically prescribing vitamin D to their patients aged 70 years and older. Uncertainty in the prescribing behaviour of GPs was attributed to the heterogeneity of their patient population, ranging from the healthy and active to frail people with significant comorbidity. Half of all GPs claimed to regularly monitor serum 25(OH)D before starting supplementation.

In **chapter 4**, we describe our systematic review of literature on the effect of ultraviolet (UV) light, when applied to the skin or eyes, on mood, depression and well-being. A PICO (population, intervention, control, and outcome)-based search strategy was carried out in the following bibliographic databases: PubMed, Embase, Web of Science, Cochrane, Psycinfo, CINAHL, Academic Search Premier and Science Direct. Finally, seven studies were selected as eligible

for this literature review: one observational study and six clinical trials. Participants in the selected studies were healthy volunteers, patients with fibromyalgia syndrome, dermatological conditions, multiple sclerosis or seasonal affective disorders.

Two of the studies examined the effect of UV light applied to the skin on mental state, finding significant improvements in mood. Five of the studies investigated the effect of UV light applied to the skin or eyes on depressive symptoms and seasonal affective disorders in participants with or without depressive disorders. Four of the five studies showed a positive effect on depressive symptoms.

Though the overall effect of UV light intervention on mood and depressive symptoms was positive, the small number of studies and certain methodological problems make drawing general conclusions difficult.

In **Chapter 5**, we present the results of our randomized multicentre controlled trial on the effect of ultraviolet B (UVB) irradiation versus vitamin D (VD) supplementation on the well-being of nursing home residents with dementia. Participants were recruited from three nursing homes in the Netherlands connected to the University Network for the Care sector South Holland (UNC-ZH), and the intervention consisted of half-body UVB irradiation with 1 standard erythema dose of 8 minutes, twice a week. The control group received VD capsules (5600 IU cholecalciferol weekly). At baseline and after three and six months, the participants in both arms were evaluated on the primary outcome, wellbeing, monitored with the CMAI (Cohen-Mansfield agitation inventory) scale and Cornell scale for depression in dementia. Secondary outcomes were quality of life monitored with QUALIDEM (shortened version) and biochemical parameters of bone homeostasis such as VD serum concentration, creatinine, parathyroid hormone (PTH), calcium and phosphate.

Seventy-nine nursing home residents participated in the study. There were no significant differences between baseline characteristics of the intervention and control groups, apart from VD concentration which was higher in the vitamin D group ( $p=0.04$ ). No significant between-group differences were found regarding agitated behaviours or depressive symptoms for the UVB and VD groups, either at 3 months or 6 months from the start of treatment. Interestingly, at six months the UVB group showed less restless/tense behaviour (maximal score on the scale 9) compared to the VD group. The difference in estimated means (adjusted for other variables in the model) over time was 2.2 (95% CI 0.8 to 3.6). There was no difference in biochemical parameters at three months between the two groups, although at six months VD serum concentration was higher in the VD group (difference in means -21.9; 95% CI -32.6 to -11.2). We concluded that the exposure of nursing home residents with dementia to UVB light showed no positive benefits in terms of wellbeing. UVB treatment may have a positive

effect on the restless/tense behavioural characteristics of advanced dementia, but more research is needed to confirm this finding.

In **chapter 6**, we examined the effect of ultraviolet (UV) irradiation versus vitamin D (VD) supplementation on blood pressure in a particularly sun-deprived population, nursing home residents with dementia.

Cardiac output and peripheral resistance are the determinants of arterial blood pressure. Ultraviolet A light from sun exposure is known to increase circulating nitric oxide, which results in a decrease in peripheral resistance. VD may also effect blood pressure through the correction of abnormalities in calcium homeostasis and regulation of the renin-angiotensin system.

This study consisted of a post-hoc analysis of medical records detailing the blood pressure measurements of participants in the randomized control trial described in chapter 5. The participants (N=61, 41 women, mean age 84.8 years) received half-body UV irradiation for 8 minutes twice weekly or 5600 IU of cholecalciferol once a week over 6 months. Short-term effects were evaluated after 1 month and long-term effects after 3 and 6 months. Differences in blood pressure changes were assessed using linear mixed models. The baseline characteristics of both groups did not differ significantly. After one month of treatment the participants in the UV group had a lower blood pressure, with a difference between the two groups of  $-23$  mmHg (95% CI  $-37.1, -10.1, p=0.001$ ) in estimated mean systolic blood pressure and  $-9.5$  mmHg (95% CI  $-9.8, -4.4, p=0.001$ ) in diastolic blood pressure, with VD group as reference. At three and six months there were no significant between-group differences in either systolic or diastolic blood pressure.

We concluded that UV light has only a short-term effect on blood pressure reduction compared to VD supplementation in this sample of normotensive to mild hypertensive nursing home residents with dementia.

The general discussion in **chapter 7** outlines the main findings of this thesis. We deliberate on the topic of vitamin D supplementation in older people in light of the current guidelines and on the possible additional effects of ultraviolet light beyond vitamin D synthesis on nursing home residents. The most recent guidelines advise more research on the cut-off that defines vitamin D deficiency and whether it varies by specific clinical outcome. Nevertheless, it is well known that the physiology of aging makes older people particularly susceptible to vitamin D deficiency and that, if untreated, it can have serious health consequences. We also discuss the different supplementation strategies for nursing home residents and community dwelling persons aged 70 years and older.

We then elaborate on the effects of ultraviolet light on the well-being of nursing home residents. Our findings showed no improvement in the general well-being of nursing home residents after UV irradiation but some aspects of quality of life such as restless/tense behaviour showed improvement. We assume that reduced well-being in dementia is a multifactorial problem that requires a broader approach.

Our findings regarding decreased blood pressure in the first month of UV light treatment in normotensive to mildly hypertensive nursing home residents with dementia raise three issues for future research: 1) our study might have lacked sufficient power to detect more subtle changes in blood pressure at three and six months, 2) older people on hypertensive medication may need adjustment of medication during the summer months, and 3) UV light might have a positive effect on the regulation of blood pressure in hypertensive patients.

Excessive sun exposure has long been a staple of health campaigns but there is now increasing evidence that insufficient sun exposure may also be a significant public health problem. Older people with dementia are particularly sun-deprived due to disability and spending insufficient time outside. In our study, the use of sunbeds in this population presented practical problems that led to low adherence. In comparison, spending time outside is less problematic for people with dementia and should be stimulated and incorporated into daily activities as a part of a healthy lifestyle program.



