Mahidol University
Faculty of Medicine Siriraj Hospital

Vitamin D Status in Thai Patients with Cardio-Metabolic Disorders

From a cross- sectional study to further research on vitamin D

Sutin Sriussadaporn, M.D.
Nipith Charoenngam, M.D.
Division of Endocrinology and Metabolism
Department of Medicine, Faculty of Medicine Siriraj Hospital

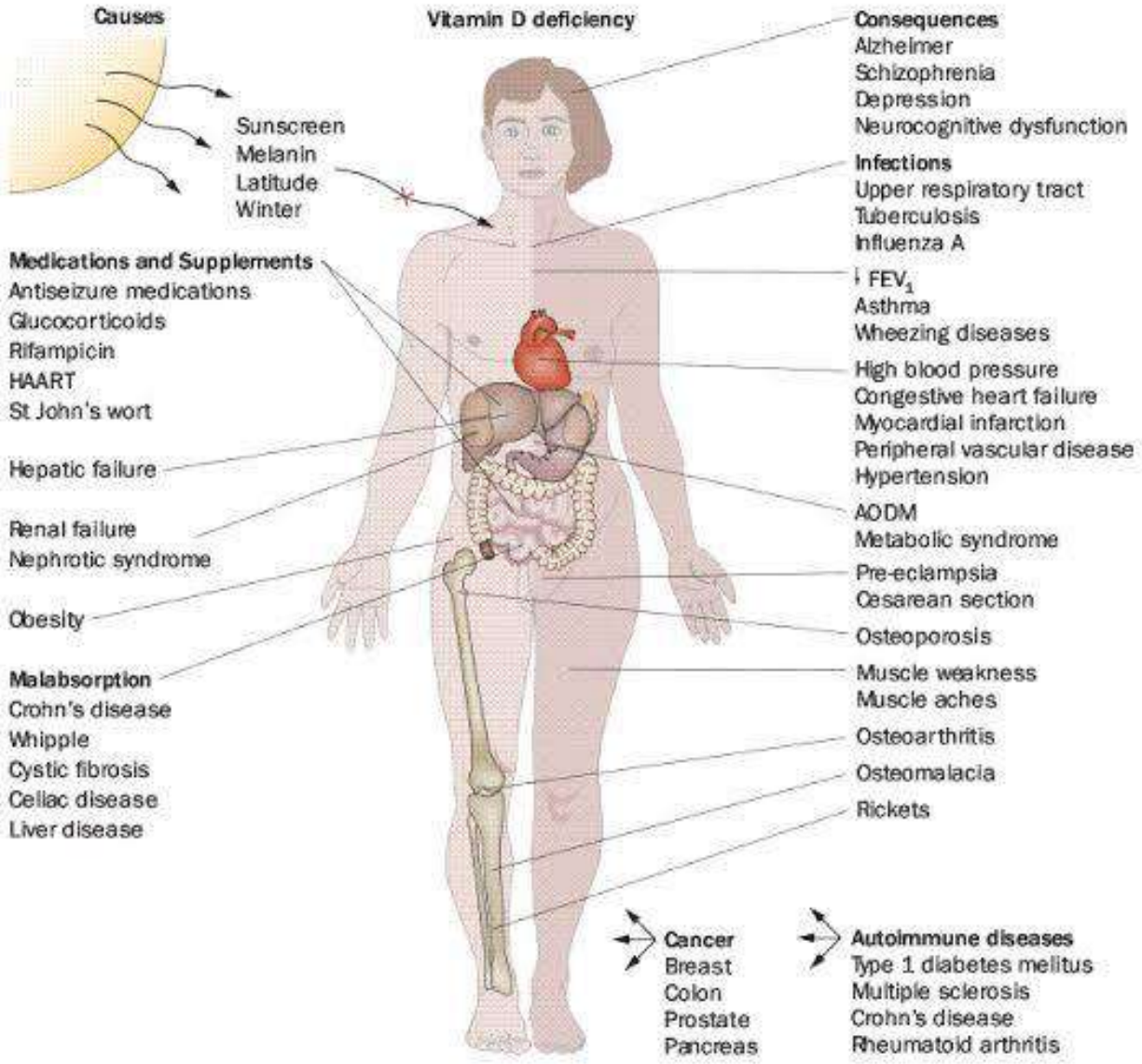
Vitamin D and health status

- Vitamin D has major roles in calcium and bone metabolism and also functions of other body systems.
- Consequences of vitamin D deficiency
  - Musculoskeletal diseases
    - Rickets/osteomalacia, growth retardation
    - Osteoporosis
  - Non-musculoskeletal diseases
    - Autoimmune diseases
    - Cancers
    - Neuropsychiatric disorders
    - Cardio-metabolic diseases: type 2 DM, HT, DLP CVD, CHF, metabolic syndrome, and CKD

Matthias Wacker and Michael F. Holick. Sunlight and Vitamin D. Dermato-Endocrinology 2013;5:1, 51-108.

VITAMIN D DEFICIENCY AND HEALTH STATUS

CAUSES AND CONSEQUENCES



Matthias Wacker and Michael F. Holick. Sunlight and Vitamin D. Dermato-Endocrinology 2013;5:1, 51-108.

Vitamin D insufficiency in Thai populations

No studies defined whether the participants had CMDs and vit. D sup

Authors	Year	Sample size	Populations in study	Prevalence of inadequate vitamin D status	Cut-point (ng/mL)
Chailurkit et al.	2011	2,641	Thai population	34.2-64.6%	< 30
Chailurkit et al.	2011	446	Thai elderly women	54.0%	< 30
Kruavit et al.	2012	93	Thai nursing home residents	61.3%	< 28
Nimitphong et al.	2013	1,449	Male subjects	13.9%	< 20
		541	Female subjects	43.1%	
Soontrapa et al.	2015	66	Rural elderly males	13.6%	< 40
		100	Urban elderly males	48.0%	

Original Article

Prevalence of Inadequate Vitamin D Status in Ambulatory Thai Patients with Cardiometabolic Disorders Who Had and Had No Vitamin D Supplementation

Nipith Charoenngam MD[1], Sutin Sriussadaporn MD[1]

[1] Division of Endocrinology and Metabolism, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Background: Data regarding the prevalence of inadequate vitamin D status in ambulatory Thai population with cardiometabolic disorders (CMDs) are scarce.

Objective: To investigate the prevalence of hypovitaminosis D in ambulatory Thai patients with CMDs with and without vitamin D supplementation (DS).

Materials and Methods: This descriptive cross-sectional study randomly recruited patients with one or more CMDs that attended the outpatient clinic during December 2016 to May 2017. CMDs included type 2 diabetes (T2DM), hypertension (HT), dyslipidemia (DLP), and coronary artery disease (CAD). Serum 25-hydroxyvitamin D (25-OHD) levels were measured by electrochemiluminescence immunoassay.

Results: Four hundred and forty-four patients were included. Mean age was 65.79±10.12 years, 72.3% were aged >60 years, and 35.1% were male. CMDs included T2DM (75.9%), prediabetes (11.7%), HT (72.1%), DLP (98.3%), and CAD (7.4%). Mean serum 25-OHD was 26.12±10.10 ng/mL, with 29.7%, 42.1%, 25.5%, and 2.7% of patients having serum 25-OHD level of ≥30, 20-<30, 10-19.9, and <10 ng/mL, respectively. Twenty percent of patients had DS. Prevalence of 25-OHD <20 ng/mL and <30 ng/mL were lower in patients with DS than in patients without DS (19.1% *vs.* 30.6% and 61.7% *vs.* 72.6%, respectively, both p <0.05). Among the 350 patients without DS, prevalence of 25-OHD <10 ng/mL was higher in patients with HT and patients with CAD than in those without (3.9% *vs.* 0.0% and 14.8% *vs.* 1.9%, respectively, both p<0.05). Male patients had higher serum 25-OHD levels and lower prevalence of 25-OHD <30 ng/mL and 25-OHD <20 ng/mL than did the female patients (29.10±11.61 vs. 23.76±8.69 ng/mL, 57.4% *vs.* 81.4%, and 20.9% *vs.* 36.2%, respectively, all p <0.005). Non-elderly patients (age ≤60) had lower serum 25-OHD levels and higher prevalence of 25-OHD <30 ng/mL and 25-OHD <20 ng/mL than did the elderly patients (age >60) (23.23±9.20 *vs.* 26.81±10.41 ng/mL, 82.1% *vs.* 68.4%, and 43.4% *vs.* 25.0%, respectively, all p<0.01).

Conclusion: Prevalence of inadequate vitamin D status in ambulatory Thai patients with one or more CMDs was high in patients with and without DS. It was higher in patients without DS than in both patients with DS and all patients regardless of DS status. Factors associated with higher prevalence of inadequate vitamin D status in patients with CMDs included HT, CAD, age ≤60 years, and female gender.

Keywords: Thailand prevalence, Inadequate vitamin D status, Ambulatory Thai patients, Cardiometabolic disorders, Vitamin D supplementation

J Med Assoc Thai 2018; 101 (6): 739-52
Website: http://www.jmatonline.com

Prevalence of inadequate vitamin D status in ambulatory Thai patients with cardiometabolic disorders who had and had no vitamin D supplementation

Table 1. Demographic characteristics, vitamin D status, and clinical characteristics of all patients, and vitamin D status of patients that did and that did not receive vitamin D supplementation

Characteristics	Mean±SD or n (%)	Range (min–max)
Age (years)	65.79±10.12	(34 to 92)
Elderly patients (age >60 years)	321 (72.3%)	
Male gender	156 (35.1%)	
Having vitamin D supplementation	94 (21.2%)	
All patients	(N=444; 100%)	
Serum 25-OHD (ng/mL)	26.12±10.10	(3.00 to 70.00)
25-OHD ≥30 ng/mL	132 (29.7%)	
25-OHD = 20 to <30 ng/mL	187 (42.1%)	
25-OHD = 10 to <20 ng/mL	113 (25.5%)	
25-OHD <10 ng/mL	12 (2.7%)	
Patients with vitamin D supplementation	(n=94; 21.2%)	
Serum 25-OHD (ng/mL)	27.56±9.72	(11.74 to 45.71)
25-OHD ≥30 ng/mL	36 (38.3%)	
25-OHD = 20 to <30 ng/mL	40 (42.6%)	
25-OHD = 10 to <20 ng/mL	16 (17.0%)	
25-OHD <10 ng/mL	2 (2.1%)	
Patients without vitamin D supplementation	(n=350; 78.8%)	
Serum 25-OHD (ng/mL)	25.72±10.18	(3.00 to 70.00)
25-OHD ≥30 ng/mL	96 (27.4%)	
25-OHD = 20 to <30 ng/mL	147 (42.0%)	
25-OHD = 10 to <20 ng/mL	97 (27.7%)	
25-OHD <10 ng/mL	10 (2.9%)	
Underlying diseases		
Type 2 diabetes mellitus	337 (75.9%)	
Prediabetes	52 (11.7%)	
Hypertension	320 (72.1%)	
Dyslipidemia	392 (88.3%)	
Coronary artery disease	33 (7.4%)	

Abbreviations: SD, standard deviation; serum 25-OHD, serum 25-hydroxyvitamin D

Charoenngam N and Sriussadaporn S. J Med Assoc Thai 2018; 101:739-52.

Ambulatory Thai patients with cardiometabolic disorders who had no vitamin D suppl. had higher prevalence of inadequate vitamin D status than those who had vitamin D suppl.

Table 2. Vitamin D status in patients with cardiometabolic disorders compared between patients with and without vitamin D supplementation

Patients	Serum 25-OHD (ng/mL) Mean±SD	25-OHD <10 ng/mL n (%)	25-OHD <20 ng/mL n (%)	25-OHD <30 ng/mL n (%)
All patients (N=444)	26.12±10.10	12 (2.7%)	125 (28.2%)	254 (70.3%)
Patients with vitamin D supplementation (n=94; 21.2%)	27.56±9.72	2 (2.1%)	18 (19.1%)[a]	58 (61.7%)[b]
Patients without vitamin D supplementation (n=350; 78.8%)	25.72±10.18	10 (2.9%)	107(30.6%)[a]	253 (72.6%)[b]

A *p*-value<0.05 indicates statistical significance

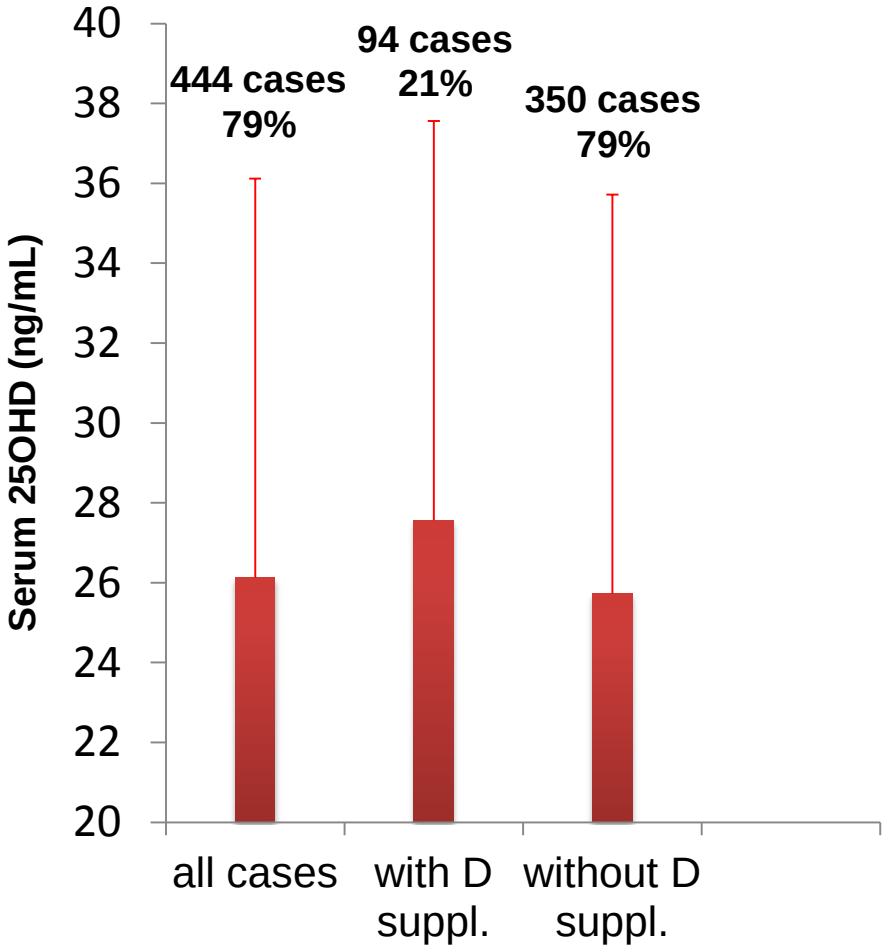
[a] denotes statistically significant difference between patients with and without vitamin D supplementation (p=0.029)

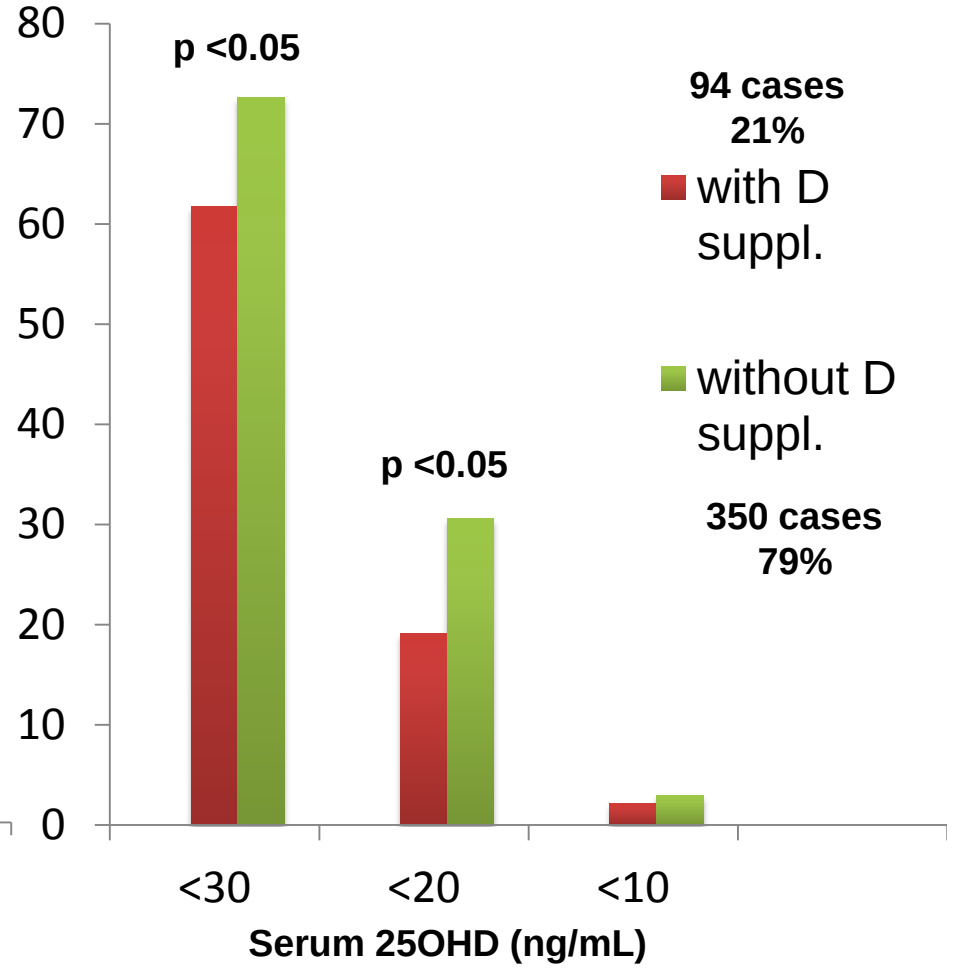
[b] denotes statistically significant difference between patients with and without vitamin D supplementation (p=0.041)

Abbreviations: serum 25-OHD, serum 25-hydroxyvitamin D; SD, standard deviation

Charoenngam N and Sriussadaporn S.
J Med Assoc Thai 2018; 101:739-52.

Serum vitamin D levels and prevalence of inadequate vitamin D status in ambulatory Thai patients with cardio-metabolic disorders who had and had no vitamin D supplementation





Of the 444 cases, there were 94 cases or 21 % had D suppl. and 350 cases or 79% had no D suppll. Patients with CMDs who had no D suppl. had higher prevalence of inadequate vitamin D status than those who had D suppl. This finding suggests that studying without data on D suppl. of the participants can lead to the underestimation of the prevalence of inadequate vitamin D status.

Vitamin D status in 350 patients with cardiometabolic disorders that did not receive vitamin D supplementation stratified by specific disorders

Table 3. Vitamin D status in 350 patients with cardiometabolic disorders that did not receive vitamin D supplementation stratified by specific disorders

Metabolic disorder	n (%)	Serum 25-OHD (ng/mL) Mean±SD	25-OHD <10 ng/mL n (%)	25-OHD <20 ng/mL n (%)	25-OHD <30 ng/mL n (%)
All patients	350 (100%)	25.72±10.18	10 (2.9%)	107 (30.6%)[2]	254 (72.6%)
Type 2 diabetes mellitus	264 (75.4%)	25.85±10.33	9 (3.4%)	78 (29.5%)	189 (71.6%)
Prediabetes	40 (11.4%)	25.23±8.32	1 (2.5%)	12 (30.0%)	32 (80.0%)
No diabetes mellitus	46 (13.2%)	25.46±10.99	0 (0.0%)	17 (37.0%)	33 (71.7%)
Hypertension	255 (72.9%)	25.85±10.45	10 (3.9%)[a]	74 (29.0%)	186 (72.9%)
No hypertension	95 (27.1%)	25.65±9.46	0 (0.0%)[a]	31 (32.6%)	66 (69.5%)
Dyslipidemia	309 (88.3%)	25.81±10.14	8 (2.6%)	93 (30.1%)	223 (72.2%)
No dyslipidemia	41 (11.7%)	25.63±10.61	2 (4.9%)	12 (29.3%)	29 (70.7%)
Coronary artery disease	27 (7.7%)	26.15±13.93	4 (14.8%)[b]	9 (33.3%)	18 (66.7%)
No coronary artery disease	323 (92.3%)	25.76±9.82	6 (1.9%)[b]	96 (29.7%)	234 (72.4%)

A p-value<0.05 indicates statistical significance

[a] denotes statistically significant difference between patients with and without HT (p=0.05)

[b] denotes statistically significant difference between patients with and without coronary artery disease (p<0.001)

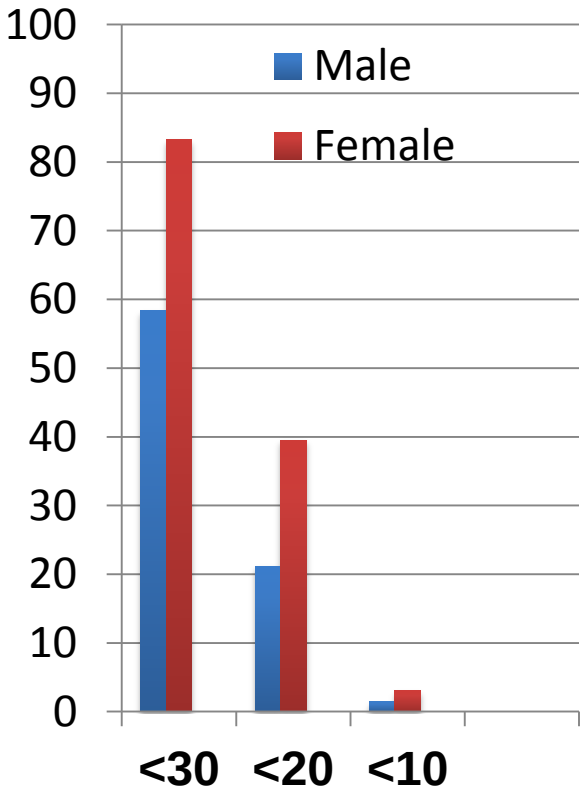
Abbreviations: serum 25-OHD, serum 25-hydroxyvitamin D; SD, standard deviation

Prevalence of vitamin D insuff. and deficiency in CMDs patients were higher than those reported in previous studies which did not clearly define whether the subjects had CMDs and vit D sup. or not.

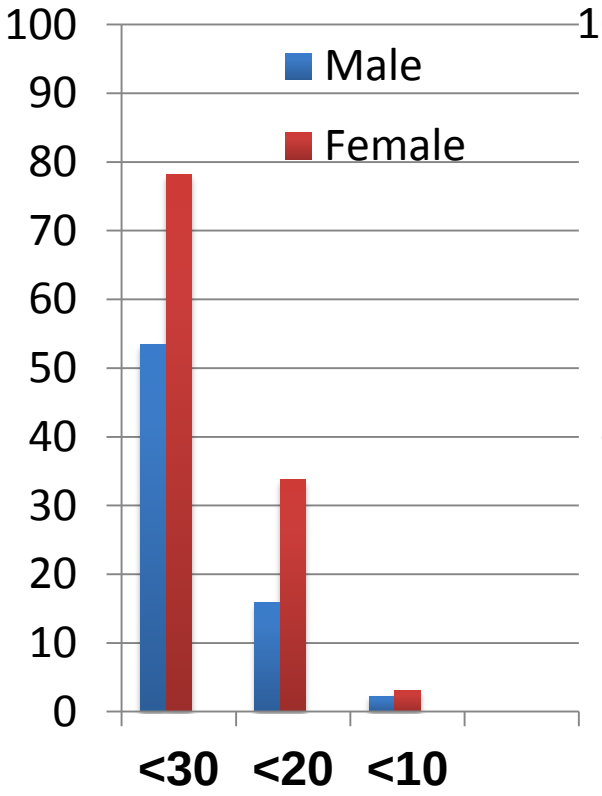
Authors	Year	Sample size	Populations in study	Prevalence of inadequate vitamin D status	Cut-point (ng/mL)
Chailurkit et al.	2011	2,641	Thai population	34.2-43.8%	< 30
Chailurkit et al.	2011	446	Thai elderly women	54.0%	< 30
Kruavit et al.	2012	93	Thai nursing home residents	61.3%	< 28
Nimitphong et al.	2013	1,449	Male subjects	13.9%	< 20
		541	Female subjects	43.1%	
Soontrapa et al.	2015	66	Rural elderly males	13.6%	< 40
		100	Urban elderly males	48.0%	
Charoenngam and Sriussadaporn	2017	350	CMDs patients without vit. D supplement	74.94% 33.42%	< 30 <20

Female patients had higher prevalence of vitamin D insuff. and deficiency than male patients both in elderly aged >60 years and non-elderly.

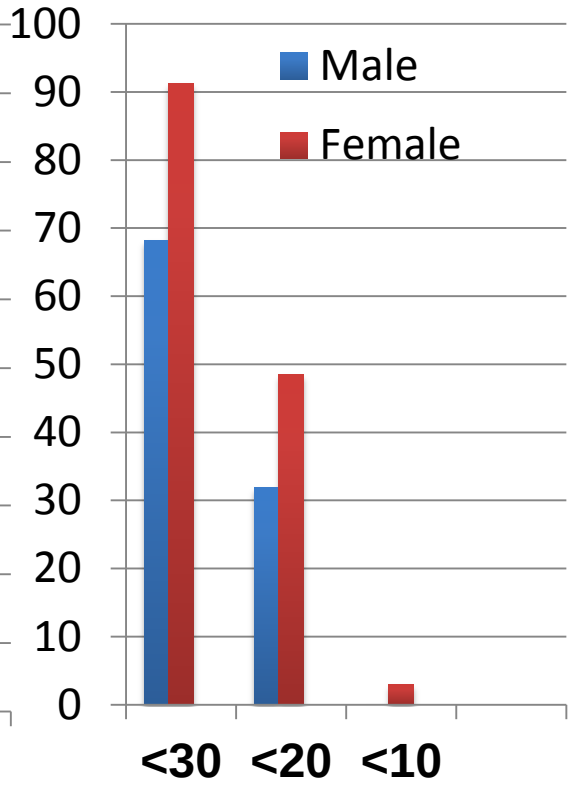
All cases
350 cases



Elderly, age >60 y
284 cases



Non-elderly, age <60 y
106 cases



Factors		Male	Female	P-value
All subjects	Serum 25-OHD levels (ng/mL)	28.92 ± 11.54	23.16 ± 8.42	<0.001*
Younger subjects	Serum 25-OHD levels (ng/mL)	26.00 ± 8.87	21.44 ± 8.20	0.003*
Elderly subjects	Serum 25-OHD levels (ng/mL)	30.38 ± 12.46	24.26 ± 8.40	<0.001*

Vitamin D status in 350 CMDs patients without vitamin D suppl. stratified by specific metabolic disorders

Table 3. Vitamin D status in 350 patients with cardiometabolic disorders that did not receive vitamin D supplementation stratified by specific disorders

Metabolic disorder	n (%)	Serum 25-OHD (ng/mL) Mean±SD	25-OHD <10 ng/mL n (%)	25-OHD <20 ng/mL n (%)	25-OHD <30 ng/mL n (%)
All patients	350 (100%)	25.72±10.18	10 (2.9%)	107 (30.6%)[2]	254 (72.6%)
Type 2 diabetes mellitus	264 (75.4%)	25.85±10.33	9 (3.4%)	78 (29.5%)	189 (71.6%)
Prediabetes	40 (11.4%)	25.23±8.32	1 (2.5%)	12 (30.0%)	32 (80.0%)
No diabetes mellitus	46 (13.2%)	25.46±10.99	0 (0.0%)	17 (37.0%)	33 (71.7%)
Hypertension	255 (72.9%)	25.85±10.45	10 (3.9%)[a]	74 (29.0%)	186 (72.9%)
No hypertension	95 (27.1%)	25.65±9.46	0 (0.0%)[a]	31 (32.6%)	66 (69.5%)
Dyslipidemia	309 (88.3%)	25.81±10.14	8 (2.6%)	93 (30.1%)	223 (72.2%)
No dyslipidemia	41 (11.7%)	25.63±10.61	2 (4.9%)	12 (29.3%)	29 (70.7%)
Coronary artery disease	27 (7.7%)	26.15±13.93	4 (14.8%)[b]	9 (33.3%)	18 (66.7%)
No coronary artery disease	323 (92.3%)	25.76±9.82	6 (1.9%)[b]	96 (29.7%)	234 (72.4%)

Patients with HT had higher prevalence of severe vitamin D deficiency defined by serum 25-OHD <10 ng/mL than those with no HT.

And also Patients with coronary artery disease had higher prevalence of severe vitamin D deficiency defined by serum 25-OHD <10 ng/mL than those with no coronary artery disease.

Patients with coexisting T2DM, HT, DLP and CAD had higher prevalence of severe vitamin D deficiency defined by serum 25-OHD <10 ng/mL than those with other combinations of CMDs.

Table 4. Vitamin D status in 350 patients with multiple cardiometabolic disorders that did not receive vitamin D supplementation

Cardiometabolic disorder combinations	n (%)	Serum 25-OHD (ng/mL) Mean±SD	25-OHD <10 ng/mL n (%)/n (%)	25-OHD <20 ng/mL n (%)/n (%)	25-OHD <30 ng/mL n (%)/n (%)
All patients	350 (100%)	25.72±10.18	12 (2.9%)	125 (28.2%)	254 (72.6%)
T2DM+HT	13 (3.7%)	27.06±8.75	0 (0%)/ 10 (3.0%)	3 (23.1%)/ 104 (30.9%)	10 (76.9%)/ 244 (72.4%)
T2DM+DLP	47 (13.4%)	26.05±9.83	0 (0%)/ 10 (3.3%)	12 (25.5%)/ 95 (31.4%)	33 (70.2%)/ 221 (72.9%)
T2DM+CAD	0 (0.0%)	-	-	-	-
HT+DLP	35 (10.0%)	25.75±8.52	0 (0%)/ 10 (3.2%)	8 (22.9%)/ 99 (31.4%)	25 (71.4%)/ 229 (72.7%)
HT+CAD	0 (0.0%)	-	-	-	-
DLP+CAD	0 (0.0%)	-	-	-	-
T2DM+HT+DLP	169 (48.3%)	25.85±10.20	5 (3.0%)/ 5 (2.8%)	50 (29.6%)/ 57 (31.5%)	123 (72.8%)/ 131 (72.4%)
T2DM+HT+CAD	3 (0.9%)	23.64±17.32	1 (33.3%)/ 9 (2.6%)[a]	1 (33.3%)/ 106 (30.5%)	2 (66.7%)/ 252 (72.6%)
T2DM+DLP+CAD	3 (0.9%)	20.99±9.70	0 (0%)/ 10 (2.9%)	1 (33.3%)/ 106 (30.5%)	2 (66.7%)/ 252(72.6%)
HT+DLP+CAD	4 (1.1%)	32.97±16.16	0 (0%)/ 10 (2.9%)	1(25.0%)/ 106(30.6%)	2 (50.0%)/ 252 (72.8%)
T2DM+HT+DLP+CAD	17 (4.9%)	25.90±14.12	3 (17.6%)/ 7 (2.1%)[b]	6(35.3%)/ 101(30.3%)	12 (70.6%)/ 242 (72.7%)

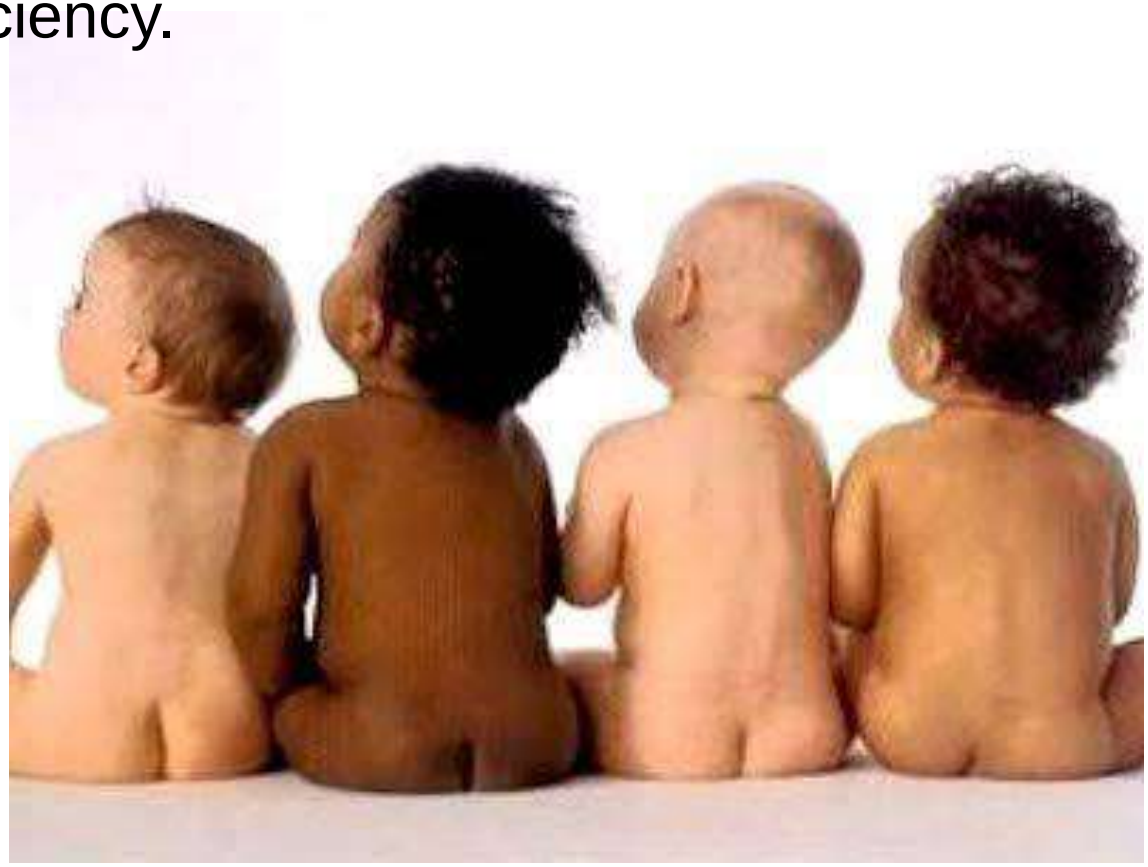
n (%)/ n (%) = number and (proportion) of patients with combination of diseases/ number and (proportion) of patients without combination of diseases

A p-value<0.05 indicates statistical significance

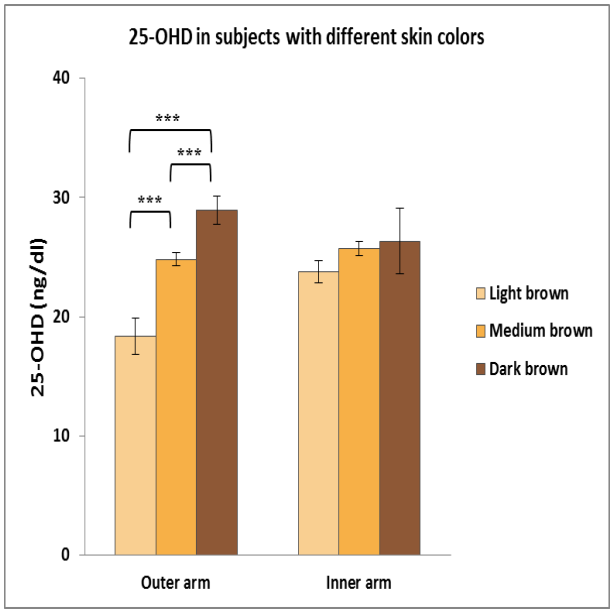
[a, b] denotes statistically significant differences between patients with and without stated multiple underlying diseases (p<0.001)

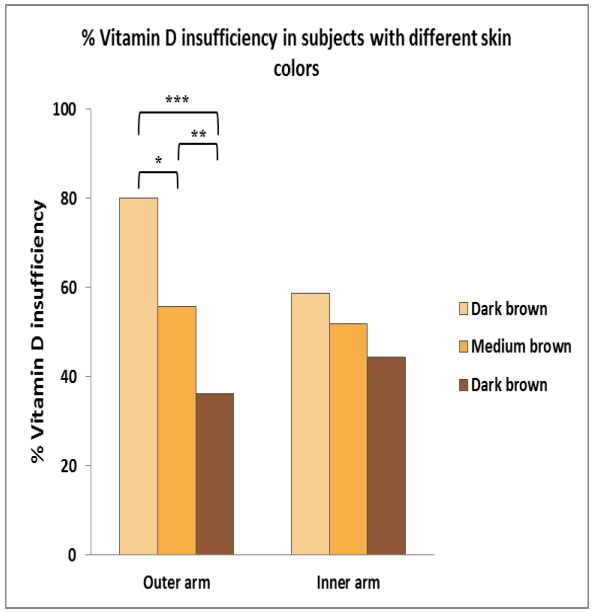
Skin color and photobiosynthesis of vitamin D

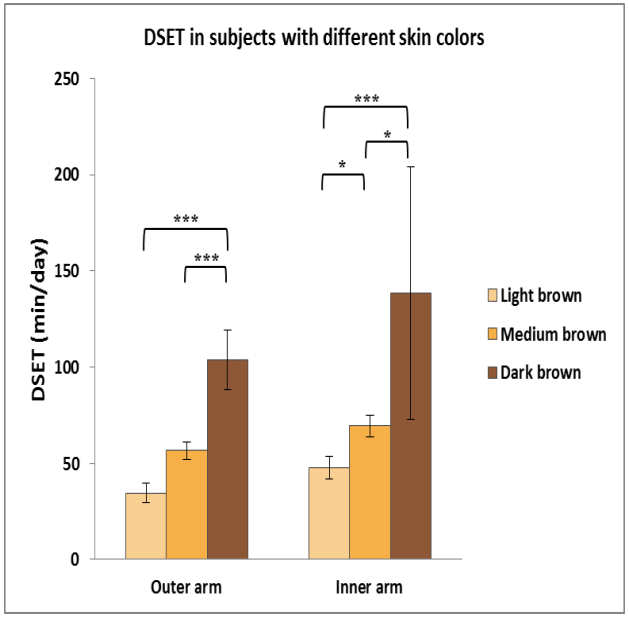
- Dark skin color is the barrier of sunlight UVB for skin photobiosynthesis of vitamin D.
- Ethnic black population has higher prevalence of vitamin D deficiency.



Relationships among skin color, vitamin D status and sunlight exposure time in patients with no vit. D suppl.







- The skin color and vitamin D status in Thai CMDs patients is related to the daily sunlight exposure time.
- Patients with darker skin color had higher serum 25-OHD levels and lower prevalence of vitamin D insufficiency and deficiency than those with lighter skin color.
- Patients with higher daily sunlight exposure time had higher serum 25-OHD levels and lower prevalence of vitamin D insufficiency and deficiency than those with lighter skin color.

Von Luschan Chromatic Skin Scale

1 – 20: Light brown

21 – 24: Medium brown

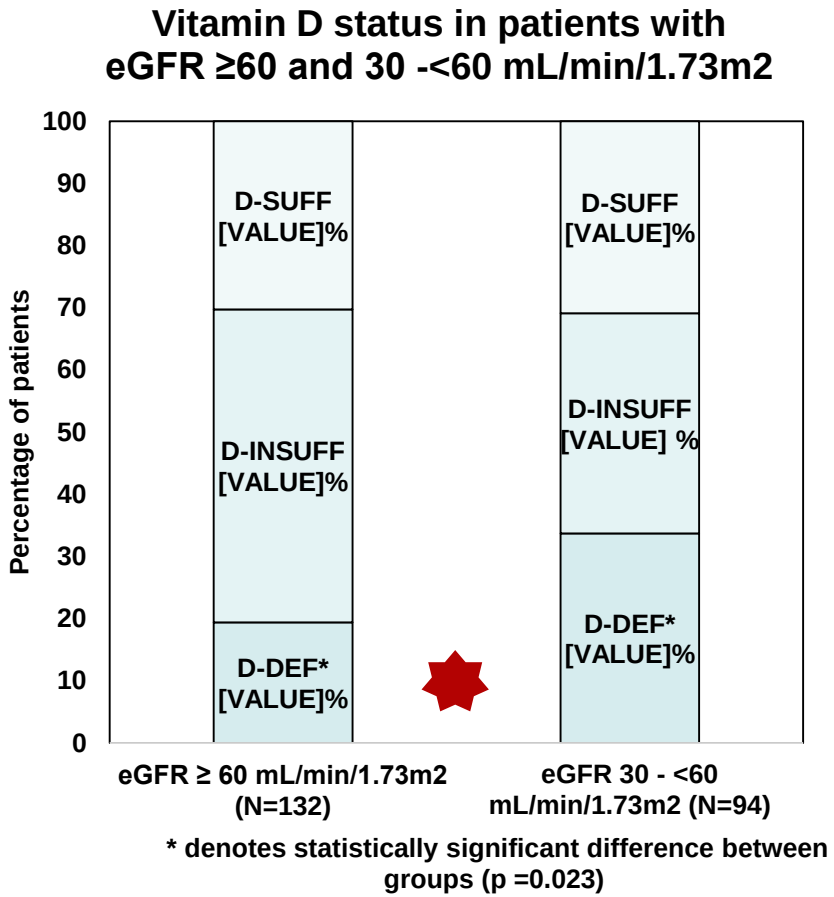
> 25: Dark brown

Relationships among skin color, vitamin D status and sunlight exposure time in patients with no vit. D suppl.

Table 2 Correlations between two factors	R	p value	
- Daily sunlight exposure time (DSET) vs. 25-OHD	0.236	< 0.001	**
- DSET vs. Skin color score at sun exposure area (VLSC of Outer arm)	0.206	< 0.001	**
- DSET vs. Skin color score at non-sun exposure area (VLSC of Inner arm)	0.191	< 0.001	**
- VLSC of Outer arm vs. VLSC of Inner arm	0.697	< 0.001	**
- 25-OHD vs. Skin color score at sun exposure area (VLSC of Outer arm)	0.261	< 0.001	**
- 25-OHD vs. Skin color score at non-sun exposure area (VLSC of Inner arm)	0.171	< 0.001	**

- Daily sunlight exposure time had a significant correlation with serum 25OHD and skin color score.
- Serum 25OHD had a significant correlation with skin color score.

Prevalence of vitamin D status in mild to moderate CKD in Thai CMD patients with no vitamin D supplement



Rationale:

- Prevalence of vitamin D def. is high in advanced CKD stage 4-5.
- Data on the prevalence of vitamin D status in patients with mild to moderate CKD are limited.

Results

- Patients with stage 3-4 CKD (eGFR30-60 mL/min/1.73 m^2) had higher prevalence of severe vitamin D deficiency than those with mild kidney impairment or stage 1-2 CKD (eGFR>60 mL/min/1.73 m^2)

Nipith Charoenngam and Sutin Sriussadaporn. Submitted for publication

Vitamin D status in Thai patients with Cardiometabolic disorders

Summary

- Prevalence of vitamin D insufficiency (70.3%) and deficiency (28.%) are high in CMDs and comparable to or higher than those previously reported in Thai general population (64.6%/14.3%) in whom the presence of CMDs in the subjects was not specifically defined.
- The prevalence are comparable to those in other countries in the similar latitudes such as India (>70%) and Singapore (68%/14%) in where sunlight is abundant all year.

Vitamin D status in Thai patients with Cardiometabolic disorders

Summary

- The prevalence are higher in patients with combination of multiple CMDs especially combination of DM, HT and CAD with or without DLP.
- The prevalence are higher in women than men.
- The prevalence are higher in non-elderly (age <60 years) than elderly (age >60 years)
- The prevalence are higher in patients with moderate kidney impairment or stage 3-4 CKD (eGFR<60 mL/min/1.73 m^2) than those with mild kidney impairment or stage 1-2 CKD (eGFR>60 mL/min/1.73 m^2)

Vitamin D status in Thai patients with Cardiometabolic disorders

Summary

- The skin color, serum vitamin D level and vitamin D status in Thai CMDs patients are significanly related to the daily sunlight exposure time.
- Adequate sunlight exposure is useful in maintaining adequate vitamin D status.
- The longer sunlight exposure time, higher serum 25-OHD levels and lower prevalence of vitamin D insufficiency and deficiency in patients with darker skin color suggest that darker skin color in Thai patients is the marker of adequate skin vitamin D synthesis not the barrier of skin vitamin D synthesis as shown in ethnic black populations.

Vitamin D status in Thai CMD patients
From clinical data to further studies

Clinical observations leading to research questions

- A number of patients still have low serum 25-OHD levels that do not increase despite taking adequate vitamin D supplementation.
- A number of patients have high serum 25-OHD despite low sunlight exposure and no vitamin D supplement.

Vitamin D status in Thai CMD patients
From clinical data to further studies

Research questions: What is or are the explanations?

- Stability and consistency of the amount of vitamin D in the vitamin D supplements available in Thailand.
- Vitamin D absorption and metabolism
  - Effects of dietary fat on vitamin D absorption
  - Role of gut microbiota
  - Role of vitamin D binding protein

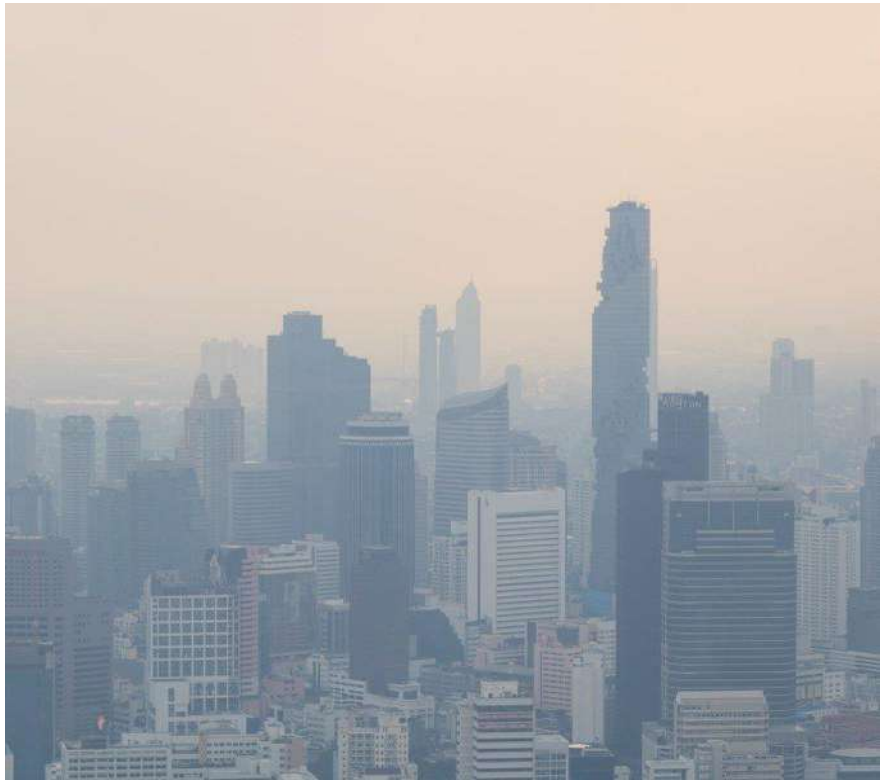
Actions

- Dr. Nipith Chareonngam, the Prince Mahidol Award Youth Scholar is working on these issues with Prof. Michael Holick at The Boston University and will present his research works in the next session.

Current hot issues on health care policies and more research on vitamin D in Thailand

Effects of pollutions on vitamin D

Particulate matter 2.5 micron (PM2.5)



More liberation of medical use of cannabis in Thailand in 2019

Effects of environmental pollutants on skin vitamin D synthesis

Air Pollutants PM 2.5

Indirect effect

Direct effect

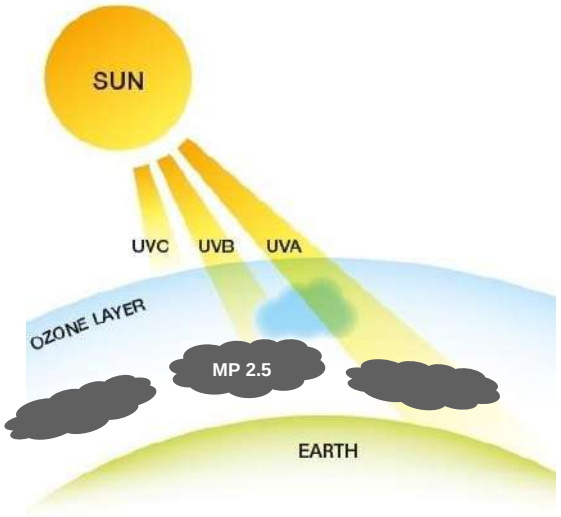
Outdoor activity

Sunlight exposure

Blocking of UVB

Cutaneous biosynthesis of previtamin D

Vitamin D deficiency



Heavy Cannabis Use Is Associated With Low Bone Mineral Density and an Increased Risk of Fractures

Antonia Sophocleous, PhD,[a] Roy Robertson, MD,[b,c] Nuno B. Ferreira, PhD,[d] James McKenzie, RGN,[a,b] William D. Fraser, MD,[e] Stuart H. Ralston, MD[a]

Table 1 Demographic and Lifestyle Characteristics of Study Population

	Controls (n = 114)	Moderate Cannabis Users (n = 56)	Heavy Cannabis Users (n = 114)
Age (y)	49.5 ± 9.8	43.3 ± 12.3***	40.5 ± 9.3***
Females	79 (69.3%)	36 (64.3%)	51 (44.7%)***
(of which postmenopausal)	50 (63.3%)	13 (36.1%)**	14 (27.5%)***
Spine Z-score	0.0 ± 1.2	0.0 ± 1.5	−0.5 ± 1.2***
Femoral neck Z-score	0.1 ± 1.0	0.3 ± 1.3	−0.2 ± 0.8*
Total hip Z-score	0.3 ± 0.9	0.3 ± 1.2	−0.2 ± 0.9***
Previous fracture	44 (38.6%)	17 (30.4%)	52 (45.6%)
Number of previous fractures	66	22	102
Clinical fracture rate ratio	1	0.84 (0.52-1.37)	2.17 (1.59-2.95)***
BMI (kg/m^2)	29.0 ± 7.0	27.7 ± 7.3	26.5 ± 6.0**
Serum 25(OH)D (nmol/L)	36.9 ± 26.7	33.9 ± 23.1	25.3 ± 16.8***
Serum P1NP µg/L	41.2 ± 17.8	39.8 ± 18.4	47.1 ± 19.2
Serum CTX µg/L	0.2 ± 0.1	0.2 ± 0.1	0.3 ± 0.1*
Dietary calcium (mg/day)	880 ± 453	1047 ± 891	1243 ± 841***
Alcohol users	47 (41.2%)	23 (41.1%)	37 (32.5%)
Alcohol (units/week)†	21.2 ± 22.3	14.2 ± 9.2	32.8 ± 37.9
Tobacco (pack years)	32.4 ± 23.7	21.3 ± 18.0*	26.9 ± 46.6
Cannabis exposures (n)	0.3 ± 1.0	1031.3 ± 1238.4***	47491.6 ± 37225.8***
Other illegal drug use	3 (2.6%)	12 (21.4%)***	73 (64.0%)***
Standing > 4 h/d	92 (80.7%)	48 (85.7%)	74 (64.9%)**
Parental hip fracture	8 (7.0%)	3 (5.4%)	4 (3.5%)
Taking part in sports regularly	52 (45.6%)	30 (53.6%)	44 (38.6%)

Values are number (%) or mean ± standard deviation, except incidence fracture rate ratio, which is presented as the risk ratio with 95% confidence intervals. Differences between groups as assessed by general linear model on bootstrapped values or chi-squared test.

25(OH)D = total 25-hydroxyvitamin D; BMI = body mass index; CTX = cross-linked C-telopeptide of type 1 collagen; P1NP = amino terminal propeptide fragment of type I collagen.

*$P < .05$, **$P < .01$, ***$P < .005$ from controls.

†Among alcohol users.

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