The effect of vitamin D supplementation on psoriasis severity in patients with lower range serum 25-hydroxyvitamin D levels - a randomised placebo-controlled trial

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3 Key Points

Question: Does vitamin D supplementation reduce psoriasis severity through the winter?

Findings: In this RCT, including 122 participants with plaque psoriasis (average PASI 3.1), we found no measurable effect on psoriasis severity of vitamin D 20000 IU/week for 4 months during winter. 25-hydroxyvitamin D (25(OH)D) levels in the intervention group increased less-than-expected based on previous experimental data in the same source population.

Meaning: Vitamin D supplementation did not affect psoriasis severity in this study, however, low baseline severity scores and lower-than-expected increase in 25(OH)D levels in the intervention group may have affected the results.

Abstract

Importance: Topical vitamin D analogues are routine treatment for psoriasis, but effect of per oral supplementation is not established.

Objectives: To examine the effect of vitamin D supplementation on psoriasis severity through winter.

Design: Randomised, double-blind placebo-controlled trial with two parallel groups performed through two winter seasons (2017/18 and 2018/19). Randomisation was computer generated. All participants, health care providers and outcome assessors were blinded to group assignment. Each participant was followed for 4 months. The presented analyses were conducted in May 2022.

Setting: The Clinical Research Unit, University Hospital of North Norway (UNN), Tromsø (located at 69^{o} north).

Participants: Adults from the general population in Tromsø (Norway) with active plaque psoriasis and 25-hydroxyvintamin D (25(OH)D) <24 ng/mL (<60 nmol/L).

Intervention: Vitamin D (cholecalciferol 100 000 IU loading dose, followed by 20 000 IU/week) or placebo for 4 months.

Main outcome(s) and Measure(s): Psoriasis Area Severity Index (PASI) (primary outcome), Physician Global Assessment (PGA), Self-administered PASI (SAPASI), and Dermatology Life Quality Index (DLQI) (secondary outcomes).

Results: 122 participants (76 male/46 female) with mean (SD) age 53.6 (10.0) years, PASI 3.1 (2.0) and serum 25(OH)D 14.9 (3.9) ng/mL were included. Of these, 60 were randomised to the vitamin D group and 62 to the placebo group. 120 participants (59 vitamin D/61 placebo) completed the study. By completion mean 25(OH)D was 29.7 (5.2) ng/mL (vitamin D) and 12.0 (3.8) ng/mL (placebo). There was no significant difference in change in PASI score between the groups (adjusted difference 0.11, 95% Confidence Interval [-0.23; 0.45]). There was no significant difference in change in PGA (adjusted odds ratio 0.66 [0.27; 1.63]), SAPASI (adjusted difference -0.60 [-1.76; 0.55]) or DLQI

(adjusted difference -0.86 [-1.9; 0.19]) between the groups. No adverse effects of the intervention were registered.

Conclusion and Relevance: Vitamin D supplementation did not affect psoriasis severity. Low baseline severity scores may explain the lack of measurable effect. Surprisingly, 25(OH)D levels in the intervention group increased less-than-expected based on previous experimental data from the same source population, and this may have affected the results.

Trial registration: ClinicalTrials.gov NCT03334136

Introduction

Vitamin D (vitD) has several effects which are of relevance to psoriasis[1,2]. Most important is the regulatory effects on the immune system, and on keratinocyte proliferation and maturation[3], which are both disturbed in psoriasis[1-3]. These vitD effects are utilized in daily clinical management of psoriasis through the use of topical vitD analouges[4]. As UV(B) increases vitD production in the skin, it has been questioned whether vitD effects partly account for the treatment effect of UV(B) on psoriasis[5,6].

Studies that establish a treatment effect of oral vitD on psoriasis are lacking. Favourable outcomes following vitD supplementation have been described in open trials and case reports[7-10], but results from the three previous randomised controlled trials (RCTs) are inconsistent[11-15]. These RCTs did not consider possible effect modification by season[13-15], and only one included subjects with lower serum 25-hydroxyvitamin D (25(OH)D) levels[15] (the preferred marker of an individual's vitD status[16]).

The present study was conducted during winter in North-Norway, by which we could separate the effects of vitD from that of UV exposure. Moreover, we included subjects with lower 25(OH)D levels, who are those most likely to benefit from supplementation.

We hypothesised that elevating 25(OH)D to recommended levels in psoriasis patients with lower 25(OH)D levels would reduce psoriasis severity during winter. We examined the effect of vitD supplementation on psoriasis severity, measured by Psoriasis Area Severity Index (PASI), Physician Global Assessment (PGA), Self-administered PASI (SAPASI), and Dermatology Life Quality Index (DLQI).

Materials and methods

Trial design/location/setting

This randomised placebo-controlled trial with two parallel groups was performed at the Clinical Research Unit, University Hospital of North Norway (UNN), Tromsø (located at 69^{o} north). The trial ran during winter, when UV-exposure is insufficient for pre-vitD production in the skin[17].

Ethics, trial registration, monitoring and reporting

The Regional Ethics Committee of North-Norway (2016/1789/REK nord) and the Norwegian Medicines Agency (EUDRACT NO 2016-003378-42) approved the study (trial protocol in eSupplements). It was performed in accordance with the Helsinki Declaration and ICH guidelines E6 for GCP, and preregistered in ClinicalTrials.gov (NCT03334136) All participants signed an informed written consent. Data was collected in a study specific electronic database (RedCAP®). An independent monitor from the Clinical Research Department UNN, monitored the study. We followed the CONSORT guideline when reporting our findings.

Eligibility criteria/Recruitment

We included adults from the general population in Tromsø aged 18-79 with active plaque psoriasis (PASI>0) and baseline 25(OH)D <24 ng/mL (<60 nmol/L [conversion factor: 2.496]). We primarily recruited subjects from the Tromsø Study cohort. The Tromsø Study is a population-based multipurpose health survey performed for the 7th time in 2015-2016 (Tromsø7)[18]. Everyone aged 40 to 99 living in the municipality of Tromsø was invited (n=32 591), and 21 083 attended[18]. The survey included serum 25(OH)D measurement and self-reported psoriasis[18,19].

During the winter 2016/2017 we conducted a pilot study as a part of another vitD intervention trial (the D-COR study), which invited participants in Tromsø7 with 25(OH)D <16.8 ng/mL[20]. We included seven participants through the pilot study (eMethods).

Our main study was performed through two winter seasons; 2017/2018 (season 1) and 2018/2019 (season 2). We sent invitations to the participants in Tromsø7 with 25(OH)D <24 ng/mL, who reported active psoriasis the last 12 months. As recruitment was slower than anticipated, and the enrolment window limited by season, we decided to expand recruitment in season 2. In November 2018 we invited subjects from the general population aged 18-79 who did not participate in Tromsø7. By response to advertisement, we sent a formal invitation.

A study nurse performed a phone pre-screening of subjects who replied, to assess eligibility. A dermatologist (MJ) screened eligible subjects to confirm active plaque psoriasis. Blood samples were

drawn to confirm 25(OH)D <24 ng/mL and assess for exclusion criteria (listed in Figure 1). The flow of participants through the trial is presented in Figure 2.

Data collected at study visit 1

Enrolment ranged from mid-October to mid-January. Study visit 1 included blood samples, medical history (covering general health, psoriasis, systemic and topical medication, physical activity, smoking habits, vitD intake and solar exposure), measurement of height, weight, hip and waist circumference and conventional blood pressure. The participants brought their topical medication for weighing.

The dermatologist (MJ) assessed psoriasis severity using PASI and PGA 6-point scale. The participants completed the questionnaires SAPASI and DLQI. Description of the scoring instruments is available in eMethods.

The dermatologist used Psoriasis Epidemiology Screening Tool and examined joints to screen for psoriatic arthritis. Participants reported severity of current joint symptoms using a Visual Analog Scale (VAS) from 0-10 (recorded in mm).

Randomisation/allocation concealment/blinding

Randomisation was computer generated using block randomisation stratified by vitD status ($<$ or $\geq$ 10 ng/mL), PASI ($<$ or $\geq$ 5) and body mass index (BMI) ($<$ or $\geq$ 27 kg/m^2), allocation ratio 1:1. The study drug was Dekristol (20 000 IU cholecalciferol, Mibe, Brehna, Germany) or identically looking placebo (Hasco-Lek, Siechnice, Poland). Independent personnel at the Hospital Pharmacy UNN prepacked the drugs in numbered identical containers. At visit 1, a study nurse dispensed the drugs in accordance with the assigned randomisation number. All participants, health care providers and outcome assessors were blinded to group assignment. The study staff could not access the randomisation key until monitoring was completed and the database locked. Post-intervention 25(OH)D levels were analysed after study completion.

Intervention

The intervention was either cholecalciferol (100 000 IU loading dose, then 20 000 IU/week) or placebo for 4 months. The vitD dose was chosen based on experience from previous vitD intervention

trials[20-22], aiming to raise 25(OH)D to >32 ng/mL in the vitD group. The participants took five capsules while at the Clinical Research Unit, thereafter one capsule weekly (registered on a diary card).

8-weeks follow-up

A study nurse performed a phone follow-up after 8 weeks to register any adverse events. The participants returned an 8-weeks-questionaire (incl. details on medication used, VAS for joint pain, DLQI and SAPASI).

4 months follow-up, visit 2

At study visit 2 after four months we repeated the data collection performed at visit 1, and registered any adverse events. The same dermatologist (MJ) did the assessments. We reweighed any tube(s) of topical medication, and calculated the amount used.

The participants returned their diary card and remaining study capsules. We calculated compliance (used capsules [dispensed capsules - remaining capsules] divided by number of Mondays since inclusion).

We advised participants to take vitD 800 IU/day after study completion, and to ask their general practitioner to remeasure 25(OH)D the following winter. The participants received a gift card (NOK 200) to cover travel expenses.

Outcome variables

The primary endpoint was the group difference in change in psoriasis severity measured by PASI score at baseline and after four months.

The secondary endpoints were difference in change in PGA-, SAPASI- and DLQI-scores, and difference in use of topical treatment for psoriasis.

Measurements

The Department of Laboratory Medicine UNN measured serum 25(OH)D using an in-house liquid chromatography–tandem mass spectrometry method which detects both $25(OH)D_3$ and $25(OH)D_2$.

The sum of these is presented as 25(OH)D in the results. In order to confirm the unexpected low rise in 25(OH)D, and minimize variance, we reanalysed frozen serum for all 25(OH)D measurements in one batch. The reanalysed values are reported. For details regarding biochemical analyses, see eMethods.

BMI was calculated as weight in kilograms (kg) divided by height in meters squared (m^2).

Power calculation and statistical analysis

To have 80 % power to detect a 0.5 standard deviation change in PASI using a 0.05 significance level, we needed 64 participants in each group (intervention or placebo). We aimed at including 130 participants, with a maximum of 160.

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 27. All analyses were done two-sided. Presented results are analysed per-protocol. Intention to treat analyses (last observation carried forward) was performed, but did not alter the result.

We assessed difference in change in all continuous outcome variables using linear regression (ANCOVA) with the respective change variable as outcome, treatment group as fixed factor and the respective baseline value as covariate. We evaluated fit of the models, including normality, outliers, and homogeneity of variance, by assessing the standardized residuals (histograms, scatterplots of residuals against predicted values). All deemed a reasonably good fit without transformation of the data. We used Cook's distances and Leverage values to identify influential cases, and ran sensitivity analyses to explore the effects of these. We evaluated the homogeneity of regression slopes-assumption by inspecting scatterplots of the outcome variable against the covariate, and by assessing baseline-by-treatment interaction terms in the regression models. If violated, we performed sensitivity analyses including the interaction term and re-evaluated fit of the model. Difference in change in PGA-score was assessed using ordinal logistic regression with baseline PGA as covariate. Change in PGA-score had three levels (-1, 0, 1). The assumption of proportional odds was met. The placebo group was reference group in all regression models.

We performed sensitivity analyses by adjusting the main models for smoking, baseline 25(OH)D, BMI, and joint symptoms. We applied linear regression to assess the contribution of known predictors of 25(OH)D response to supplementation (baseline BMI, age, sex, baseline 25(OH)D)[23], and travel to the tropics.

Results

Baseline characteristics of the 122 included participants are shown in Table 1. Detailed psoriasis-related anamnestic information is available in eTable 1. Only 53 participants (43.3 %) had affected body surface area (BSA) of >10 % in any area at baseline (Table 1).

120 participants completed the study (Figure 2). Compliance with the intervention was 98.6 %.

The use of both systemic and topical treatment was balanced between the groups. No participant used systemic medication for psoriasis. Three participants used disease modifying drugs for psoriatic arthritis in stable dose through the study.

Post-intervention 25(OH)D levels are shown in Table 1. Only 24 (41.1 %) participants in the vitD group reached 25(OH)D ≥30 ng/mL post-intervention.

Primary analyses:

Primary outcome

There was no significant difference in change in PASI scores between the groups (adjusted difference 0.11, 95 % Confidence Interval [-0.23; 0.45], p=0.52) (Table 2).

Secondary outcomes

Participants in the vitD group had 34 % decreased odds of being in the higher PGA change categories (0 or +1), compared to the placebo group. However, the result was not significant (adjusted odds ratio 0.66 [0.27; 1.63], p=0.37) (Table 2).

There was no significant difference in change in SAPASI scores (adjusted difference -0.60 [-1.76; 0.55], p=0.30) or DLQI scores overall (adjusted difference -0.86, [-1.9; 0.19], p=0.11) between the groups (Table 2).

The used amount of topical medication (measured in grams) was not significantly different between the groups. Details regarding topical therapy used are available in eResults.

Sensitivity analyses did not change the results (eResults). Correlations between the outcome measures are shown in eTable 4.

Explorative analyses:

In order to assess a potential change in severity for those with more disease activity, we performed explorative analyses in subgroups defined by the respective median baseline value for the continuous outcomes (Table 3). These analyses revealed no new findings for PASI or SAPASI, or DLQI below median. However, in those with DLQI above median (DLQI≥4), difference in DLQI change was significant in favour of the vitD group (adj. diff -2.07, [-3.67; -0.46], p=0.01). The difference was seen mainly on the DLQI subscales Symptoms and feelings, Personal relationships, and Treatment (eTable 5).

Explorative analysis of subgroups with moderate or higher PGA (n=26) led to a substantial loss of power, and did not reveal new findings (results not shown).

Explorative analysis restricted to participants with affected BSA >10 % in any area (n=53) had only minor impact on the adjusted difference in change values and odds ratios (results not shown). The same was found when excluding participants who travelled to the tropics during the study (n=10).

A linear model including baseline BMI, age, sex, baseline 25(OH)D[23], and travel to the tropics explained 15 % of the variation in post-intervention 25(OH)D level in the vitD group (eTable 3).

Safety:

No treatment specific adverse effects were registered during the study.

Discussion

Our study did not show an effect of weekly vitD supplementation on psoriasis severity measured by PASI, PGA, SAPASI or use of topical treatment. Neither did we find an effect on psoriasis-related quality of life measured by DLQI.

Our general population approach resulted in very low average baseline psoriasis severity, and the anticipated worsening of severity in winter did not arise. PASI has limited responsiveness in mild disease, particularly when psoriasis affects <10 % BSA in any area[24]. Change in PASI then depends entirely on change in plaque severity scores, and may be underestimated[24]. Only 53 participants (43.3 %) in our sample had baseline BSA >10 % in any area; making it close to impossible to detect change. Both improvement and deterioration may therefore have been missed. SAPASI has the same limitations as PASI when BSA is <10 % in any area. Change in PGA scores showed a favourable response to vitD supplementation, but the results were not statistically significant. Difference in use of topical treatment could have been a surrogate marker for difference in treatment effects. However, our participants used on average small amounts (if any) topicals, making the measure less valuable.

Psoriasis can have substantial impact on quality-of-life, which does not always correlate with disease severity measurements[25]. Our participants had on average low DLQI scores, and these were only weakly correlated with SAPASI, PGA and PASI post-intervention. DLQI captures other symptoms of disease than solely visible ones (e.g. pruritus and pain)[25], and could point to changes not captured by the severity measures. However, an effect of vitamin D supplementation on DLQI was not apparent in our trial.

Considering the low baseline severity scores, lack of (or possibly undetected) winter deterioration, and the weak PASI/SAPASI responsiveness in mild disease, we found it warranted to explore the effects in subgroups based on median split. For PASI and SAPASI this revealed no new insight. Those with BSA <10 % were close to evenly distributed among the median split groups, which left us with the same limitations as in the primary analysis. In those with baseline DLQI above median (≥4) we found a significant difference in DLQI change in favour of vitD. A DLQI change of -2 points is considered small[26]. However, in our subsample, this represents a 29 % improvement. This finding may suggest a

small favourable response to vitD on psoriasis-related symptoms that we were not able to detect using the chosen severity scoring instruments.

Our findings regarding PASI and PGA are in line with two previous RCTs from New Zealand[13,14]. Low baseline severity scores make them suffer the same limitations in effect assessment as in our study. Moreover, their participants had sufficient average baseline 25(OH)D, making them less likely to benefit from supplementation. Their results may also have been affected by increase in 25(OH)D in the placebo groups[13,14]. Opposed to our findings, an RCT from Thailand including cases with mild psoriasis and low baseline 25(OH)D, found a small significant effect on PASI in favour of vitD after 3 months, but just borderline significant after 6 months[15]. The study was small, did not consider effect of concomitant topical therapy, and reported small differences in 25(OH)D post-intervention between the intervention and placebo group. A recent meta-analysis including the three mentioned RCTs was inconclusive[11].

Immunomodulatory effect of vitD is believed to depend on maintaining 25(OH)D >30 ng/mL[12]. The vitD dose given in our trial exceeds the ≥1500-2000 IU/d recommended by the Endocrine Society to maintain 25(OH)D >30 ng/mL[16]. Based on response to an equal vitD supplementation regimen given in previous RCTs performed in the same population, we expected the vitD group to reach average 25(OH)D >32 ng/mL[20-22]. One of these previous trials (D-COR) also had equal intervention length and similar inclusion and exclusion criteria as our study[20]. In the D-COR subsample enrolled from mid-October to mid-January, mean 25(OH)D in the vitD group was 34.4 ng/mL post-intervention, and 75 % reached 25(OH)D ≥30 ng/mL (personal communication, primary investigator Rolf Jorde). In contrast, only 41.1 % reached 25(OH)D ≥30 ng/mL in our vitD group, although compliance was excellent. This was surprising, and may have influenced our results. Higher average BMI in our study compared with D-COR[20], may explain some of the observed difference in 25(OH)D response. However, when exploring this, much of the variation in post-intervention 25(OH)D was unexplained by known predictors of response to vitD supplementation (BMI, baseline 25(OH)D, age, sex)[23] or travel to tropical areas during the study. We hypothesise that there may be genetic differences in uptake, distribution, and enzymatic processing of cholecalciferol in persons with psoriasis compared

with the general population. VitD non-responsiveness, possibly caused by genetic differences, has been suggested in relation to psoriasis[7] and autoimmune diseases in general[12,27]. Favourable outcomes of high vitD doses on psoriasis severity has been reported[7,8], but not evaluated in RCTs. A recent American study suggested a preventive effect of vitD supplements on autoimmune disease risk[28]. Moreover, a recent mendelian randomisation study found evidence of a causal relationship between genetically predicted lower 25(OH)D and incident psoriasis[29]. VitD may therefore play a role in both prevention and treatment of psoriasis.

Our study has several strengths. Foremost, the thorough randomised controlled design and elimination of sunshine as a source of vitD, creating a true placebo group. We also have detailed information on possible confounders, few drop outs, and high compliance. Furthermore, the same dermatologist did all assessments, minimizing differences in severity scoring.

Based on our findings, any large effect of vitD supplementation on psoriasis severity seems unlikely in those with mild disease (PASI <5). We cannot conclude on whether vitD supplementation has a small to moderate effect based on our data, considering the discussed limitations. Future trials should include cases with more extensive psoriasis and/or use severity measurements which are more sensitive in the lower spectrum. Also, one should insure to achieve the targeted 25(OH)D level, possibly aiming at the 25(OH)D level achieved through UV(B) treatment (>40 ng/mL)[30]. Further biological analysis investigating the vitD metabolism in persons with psoriasis are warranted.

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Data access/Responsibility/Analysis: Marita Jenssen had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Supporting Information

Full trial protocol available online.

Online supplementary material:

eMethods

The pilot study

Description of outcome measures

Measurements

eResults

Details regarding topical therapy used and travels to tropical areas during the study.

Sensitivity analyses.

eTable 1: Psoriasis description anamnestic at baseline.

eTable 2: Body surface area (BSA) affected at baseline.

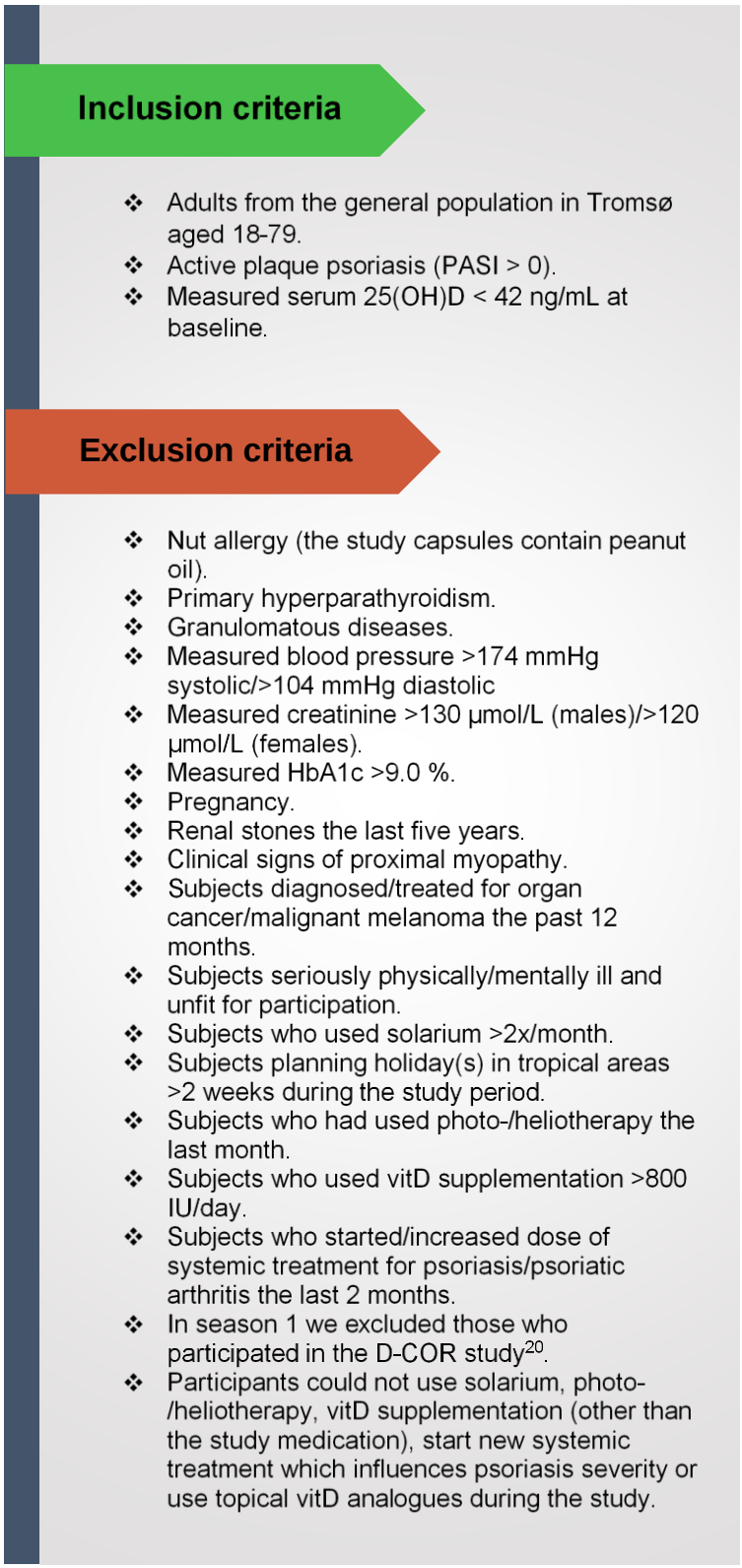
eTable 3: Linear regression assessing predictors of 25(OH)D levels post-intervention in the vitamin D group.

eTable 4: Correlations between the psoriasis severity measures and DLQI scores at baseline and after 4 months.

eTable 5: Results of linear regression analysis assessing difference in change in DLQI subscales between treatment and placebo groups after 4 months, in the participants with DLQI ≥ 4 at baseline.

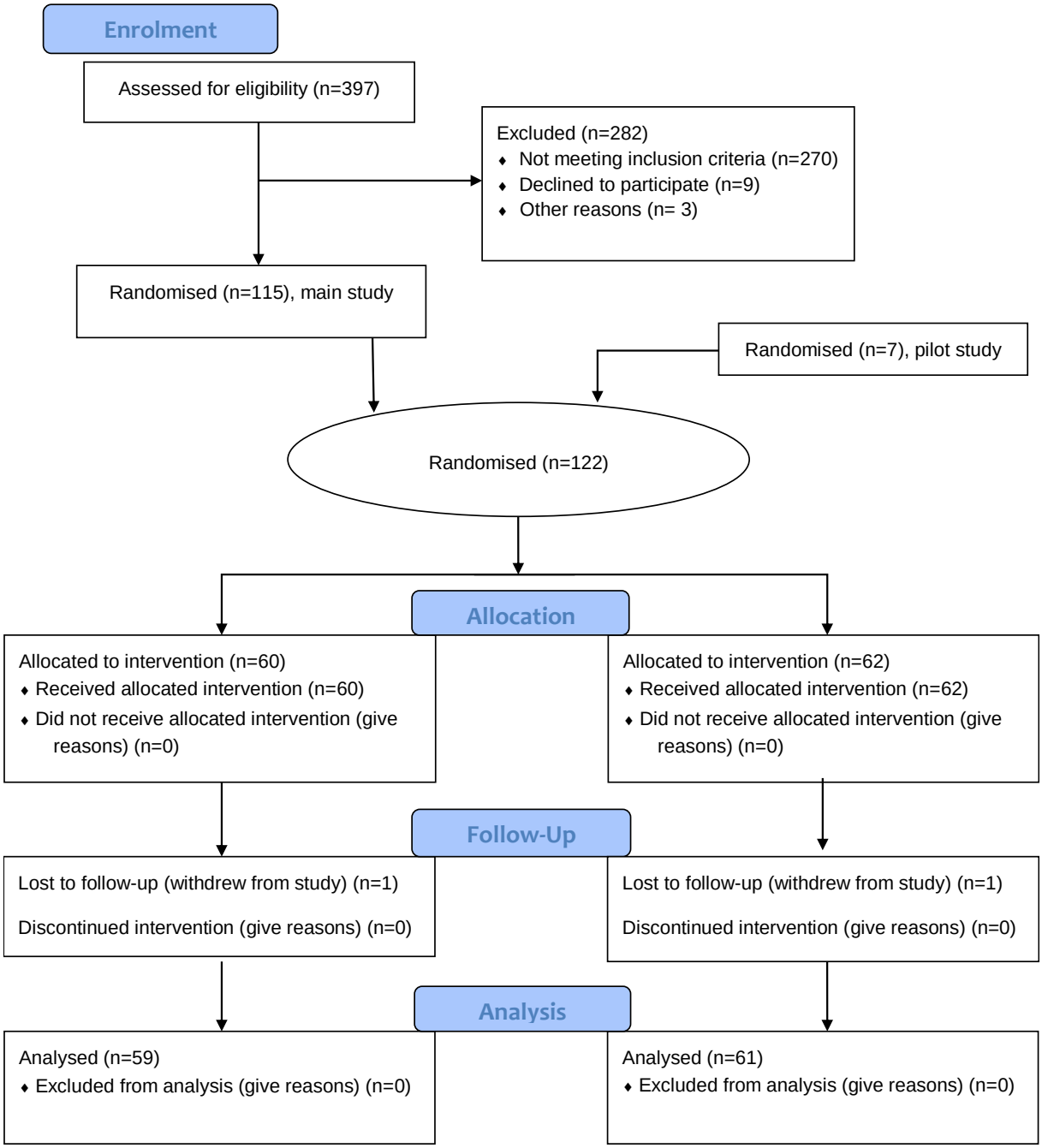
Figures

Figure 1. The trial's inclusion and exclusion criteria



BP=measured blood pressure. HbA1c= Haemoglobin A1c, vitD=vitamin D, IU=international units.

Figure 2. CONSORT Flow Diagram showing the flow of participants through the phases of the trial



n=number of participants.

Tables

TABLE 1
Characteristics of the participants in the vitamin D and placebo groups at baseline and after 4 months.

	Vitamin D		Placebo	
	Baseline	After 4 months	Baseline	After 4 months
Participants (n)				
Total	60	59	62	61
Main study	57	56	58	58
Pilot study	3	3	4	3
Age	53.3 (10.9)	-	54.0 (9.1)	-
Sex				
Male	37 / 61.7	37 / 62.7	39 / 62.9	39 / 63.9
Female	23 / 38.3	22 / 37.3	23 / 37.1	22 / 36.1
Weight, kg	86.5 (17.0)	86.9 (17.8)	83.4 (16.3)	84.3 (16.4)
BMI, kg/m2	28.9 (5.4)	29.0 (5.7)	28.0 (4.3)	28.4 (4.2)
Daily smoking	7 / 11.7	6 / 10.2	15 / 24.2	13 / 21.3
Daily snuff consumption	10 / 16.7	9 / 15.3	7 / 11.3	6 / 9.8
Previously confirmed PsA at baseline	7 / 11.7	-	6 / 9.7	-
Possible PsA diagnosed at study visit	0	0	1	0
PASI score	3.2 (2.1)	2.9 (2.2)	2.9 (1.9)	2.6 (1.7)
SAPASI score	4.0 (3.2)	3.6 (3.2)	3.5 (2.9)	3.7 (4.5)
DLQI score	4.4 (4.0)	3.8 (3.4)	4.8 (3.9)	4.9 (3.9)
PGA score				
Minimal	10 / 16.7	12 / 20.3	10 / 16.1	9 / 14.8
Mild	36 / 60.0	33 / 55.9	40 / 64.5	38 / 62.3
Moderate	14 / 23.3	14 / 23.7	12 / 19.4	14 / 23.0
Marked/Severe	0 / 0	0 / 0	0 / 0	0 / 0
BSA any area > 10 %[1]	29 / 48.3	25 / 41.7	24 / 38.7	18 / 29.0
25(OH)D total, ng/mL	15.1 (3.4)	29.7 (5.2)	14.8 (4.6)	12.0 (3.8)
Calcium, mg/dL	9.40 (0.33)	9.28 (0.39)	9.44 (0.34)	9.36 (0.32)
Phosphate, mg/dL	3.04 (0.56)	3.00 (0.52)	3.20 (0.50)	3.02 (0.55)
PTH, pg/mL	51.6 (17.5)	54.9 (15.0)	45.0 (14.0)	52.7 (15.9)

Values are given as count / % or mean (standard deviation) unless otherwise stated.
BMI=Body Mass Index. PsA=psoriatic arthritis. PASI= Psoriasis Area Severity Index. SAPASI= Self-Administered Psoriasis Area Severity Index. DLQI= Dermatology Life Quality Index. PGA=Physician Global Assessment. BSA=Body Surface Area. 25(OH)D=25-hydroxyvitamin D. PTH=Parathyroid Hormone.
25(OH)D, calcium, phosphate and PTH are measured in serum.

Conversion factors for converting measurements from conventional to SI units:
25(OH)D: ng/mL*2.496 = nmol/L. Calcium: mg/dL*0.25 = mmol/L. Phosphate: mg/dL*0.323 = mmol/L. PTH: pg/mL*0.106= pmol/L.

[1] BSA any area >10 % = having area score 2 or more in any of the four areas in the PASI scoring instrument.

TABLE 2

Difference in change in PASI, SAPASI and DLQI scores and odds ratio of difference in PGA score between treatment and placebo groups after 4 months.

	Vitamin D (n=59)	Placebo (n=61)	Difference in change (unadjusted)[1]	Difference in change (adjusted)[1,2]	p-value (adjusted)[1,2]
Change in PASI score	-0.34 (0.98)	-0.41 (0.97)	0.07 [-0.28; 0.42]	0.11 [-0.23; 0.45]	0.52
Change in SAPASI score	-0.50 (2.26)	0.25 (3.96)	-0.75 [-1.9; 0.43]	-0.60 [-1.76; 0.55]	0.30
Change in DLQI score	-0.59 (3.54)	0.10 (3.17)	-0.69 [-1.9; 0.52]	-0.86 [-1.9; 0.19]	0.11
Change in PGA score			OR (unadjusted)[1]	OR (adjusted)[1,2]	
-1	8 / 13.6	5 /8.2			
0	46 / 78.0	49 / 80.3			
1	5 / 8.5	7 / 11.5	0.64 [0.26; 1.55]	0.66 [0.27; 1.63]	0.37

Summarising raw values are given as mean (standard deviation) or count / %.

95 % confidence intervals are given in squared brackets.

PASI= Psoriasis Area Severity Index. SAPASI= Self-Administered Psoriasis Area Severity Index.

DLQI= Dermatology Life Quality Index. PGA=Physician Global Assessment. OR=odds ratio.

[1] Linear regression model for continuous outcomes and ordinal logistic regression with odds ratio estimates for PGA score.

[2] Adjusted for baseline value.

TABLE 3

Difference in change in PASI, SAPASI and DLQI scores between treatment and placebo groups after 4 months, in subgroups defined by median of baseline value.

Outcome	Subgroup	Vitamin D				Placebo						
		Baseline		4 months		Baseline		4 months		Difference in change (unadjusted)[1]	Difference in change (adjusted)[1]	p-value (adjusted)[1]
		n	Score	n	Score	n	Score	n	Score			
PASI score	<2.70	28	1.6 (0.6)	27	1.5 (0.9)	32	1.5 (0.8)	31	1.4 (0.8)	-0.07 [-0.40; 0.26]	-0.04 [-0.37; 0.29]	0.80
	≥2.70	32	4.6 (1.9)	32	4.1 (2.3)	30	4.5 (1.4)	30	3.7 (1.5)	0.26 [-0.33; 0.84]	0.26 [-0.32; 0.85]	0.38
SAPASI score	<3.12	26	1.4 (0.9)	24	1.9 (1.8)	35	1.6 (0.9)	35	2.5 (1.8)	-0.58 [-1.41; 0.25]	-0.59 [-1.43; 0.25]	0.17
	≥3.12	34	6.0 (2.9)	34	4.8 (3.4)	27	5.9 (2.8)	26	5.3 (6.3)	-0.44 [-2.63; 1.75]	-0.45 [-2.65; 1.75]	0.69
DLQI score	<4.00	28	1.5 (1.0)	27	3.0 (2.9)	28	1.9 (1.0)	28	2.6 (2.0)	0.69 [-0.53; 1.92]	0.73 [-0.52; 1.99]	0.25
	≥4.00	32	6.9 (3.9)	32	4.6 (3.6)	34	7.2 (3.8)	33	6.9 (4.0)	-1.86 [-3.66; -0.05]	-2.07 [-3.67; -0.46]	0.01

Score values are given as mean (standard deviation). 95% confidence intervals are given in squared brackets.

PASI= Psoriasis Area Severity Index. SAPASI= Self-Administered Psoriasis Area Severity Index. DLQI= Dermatology Life Quality Index.

n = number of participants.

[1]Linear regression model. The adjusted model includes baseline value.