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

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Chapter 7

General discussion

Observational studies have found associations between low vitamin D levels and a wide range of serious outcomes, including cardiovascular disease, malignancies, diabetes, autoimmune diseases and higher mortality [1-8]. Furthermore, randomized control trials, meta-analyses and Mendelian studies have confirmed the effects of vitamin D supplementation on bone health, hypertension risk, acute respiratory infections and mortality in populations with very low vitamin D levels [9-16]. However, there is increasing evidence that sun exposure may exert its positive effects on human health via mechanisms other than vitamin D synthesis alone. Sunshine appears to protect against several types of cancer, cardiovascular disease and autoimmune diseases [17-19], as well as positively influencing mood, depressive disorders and well-being [20]. As many people aged 70 years and over are both vitamin D deficient and sun-deprived, the potential for health problems is obvious [21, 22]. In this thesis we therefore explore the utility of vitamin D in older people, focusing on supplementation strategies and the possible additional effects of ultraviolet light beyond vitamin D synthesis, with the aim of improving the well-being and quality of life of nursing home residents with dementia

MAIN FINDINGS OF THE STUDIES PRESENTED IN THIS THESIS:

1) Of the 71 participants in a cross-sectional study (all nursing home residents with dementia, mean age of 83), 19 used cholecalciferol drops and 52 used cholecalciferol capsules. Mean serum 25(OH)D was 77 (SD 30) nmol/L and 55 residents (78%) were vitamin D sufficient. Among capsule users, mean serum 25(OH)D was 90 (SD 22) nmol/L (considerably higher than the expected 50 nmol/l), and 49 (94%) were vitamin D sufficient. Among users of drops, mean serum 25(OH)D was 41 (SD 8) nmol/L and only 6 (32%) were vitamin D sufficient (Chapter 2).
2) Our survey of the vitamin D prescribing behaviour of elderly care physicians (ECPs) and general practitioners (GPs) in the Netherlands for persons aged 70 years and over shows that most ECPs (94.2%) and more than a third of GPs (34.0%) prescribed vitamin D systematically (consistent with the guidelines) to their patients aged ≥70 years; a comparison with 2010 showed an increasing trend towards prescribing vitamin D supplements (Chapter 3).
3) Our systematic review of clinical trial and observational study evidence on the effects of ultraviolet light on mood, depressive disorders and well-being found that of the seven studies included, six showed a positive effect of UV light on domains of psychological health, suggesting a positive correlation between ultraviolet light and an improvement of mood (Chapter 4).
4) Half-body ultraviolet irradiation for six months in nursing home residents with dementia is not superior to oral vitamin D supplementation as regards well-being measured with the

Cornell depression scale and Cohen-Mansfield agitation inventory. However, ultraviolet light has a positive effect on restless/tense behaviour after six months of intervention (Chapter 5).

5) Compared to vitamin D supplementation, ultraviolet light has a short-term effect on blood pressure (evident at one month but not at three and six months) in a normotensive to mildly hypertensive population of nursing home residents (Chapter 6).

Vitamin D supplementation in older people: treatment or prevention of vitamin D deficiency?

Dietary reference values for vitamin D

Dutch dietary reference values for vitamin D were published in 2000 and then again in 2008, and set adequate vitamin D intake for people 70 years and over at 10 µg per day (400IE) [23]. In 2012, a committee of experts at the Dutch Health Council issued a re-evaluation of the 2008 dietary reference values on the basis of the most recent scientific evidence. For those aged 70 years and over, the committee concluded that previous recommendations may have been too low [24]. This may be related to inadequate sun exposure. It is generally assumed that two-thirds of vitamin D is derived from production in the skin following sun exposure and one third from dietary intake [24]. In the Netherlands, sunlight-induced vitamin D production in the skin is only possible in the period March to November, and requires exposing (bare) hands and face to the sun for 15-30 minutes between the hours of 11.00 and 15.00.

Foodstuffs rich in vitamin D include oily fish, liver, meat, eggs and dairy products. Owing to limited mobility and co-morbidities, the amount of sun exposure and dietary intake of vitamin D amongst older people are both often insufficient. As a consequence the Dutch Health Council now advises supplementation in this particular group, with dietary reference values set at 20 µg (800IE). These dietary reference values encompass total theoretical vitamin D supply from both diet and sunlight to help ensure that (almost) all persons aged 70 and over achieve the target value. The target value for serum 25(OH)D is a concentration of 50 nmol/l, which in older people is regarded as protective with regard to bone health and falls among the very frail.

Dietary reference values are a screening instrument designed to prevent vitamin D deficiency rather than treat it, and the values apply to healthy individuals. Vitamin D metabolism and its conversion to the active form are dependent on the correct functioning of several organs and on the availability of a number of enzymes and active substances. Impairment in the functioning of skin, intestines, liver, kidneys or cells of the immune system, as is frequently the case in older people, can lead to vitamin D deficiency, and it is not clear that supplementation at vitamin D levels suitable for healthy people actually improves the health of older persons. Older people are also likelier to use medications that can potentially influence the production

of 25(OH)D in the liver, such as antiepileptics (carbamazepine, oxcarbazepine, phenytoin, phenobarbital), immunosuppressants (corticosteroids) or diuretics (thiazides).

Dietary vitamin D reference values applied to frail people

In **chapter 2** we describe a cross-sectional study in nursing home residents. In this study we investigated the efficacy of daily vitamin D supplementation for at least three months, at a dose of 20 µg (800 IE) in the form of capsules or drops. We also collected data on various factors that may influence serum 25(OH)D levels, including age, co-morbidity, number and sort of medication use, body mass index (BMI), sun exposure, modification of diet in renal disease (MDRD) and Functional Ambulation Classification (FAC) scores as an assessment of mobility. We found that in most residents (94% of residents had a mean serum 25(OH)D concentration of 90 nmol/l, SD 22) vitamin D supplementation once a week with cholecalciferol capsules containing 5600 IU (equivalent to 800 IU daily) resulted in vitamin D sufficiency (serum 25(OH)D ≥ 50 nmol/L). Our results show that Dutch Health Council advice concerning vitamin D supplementation in people 70 years and older is adequate to maintain vitamin D sufficiency and is also applicable to the most frail people if cholecalciferol capsules are used.

The baseline concentration of serum 25(OH)D in our research population was not determined, but from literature we know that nursing home residents are almost universally vitamin D insufficient without vitamin D supplementation [21, 22]. The results of our study show that the supplementation strategy proposed by the Dutch Health Council for maintenance of vitamin D sufficiency in older people can also be used effectively in the treatment of vitamin D deficiency (serum 25(OH)D < 30 nmol/L) and insufficiency (serum 25(OH)D > 30 < 50 nmol/L) in this population. Endocrine Society clinical practice guidelines recommend a dose of 50 000 IU of vitamin D once a week for eight weeks followed by 800-1000 IU/day maintenance therapy for treatment of vitamin D deficiency and insufficiency [25]. In obese patients and patients on medications that affect vitamin D metabolism, the American Geriatrics Society and the Endocrine Society suggest use of even higher doses of vitamin D [25, 26]. However, in our study we found no association between BMI, renal function, number and kind of medication and 25(OH)D status. It seems possible that a daily dose of 800 IE vitamin D, the dietary reference value defined by the Dutch Health Council, is enough to both prevent and treat vitamin D deficiency and insufficiency in all patients aged 70 years and above, independent of any health condition (excluding patients with malabsorption syndromes. Similarly, in a study by Chel et al. [22], recommended preventive supplementation of vitamin D (600 IE or 800 IE daily, or 4200 IE or 5600 IE weekly) achieved vitamin D sufficiency in 90-94 % of deficient or insufficient older people after 3-4 months. More research in larger groups of patients is needed to confirm this finding. An accepted standard for supplementation doses of vitamin D in this population subgroup would make implementation easier and cheaper.

Towards an adequate intake of vitamin D

In **chapter 3** we explored the vitamin D prescribing behaviour of elderly care physicians (ECPs) and general practitioners (GPs) in the Netherlands using a survey approach. The study found increased awareness in these two physician groups of the importance of vitamin D supplementation in older people when compared to the results of a similar study carried out in 2010 [27]. In our study 94.2% of the ECPs and 34% of the GPs prescribed vitamin D systematically (consistent with guidelines) to their patients aged 70 years and over. In nursing homes in the Netherlands vitamin D supplementation is regarded as the standard of care because it is widely appreciated that almost all nursing home residents are vitamin D insufficient without supplementation. The prescribing behaviour of GPs is less consistent, which is possibly related to the heterogeneity of their specific older patient population, which ranges from fit and active to very vulnerable people. GPs frequently order blood tests (49.5%) to assess serum 25(OH) D before they start supplementation or when they are unsure of the utility of vitamin D supplementation (36%). This is likely related to current ambiguity of the literature concerning guidance of vitamin D supplementation.

Untreated vitamin D deficiency in older people can have serious health consequences [10, 23, 28, 29]. There are two approaches to the prevention and treatment of vitamin D deficiency and insufficiency: population or individual. The population approach entails vitamin D supplementation in an entire group of people vulnerable for vitamin D deficiency or insufficiency. An individual-based approach targets individuals with vitamin D deficiency or insufficiency. Choosing a population-based approach in the 70 years or older group is supported by solid evidence from observational studies and clinical trials, and many studies point to a vitamin D threshold below which disease risks increase and vitamin D supplementation shows beneficial effects [30].

As already mentioned, vitamin D deficiency has a high prevalence in older people. In the Longitudinal Aging Study Amsterdam (LASA), of the 1311 community-dwelling older persons tested for serum 25(OH)D levels, 48.4 % were vitamin D insufficient (25(OH)D < 50 nmol/l) and 11.3% were vitamin D deficient (25(OH)D < 25 nmol/l) [31]. In a German study of 1418 community-dwelling older people aged ≥65 years, the proportions of vitamin D deficiency, insufficiency and sufficiency were respectively 78.8, 19.2 and 1.9% in March, compared to 16.1, 63.4 and 20.5% in Augustus [32]. Vitamin D insufficiency is very common in community-dwelling older people and shows a strong seasonal pattern. This public health issue in this specific risk group argues for a population-based approach, and the proposed solution is in line with Dutch Health Council advice [24] and has a favourable cost-benefit ratio [30]. Concerns related to exceeding the tolerable upper level intake limit are unfounded, as the recommended levels of supplementation are significantly lower than tolerable upper intake levels for adults (100 µg per day per person). International research data and data from the National Institute

for Public Health and Environment (RIVM) suggest that sunlight exposure in the Netherlands leads to the production an average of 6-7 µg of vitamin D per day. In an evaluation report of dietary reference values for vitamin D, the Dutch Health Council stated that the mean vitamin D intake from foods in the age group between 7 and 70 years is 2.3 to 4.1 µg for men and 2.3 to 3.2 µg for women in the Netherlands. In conclusion, even in the case of people with a good vitamin D intake, sufficient sun exposure and vitamin D supplementation, the daily intake would still be much lower than the tolerable upper level. For older people with sufficient sun exposure and vitamin D intake, an estimated average requirement of 10 µg (400 IE) per day will ensure that the target level of 50 nmol/l serum 25(OH)D is reached independently of any medication used, BMI, co-morbidity, kidney or liver function [24].

With an average primary care visit only lasting 13-16 minutes, time to adequately address topics such as vitamin D supplementation may be limited, particularly in complex cases. To reduce costs and lengthy visits, a useful addition to the GP's electronic dossier may be a computer-aided reminder for when a patient turns 70 and an automatic message that includes a prescription and patient information leaflet covering the use of vitamin D. Special care should be taken regarding patients suffering from granuloma-forming disorders such as sarcoidosis, tuberculosis, chronic fungal infections or primary hyperthyroidism, as these patients should be monitored for serum calcium levels [25]. Another possible option is to assign the vitamin D supplementation program to the Municipal Health Services.

Effect of ultraviolet light and vitamin D on well-being and quality of life in people with dementia

Following the discovery by Niels Ryberg of the curative effect of ultraviolet (UV) light on lupus vulgaris (a skin variant of tuberculosis), additional beneficial effects of sunlight have been documented in the scientific literature. Human and animal studies have shown that exposure to ultraviolet light can incite a chain of endocrine, immunologic and neurohumoral reactions that affect mood and hence quality of life [33-36]. To collate evidence from observational studies and clinical trials concerning the effect of ultraviolet light on mood, depressive disorders and well-being, we carried out a systematic review **(chapter 4)**. Of the seven studies included, six showed a positive effect of UV light on domains of psychological health. Extrapolating from this review, we suggest that ultraviolet light and mood show a positive correlation. However, due to the small number and heterogeneity of studies more research will be needed to confirm and further document this correlation.

Consequently, we conducted a multicentre randomized controlled trial **(chapter 5)** focused on the effect of ultraviolet light and vitamin D supplementation on the well-being and quality of life of nursing home residents with dementia. We considered well-being as the personal aspect of the multidimensional concept 'quality of life', as recent research has shown that mood and

behavioural problems are important predictors of quality of life among nursing home residents with moderate to severe dementia [37]. During the observation period of six months, our study showed no significant between-group differences regarding agitation or symptoms of depression. However, at six months the group receiving ultraviolet light showed less restless/tense behaviour compared to the vitamin D group. Discussing possible explanations for these results, we highlight potential mechanisms through which ultraviolet light affects mood and well-being.

A possible mood-modulating effect of UV light via the skin is mediated by the vitamin D pathway

The major source of vitamin D for humans is exposure of the skin to sunlight (UVB 280-315 nm), resulting in the conversion of 7-dehydrocholesterol to previtamin D3. The recent discovery that the human brain also possesses vitamin D receptors indicates that mood and depressive disorders might be directly influenced by vitamin D deficiency [38, 39]. Indeed, many observational studies have reported a significant negative correlation between 25(OH)D levels and depression in people ≥60 years [29, 40-44].

In our RCT **(chapter 5)**, both the vitamin D group and the UV group were vitamin D-sufficient, which may explain the lack of an additional effect of the interventions on mood and well-being. However, a recent meta-analysis found no evidence of an effect on depression in adults with vitamin D supplementation [45]. In a study by Knipperberg et al., participants with multiple sclerosis reported their levels of sun exposure and that was inversely correlated with depression, the magnitude of the effect of sun exposure on depression remained also stable when 25(OH)D3 was included in the model [46].

A possible mood-modulating effect of UV light via the skin is mediated by the other pathway than vitamin D synthesis alone

Other pathways that may be triggered by UV light to modulate mood and act through skin exposure involve three local systems: (i) the skin analogue of the hypothalamic-pituitary-adrenal (HPA) axis,[33] (ii) the serotoninergic/melatoninergic system [34], and (iii) the immune system [35, 36]. These pathways are assumed to interact with systemic mechanisms of body homeostasis [35]. There is an increasing literature on molecular mechanisms that may play a role in depression [47]. Depression is characterized by slightly increased cerebrospinal fluid (CSF) concentrations of several pro-inflammatory cytokines [48], and pro-inflammatory cytokines in turn enhance the activity of indoleamine 2,3-dioxygenase, the first rate-limiting enzyme of tryptophan degradation. Increased tryptophan degradation can induce serotonin depletion and depression. The above mentioned mechanisms of UV action on the skin, immune and nervous system may impact the systems underlying depression and help establish a new balance. This was indeed observed in studies by Edstrom et al. [49], Knippenberg et al.

[46] and Pudikov et al. [50], in which the mean age [interquartile range (IQR)] of participants was 54 (48-59), 48 (37-59) and 36 (24-42), respectively. However, this was not the case in our study **(chapter 5)**. One possible explanation for this inconsistency is the very different age and co-morbidity of the participants in our study: people with dementia and a mean age 84 (IQR80-88). Overall, late-life depression has distinctive features that differentiate it from depressive disorders occurring at younger ages, and it is accompanied by subcortical vascular changes and hippocampal atrophy [51]. Thus depression in old age, and especially in dementia, is characterized by not only molecular changes in comparison to younger age depression but also structural changes in the brain. Confirmation of this difference came when well-controlled studies, systematic reviews and meta-analyses found no reliable or convincing efficacy for antidepressants in patients with dementia and co-occurring depressive disorders [52, 53].

The lack of an observed effect on agitation in our study, in either group, may also be associated with the multifactorial character of the agitation experienced by people with dementia. Agitation often occurs in the cognitively impaired and is a collection of symptoms that may reflect an organic psychiatric disorder (e.g. dementia), a medical illness, an adverse effect of medication or it may be secondary to insecurity, frustration, fears or misperceptions produced by impaired hearing, sight or aphasia. For the treatment of this multifactorial problem a more complex approach is likely needed

In our study, the participants allocated to the UV group showed a decrease in restless/tense behaviour after six months of treatment. This may be due to the effects of UV on the skin and the local production of serotonin, cytokines and beta-endorphin which together promote a feeling of well-being, boost the immune system, relieve pain and improve relaxation [33, 34, 54]. In a study by Gamblichler et al., UVA-exposed volunteers felt significantly more balanced, less nervous and strengthened after three weeks of UVA exposure twice a week. Following the first UVA exposure, serum serotonin was significantly higher and serum melatonin significantly lower compared to before exposure.

In reference to methodological considerations, discussed in details later in this thesis, there were some practical problems during our randomized controlled trial in terms of the variable adherence of nursing home residents to UV treatment. If this could be solved by finding a more satisfactory manner of administering UV light treatment, this intervention might be a good complementary therapy for restless/tense behaviour and improve the quality of life of older people with dementia. A replication of this RCT is warranted to confirm these findings.

Effect of ultraviolet (UV) light and vitamin D supplementation on blood pressure in people with dementia

UV type A from sun exposure is known to increase circulating nitric oxide, which in turn decreases peripheral resistance [55, 56]. Vitamin D may also influence blood pressure by correcting abnormalities in calcium homeostasis and regulating the renin-angiotensin system [2, 9]. In **chapter 6** we focused on the comparative effects of UV light versus vitamin D supplementation in relation to blood pressure reduction. The light emissions used in our study consisted of UV light A and B, which ensured production of vitamin D, allowing us to estimate additional effects of ultraviolet light on blood pressure over and above the effect of vitamin D.

We conducted a post-hoc analysis of a randomized controlled trial to assess differences in blood pressure changes between persons with dementia receiving UV light versus vitamin D supplementation. This post-hoc analysis showed only a short-term (at one month) effect of UV light on blood pressure reduction compared to vitamin D use in a vitamin D sufficient population of nursing home residents. This might be due to regulatory and counterregulatory mechanisms or to the depletion-repletion kinetics of active substances in the skin, or to increased resistance of the end target organs to these substances. In addition to these biological mechanisms, the small sample size in our study could have influenced the results. This is discussed further in the section on methodology.

Our results are in line with most other studies carried out to examine the effect of UV light on blood pressure [55-57], but none of these studies were designed to observe the long-term effects of this intervention. Future studies should investigate the effect of UV light on blood pressure in larger groups of people, over longer timeframes and in different populations (vitamin D sufficient vs. vitamin D insufficient, hypertensive vs. normotensive, young vs. old). A range of different ultraviolet light exposure regimes should be studied, including UV type A, UV type B and a combination of both in order to assess if this treatment is likely to be beneficial.

Thus far, solid evidence from large observational studies indicates that sun exposure can be a potentially beneficial environmental factor in the maintenance and regulation of blood pressure [18, 58, 59]. These observational studies had large sample sizes, long follow-up and community-based sampling, which together increases their external validity. However, the studies also had limitations regarding measurement error in the determination of sun exposure, as the hours of sun exposure were not always documented. Based on studies with adequate documentation of daily hours of sun exposure, it appears that insufficient exposure to UV radiation and/or active avoidance of sunlight may be a new risk factor for hypertension.

Amongst community-dwelling frail older people who may be particularly deprived of sun exposure, it is important to implement public health care programs that encourage people to go

outdoors and carry out outside activities. Besides environmental factors such as sun exposure, time outdoors has other positive effects that can influence blood pressure such as decreased stress, greater physical activity and a greater likelihood of social contact [60].

For nursing home residents with dementia, the passive and active use of green gardens can be a feasible and applicable option when caregivers, disciplines, managers, relatives and volunteers are involved, motivated and well-trained [61].

Methodological considerations of the randomized controlled trial

Blinding of the trial

Even while writing the protocol for the RCT "The Effect of Ultraviolet B Irradiation Compared with Oral Vitamin D Supplementation on the Well-being of Nursing Home Residents with Dementia", we were aware that blinding of the trial was impossible. We also choose not to use cluster randomisation because each nursing home included in the trial had its own program for improving resident's quality of life, a factor that might have negatively influenced the results. Excepting exposure to the intervention, we aimed to ensure that all other circumstances remained the same.

Blinding participants to the treatment was logistically difficult. The nursing home residents who participated in the trial received an explanation of the aims of the trial and expectations of the treatment. As all participants had dementia, it was not possible to be certain that they understood and remembered this information by the time of the UV light sessions.

Nursing staff were not blinded, as they administered the medication and intervention, and completed the questionnaires.

Adherence of Nursing Home Residents to the Intervention

Neglecting to examine adherence and its impact on outcome can compromise the interpretation of research finding and lead to inappropriate recommendations and decisions regarding the use and implementation of an intervention. In our study we therefore analysed the adherence of nursing home residents to the UV intervention, the methods used to partially solve problems of adherence and how adherence was related to outcomes.

A recognizable problem in our study was the variable adherence of nursing home residents to UV light treatment. Twelve of the participants (30%) in the UV group refused to adhere to the intervention procedure for a variety of reasons, including an unwillingness to remove clothes or to wear protective glasses, feeling cold or anxious, not understanding the purpose of the procedure or being unable to lie quietly on a bed during UV exposure. Furthermore, 19% of the participants joined the sessions only for the first three months and 41% continued for more

than 3 months, while 28% seemed to find the sessions pleasant and reinforcing according to nursing staff. Given the marked difficulties in adherence, and particularly the fact that those who disliked UV treatment were started on vitamin D supplementation, per protocol analysis results were also interesting. In view of the variable duration of exposure and keeping in mind sample size, we considered participants as "treated" following any duration of UV exposure, only allocating participants to the vitamin D control arm when they refused treatment. This additional analysis showed the same results for the main outcomes as the intention-to-treat analysis.

Missing data

As some participants inevitably passed away due to dementia during the course of the study, we had some missing data. When designing the study, we calculated that 56 participants would be needed to provide an 80% probability of detecting a mean between-group difference of 10 points on the CMAI. Taking into account the vulnerability and high mortality rates in this population, we chose to recruit 78 participants. Ultimately, 52 of the participants could be included in the analysis at the 6-month time point, equating to 93% of our original power estimate (5256*100% = 93%). Furthermore, we chose a linear mixed model as a bias-reducing analysis. The alternative was a complete case analysis, but this has drawbacks such as substantial loss of information and adverse effects on precision and power [62, 63]. In the linear mixed model, using direct likelihood analysis, we used the observed data without deletion or imputation. In doing so, appropriate adjustments valid under MAR (missing at random) were made to parameters at times when data were incomplete due to within-patient correlations. We did not use multiple imputations because this has advantages when both outcomes and covariates are missing and in our case only outcome data were missing.

Methodological considerations of the post-hoc analysis

We carried out a post-hoc analysis of the randomized controlled trial data with the aim of assessing differences in blood pressure change between persons with dementia receiving ultraviolet light versus vitamin D supplementation. One of the limitations of this post-hoc analysis was the technique of blood pressure measurement. Data obtained from the medical records of the nursing home residents were monthly pragmatic blood pressure measurements (1 measurement per time) rather than the standardized method for automated blood pressure measurement (the average of 3 measurements taken after 5 minute breaks) [64]. Another source of uncertainty was the power of the post-hoc analysis. The sample size of the RCT, which data were used for the post-hoc analysis, was calculated on the basis of Cohen-Mansfield Agitation Inventory. We did not calculated the power of the post-hoc analysis which primary outcome was the difference in blood pressure between intervention and control group. Power analysis used to indicate power for outcomes already observed does not provide sensible results

[65]. In addition, the lack of a statistical difference in blood pressure between the vitamin D and UV groups might have been due to the small size of our study.

CONCLUSIONS:

1. Vitamin D supplementation using cholecalciferol capsules containing 5600 IU once a week (equal to 800 IU daily) results in vitamin D sufficiency (serum 25(OH)D ≥50 nmol/l) in a population of nursing home residents regardless of gender, age, BMI, renal function, sun exposure, comorbidity, medication or mobility status.
2. Vitamin D prescribing behaviour of elderly care physicians and general practitioners in the Netherlands in relation to persons aged 70 years and over indicates an increasing awareness of the importance of vitamin D supplementation in older people.

General practitioners need more guidance regarding their prescribing behaviour due both to their often heterogeneous patient population and contradictions in international guidelines.

3. Compared to vitamin D supplementation, the effect of ultraviolet light showed no improvement of the well-being in general after UV irradiation in nursing home residents but improvement of some aspects of quality of life such as restless /tense behaviour.
4. Ultraviolet light has a short-term effect, reducing systolic and diastolic blood pressure in a vitamin D sufficient population of normotensive to lightly hypertensive nursing home residents with dementia.

RECOMMENDATIONS

1. In nursing homes residents, vitamin D supplementation with capsules (800 IE per day or 5600IE per week) is sufficient to reach a serum concentration of 50 nmol/l 25(OH)D3.
2. The data presented in this thesis and a solid evidence from large observational studies indicate that ultraviolet light may have effects beyond the synthesis of vitamin D in nursing home residents who are especially sun-deprived.

a. We recommend implementation of a public health care program that encourages outdoor activities by older people, even for (very) frail older people. Balanced sun exposure can ensure the production of vitamin D, promote relaxation of stress and improve cardiovascular and neuroendocrine regulation, all of which contribute to health and well-being. Technically approved sunbeds with appropriate ultraviolet exposure schedules can be used in the winter months and for very frail people who cannot go outdoors. The use of sunbeds by nursing home residents with dementia highlighted certain practical problems, including feeling cold, anxious, being unable to lie still or being unable to understand the purpose

of the procedure. Future research efforts in this field should first attempt to find more satisfactory approaches to administering ultraviolet light.

b. It will be interesting to reproduce our trial on the effect of ultraviolet light compared with oral vitamin D supplementation on the well-being of nursing home residents without cognitive impairment.
c. Checking up blood pressure and adjusting medication in de summer by older people with antihypertensive medication and going outside more frequently might be relevant because the possible reducing effect of UV on blood pressure
d. Further research is needed on the effect of ultraviolet light on blood pressure in a larger population sample that includes hypertensive older people, to evaluate if a more sustained effect can be reached using this intervention.

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