



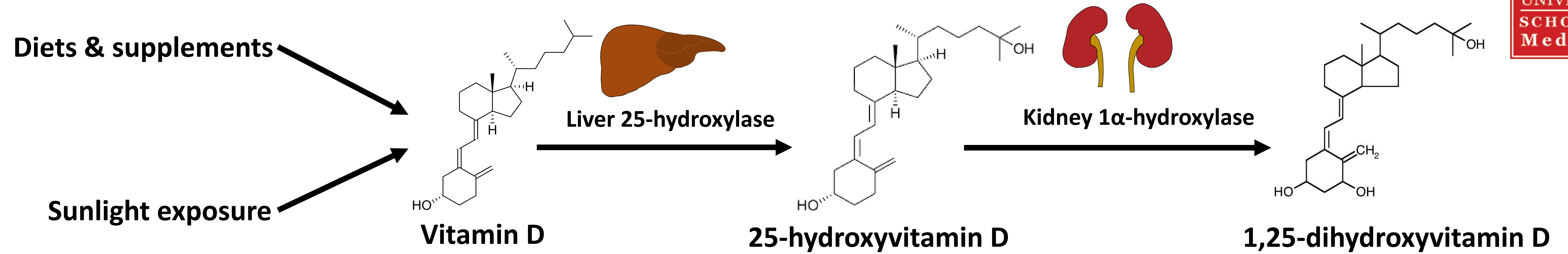
PRINCE MAHIDOL  
AWARD CONFERENCE



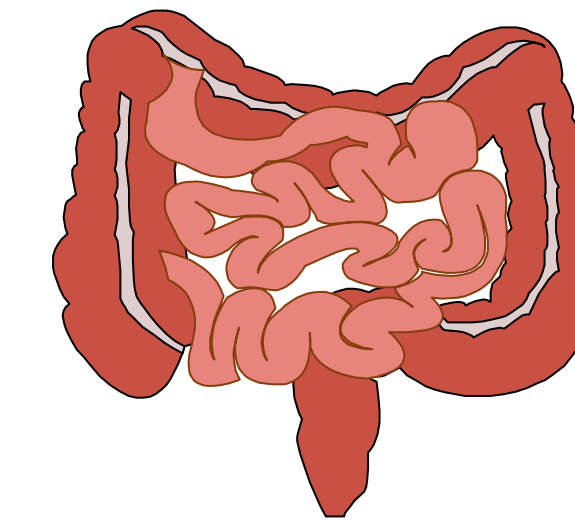
# Pharmacokinetic Evaluation of Vitamin D<sub>3</sub> and 25-Hydroxyvitamin D<sub>3</sub> in Normal and Malabsorptive Adults

Nipith Charoenngam, Tyler A. Kalajian, Arash Shirvani, Grace H. Yoon, Suveer Desai, Caroline Apovian, Ashley McCarthy, Michael F. Holick  
Section Endocrinology, Diabetes, Nutrition and Weight Management, Department of Medicine, Boston University School of Medicine

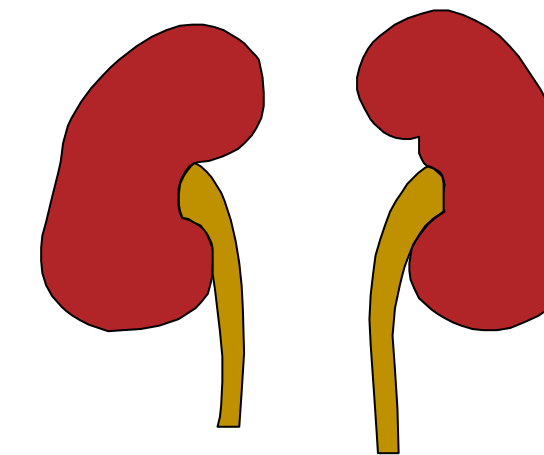
# Pharmacokinetic Evaluation of Vitamin D<sub>3</sub> and 25-Hydroxyvitamin D<sub>3</sub> in Normal and Malabsorptive Adults



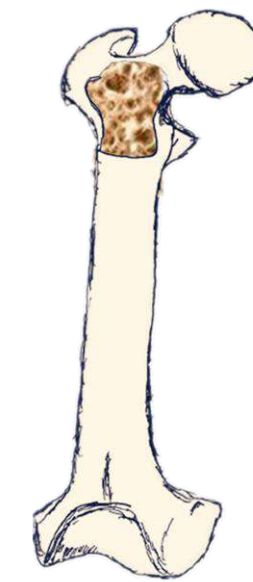
↑ Intestinal Ca and PO<sub>4</sub> absorption



↓ Urinary Ca excretion



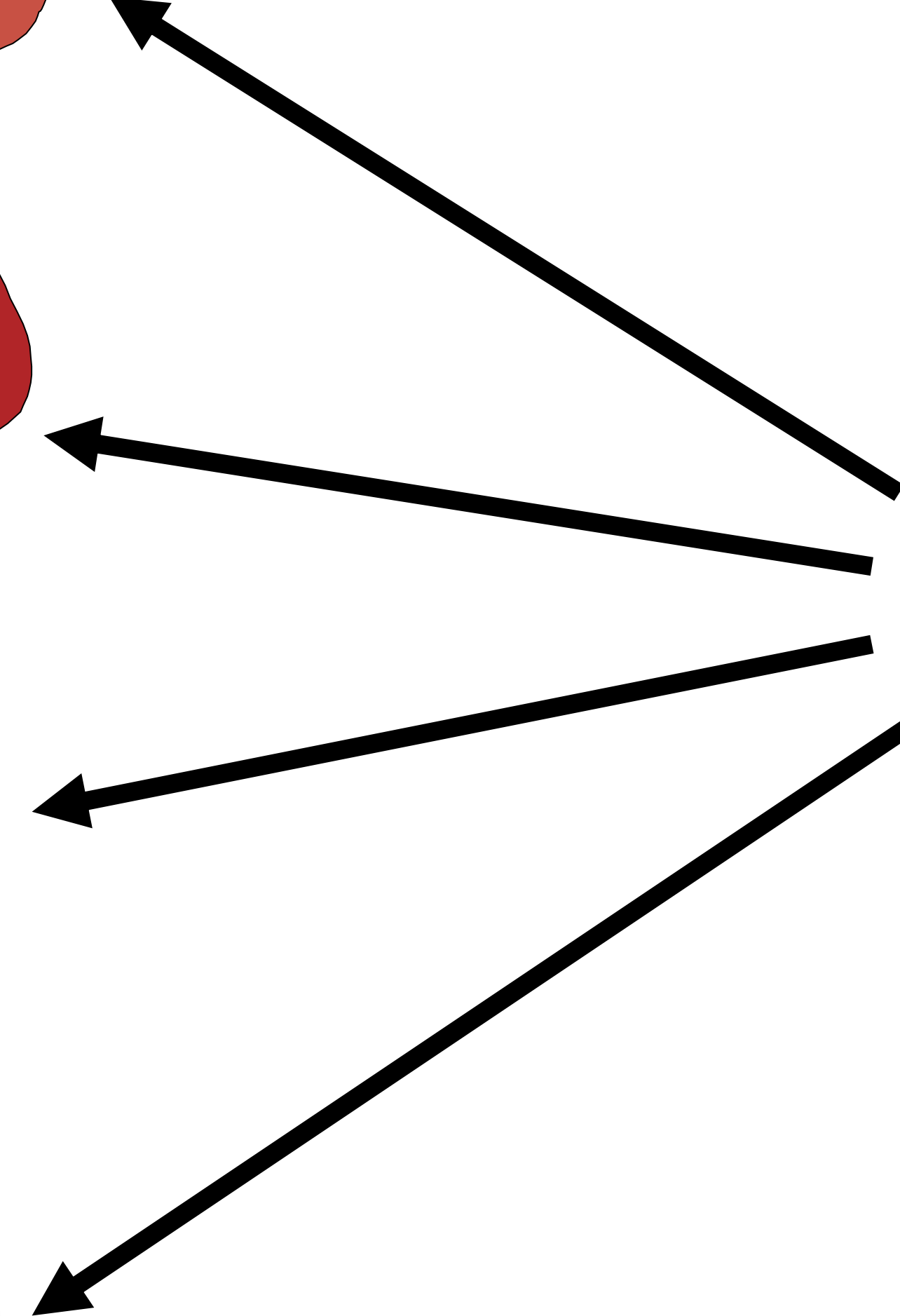
↑ Bone remodeling



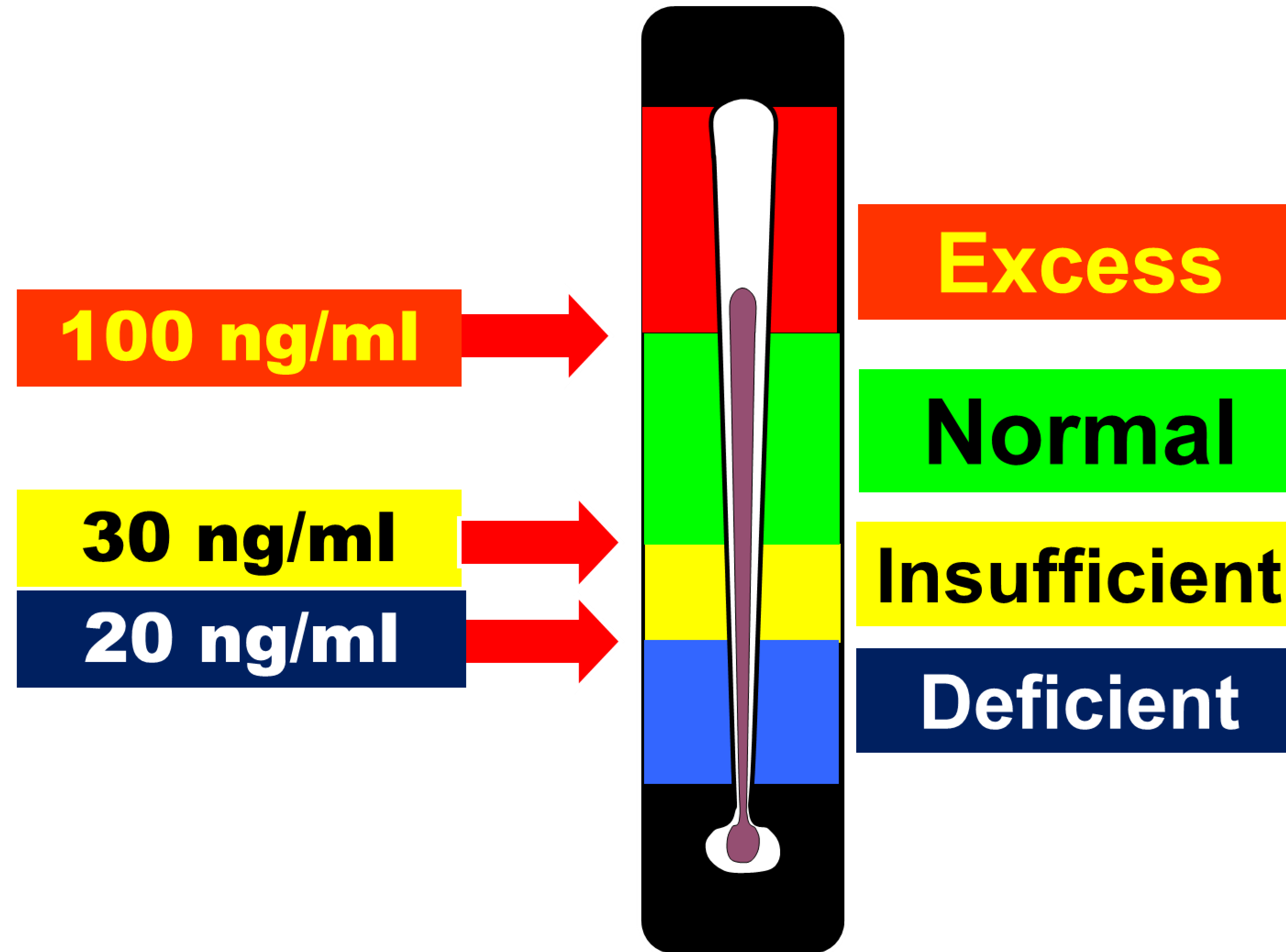
Non-skeletal effects



**Vitamin D receptor**



## 25(OH)D



**How common is vitamin D  
deficiency/insufficiency in Thailand?**

*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<sup>1</sup>, Sutin Sriussadaporn MD<sup>1</sup>

<sup>1</sup> Division of Endocrine and Metabolism, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

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

**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%) <sup>a</sup>	58 (61.7%) <sup>b</sup>
Patients without vitamin D supplementation (n=350; 78.8%)	25.72±10.18	10 (2.9%)	107(30.6%) <sup>a</sup>	253 (72.6%) <sup>b</sup>

A *p*-value<0.05 indicates statistical significance

<sup>a</sup> denotes statistically significant difference between patients with and without vitamin D supplementation (*p*=0.029)

<sup>b</sup> 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

**Table 7.** Summary of prevalence of inadequate vitamin D status in different population subgroups in Thailand

Authors	Year	Sample size	Type of population	Prevalence of inadequate vitamin D status	Cut-point (ng/mL)	Method of 25-OHD measurement
Chailurkit, et al.	2011	2,641	Thai population	34.2-64.6%	<30	LC/MS/MS (25-OHD <sub>2</sub> +D <sub>3</sub> )
Chailurkit, et al.	2011	446	Thai elderly women	54.0%	<30	RIA (25-OHD <sub>2</sub> +D <sub>3</sub> )
Kruavit, et al.	2012	93	Thai nursing home residents	61.3%	<28	RIA (25-OHD <sub>2</sub> +D <sub>3</sub> )
Nimitphong, et al.	2013	1,449	Male subjects	13.9%	<20	LC/MS/MS (25-OHD <sub>2</sub> +D <sub>3</sub> )
		541	Female subjects	43.1%		
Soontrapa, et al.	2015	66	Rural elderly males	13.6%	<40	ECLIA (25-OHD <sub>2</sub> +D <sub>3</sub> )
		100	Urban elderly males	48.0%		
The present study	2018	444	Adult ambulatory patients with cardiometabolic disorders	70.3%	<30	ECLIA
				28.2%	<20	(25-OHD <sub>2</sub> +D <sub>3</sub> )

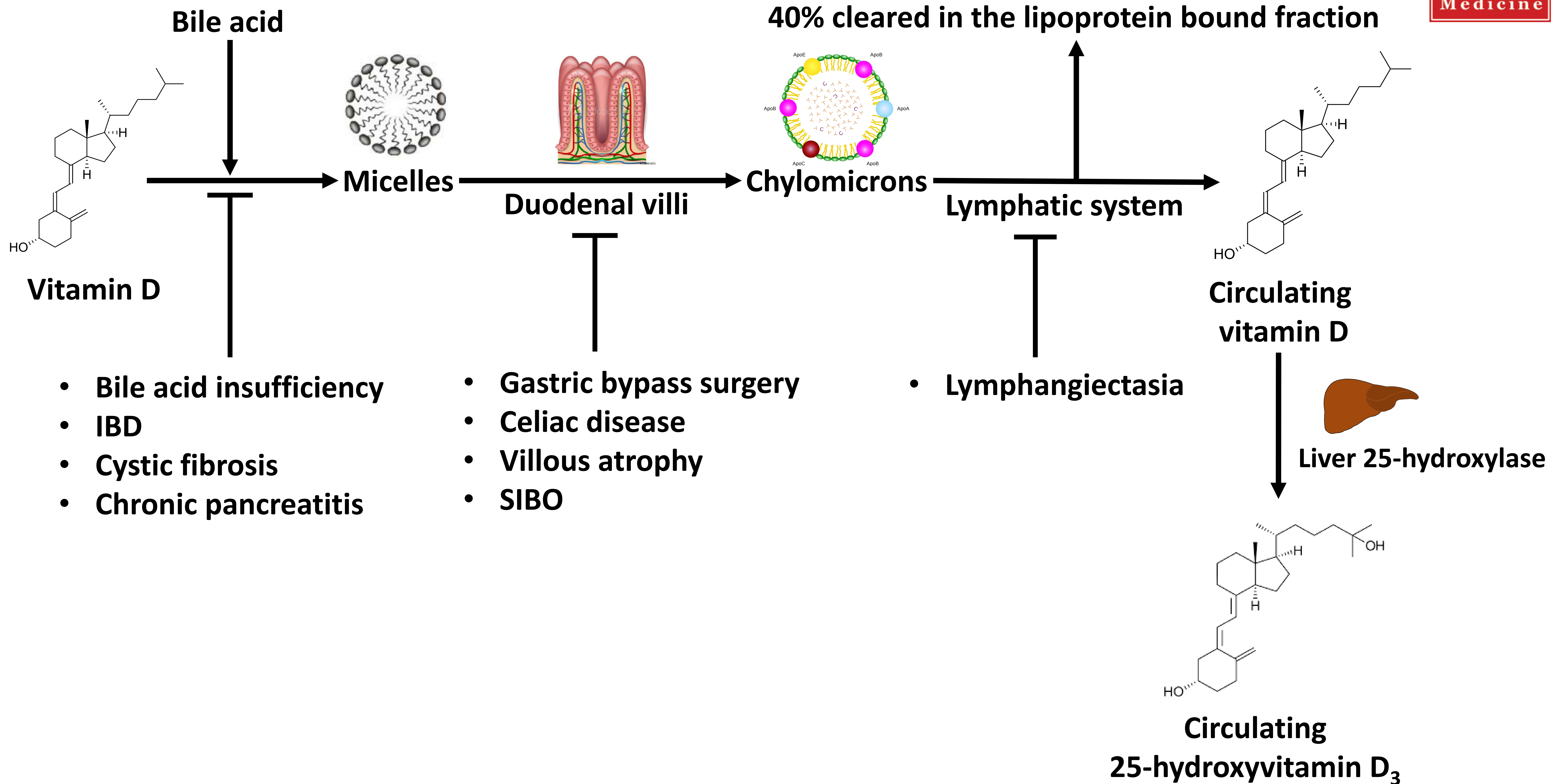
**Abbreviations:** 25-OHD, serum 25-hydroxyvitamin D; LC/MS/MS, liquid chromatography tandem mass spectrometry; RIA, radioimmunoassay; ECLIA, electrochemiluminescence immunoassay

## Sources of vitamin D

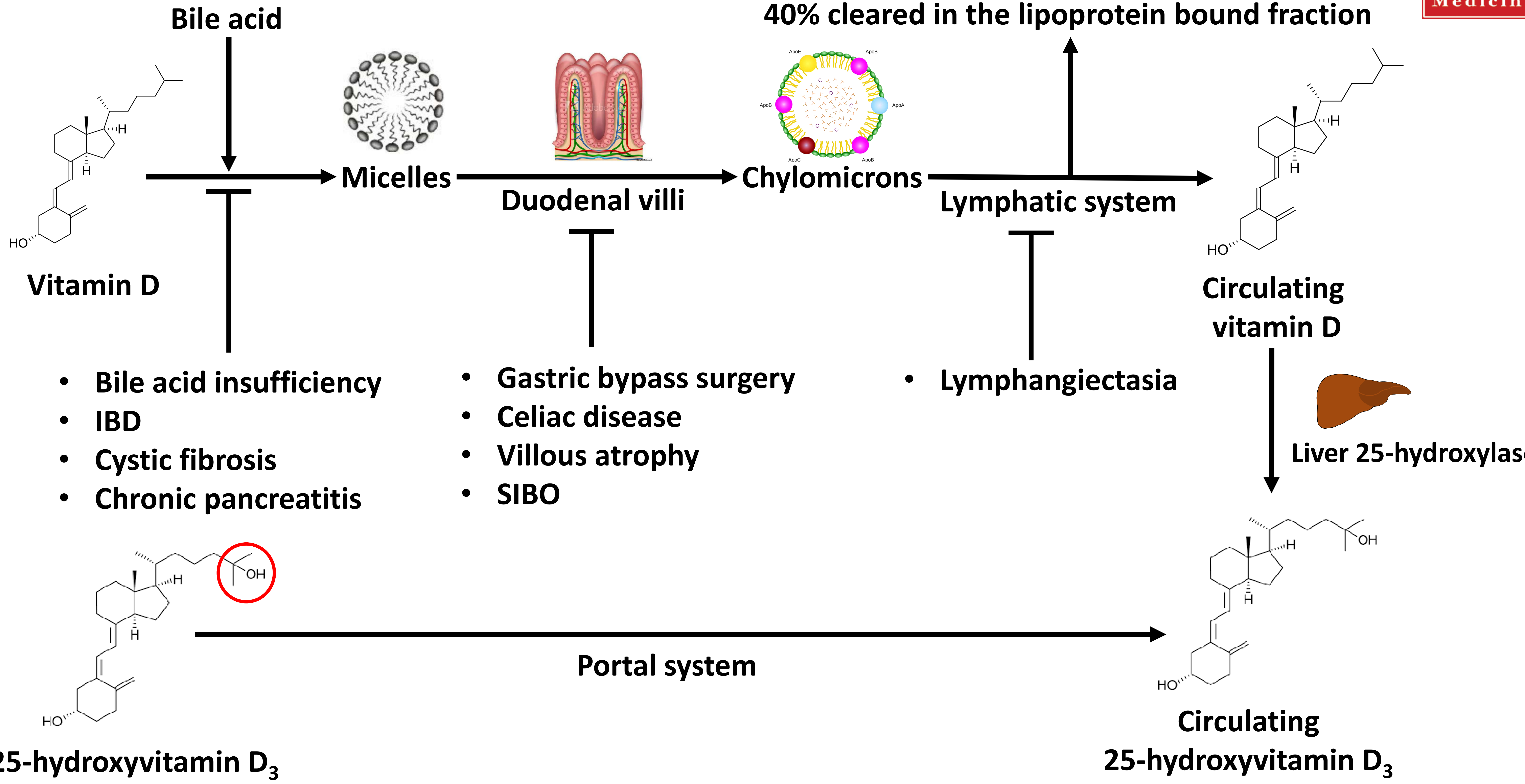
- Diet
  - D<sub>2</sub>: Sun-exposed mushroom, fortified products
  - D<sub>3</sub>: Cod liver oil, salmon, mackerel, tuna, fortified products
- Sunlight
  - Winter: No vitamin D<sub>3</sub> synthesis at latitude >33°
  - Spring, Summer, Fall: vitamin D<sub>3</sub> production 10 am – 3 pm
- Supplement



# Pharmacokinetic Evaluation of Vitamin D<sub>3</sub> and 25-Hydroxyvitamin D<sub>3</sub> in Normal and Malabsorptive Adults



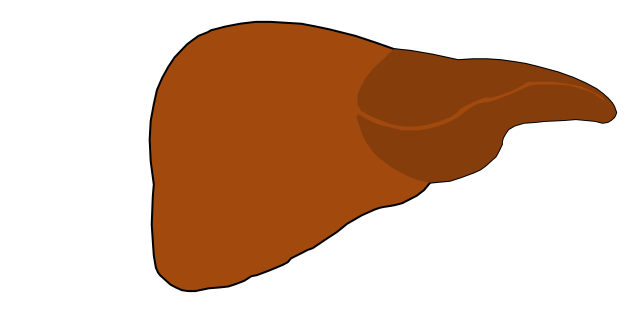
# Pharmacokinetic Evaluation of Vitamin D<sub>3</sub> and 25-Hydroxyvitamin D<sub>3</sub> in Normal and Malabsorptive Adults



- Bile acid insufficiency
- IBD
- Cystic fibrosis
- Chronic pancreatitis

- Gastric bypass surgery
- Celiac disease
- Villous atrophy
- SIBO

- Lymphangiectasia



## *A Pilot Clinical Trial to Evaluate the Pharmacokinetics of Orally Administered 25-hydroxyvitamin D<sub>3</sub> and Vitamin D<sub>3</sub> in Healthy Adults and Adults With a History of Intestinal Malabsorption*

**Study design:** Randomized double-blinded crossover study

**Subjects:** 10 healthy adults and 6 malabsorptive patients with vitamin D insufficiency or deficiency

### **Eligibility criteria**

- Age ≥18 years old (healthy or with a history of intestinal malabsorption)
- No conditions affecting vitamin D metabolism
- Vitamin D deficiency/insufficiency defined by serum total 25(OH)D <30 ng/mL
- Not taking vitamin D supplement within 2 weeks
- Not pregnant
- No contraindications to oral vitamin D



## Results

- Baseline characteristics of healthy adults and malabsorptive patients

	Healthy participants (N = 10)	Malabsorptive patients (N = 6)	p-value
<b>Age</b>	32.3 ± 2.7	46.5 ± 4.1	0.010*
<b>Number of female participants</b>	8 (80 %)	6 (100 %)	
<b>Body mass index (kg/m<sup>2</sup>)</b>	27.0 ± 2.1	32.7 ± 4.1	0.192
<b>Ethnicity</b>			
• Caucasian	5 (50 %)	4 (67 %)	
• Hispanic	0 (0 %)	1 (17 %)	
• Asian	2 (20 %)	0 (0 %)	
• Black	3 (30 %)	1 (17 %)	
<b>Diagnosis</b>			
• Gastric bypass surgery		4 (67 %)	
• Intestinal lymphangiectasia		1 (17 %)	
• Ulcerative colitis		1 (17 %)	

Data were expressed as mean ± SEM

## Results

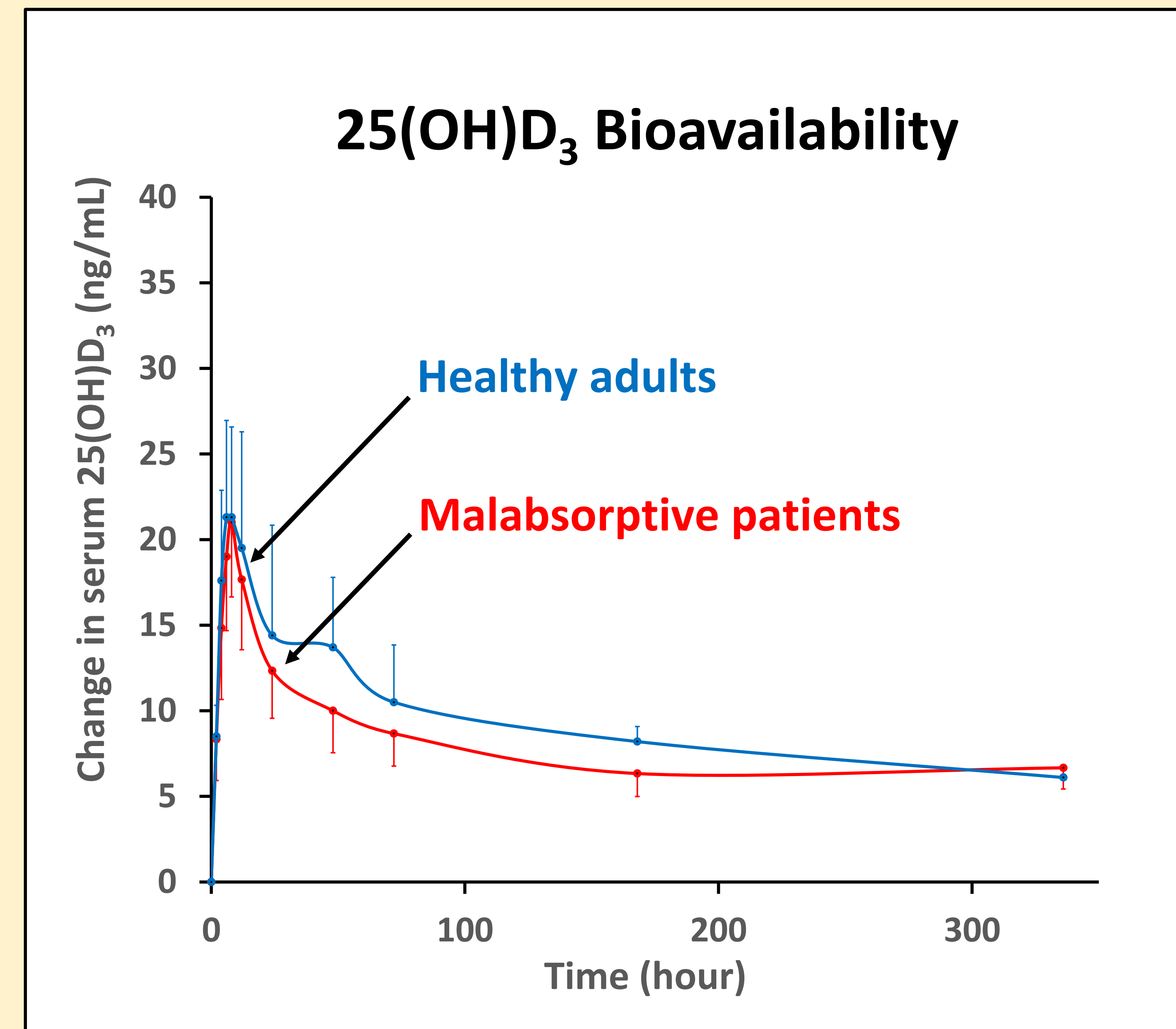
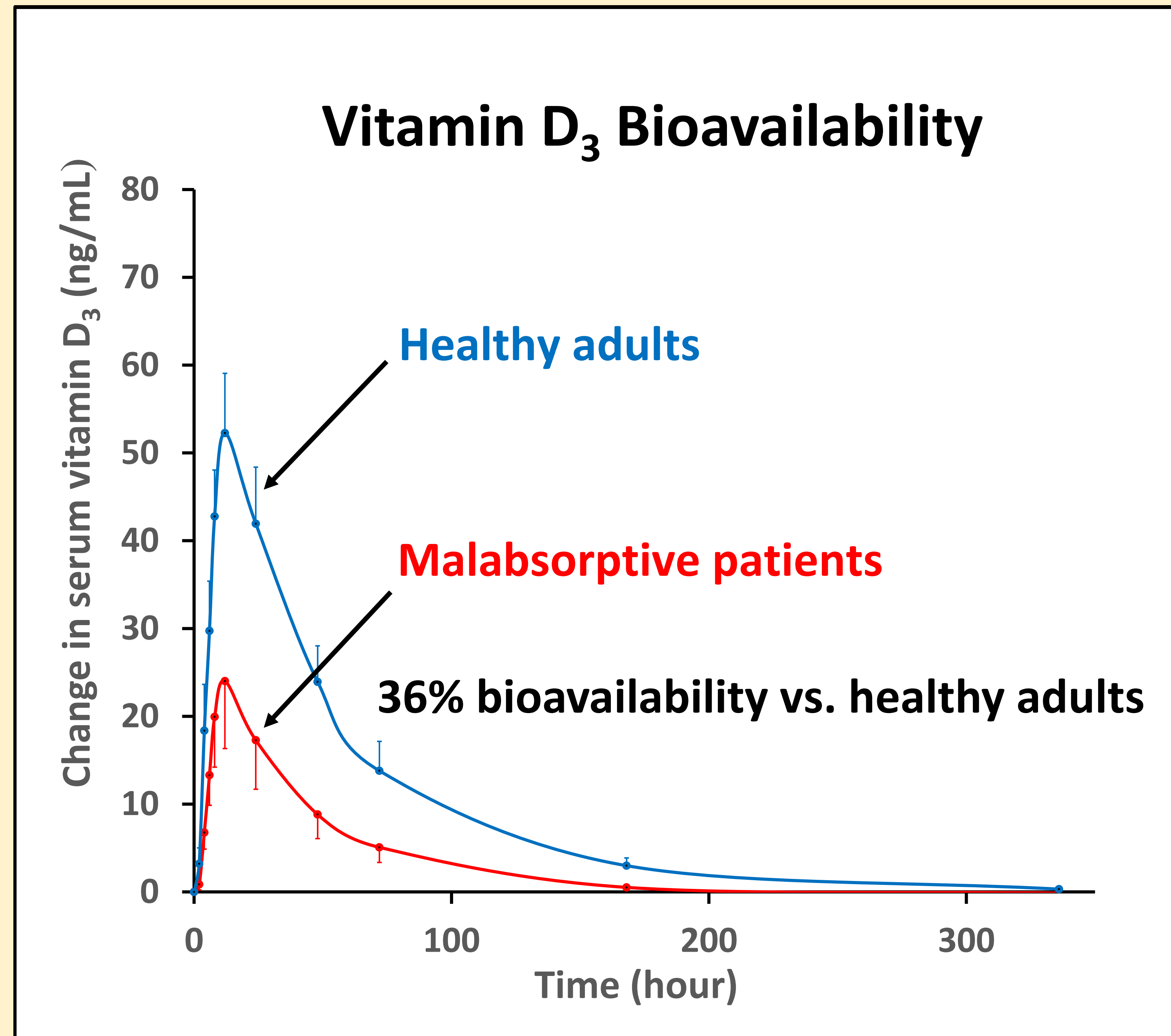
- Baseline characteristics of healthy adults and malabsorptive patients

	Healthy participants (N = 10)	Patients with fat malabsorption (N = 6)	p-value
Vitamin D <sub>2</sub> (ng/mL)	0.0 ± 0.0	0.0 ± 0.0	N/A
Vitamin D <sub>3</sub> (ng/mL)	0.0 ± 0.0	1.6 ± 1.0	0.183
Total 25-hydroxyvitamin D (ng/mL)	17.1 ± 2.3	14.7 ± 3.4	0.554
25-hydroxyvitamin D <sub>2</sub> (ng/mL)	0.4 ± 0.4	4.2 ± 3.1	0.284
25-hydroxyvitamin D <sub>3</sub> (ng/mL)	16.7 ± 2.1	10.5 ± 4.2	0.228
<b>Intact PTH (pg/mL)</b>	<b>41.5 ± 5.4</b>	<b>74.0 ± 16.9</b>	<b>0.116</b>
Total calcium (mg/dL)	9.4 ± 0.1	9.4 ± 0.1	0.796
Phosphate (mg/dL)	3.9 ± 0.3	4.0 ± 0.3	0.736
Creatinine (mg/dL)	0.8 ± 0.03	0.7 ± 0.04	0.103
eGFR (mL/min/1.73m <sup>2</sup> )	106.8 ± 4.7	104.0 ± 6.7	0.733
Glucose (mg/dL)	83.1 ± 7.5	89.8 ± 8.8	0.580
<b>Albumin (g/dL)</b>	<b>4.4 ± 0.08</b>	<b>4.1 ± 0.05</b>	<b>0.027*</b>

Data were expressed as mean ± SEM

## Results

- Pharmacokinetic studies of orally administered 900 μg vitamin D<sub>3</sub> and 900 μg 25(OH)D<sub>3</sub>



Data were expressed as mean ± SEM

## Results

- Pharmacokinetic studies of orally administered 900 µg vitamin D<sub>3</sub> and 900 µg 25(OH)D<sub>3</sub>

Pharmacokinetic parameters	900 µg vitamin D <sub>3</sub> arm			900 µg 25(OH)D <sub>3</sub> arm		
	Healthy adults (N = 10)	Malabsorptive patients (N = 6)	p-value	Healthy adults (N = 10)	Malabsorptive patients (N = 6)	p-value
<b>AUC (ng·hr /mL)</b>	<b>3258 ± 496</b>	<b>1177 ± 425</b>	<b>0.022*</b>	3128 ± 545	2667 ± 735	0.562
<b>C<sub>max</sub> (ng/mL)</b>	<b>53.5 ± 6.0</b>	<b>24.3 ± 8.4</b>	<b>0.016*</b>	23.1 ± 4.6	23.2 ± 6.8	1.000
<b>T<sub>max</sub> (hr)</b>	10.4 ± 0.7	11.3 ± 0.7	0.345	<b>11.2 ± 4.1</b>	<b>5.3 ± 0.7</b>	<b>0.031*</b>
<b>T<sub>1/2</sub> (hr)</b>	31.4 ± 3.3	28.7 ± 1.5	0.713	60.6 ± 7.9	65.7 ± 29.9	0.313
<b>C<sub>trough</sub> (ng/mL)</b>	0.3 ± 0.3	0.1 ± 0.1	0.220	6.1 ± 1.3	6.7 ± 1.5	0.875

Data were expressed as mean ± SEM



## Conclusions

- Malabsorptive patients who are unable to efficiently form micelles and chylomicrons have difficulty absorbing vitamin D.
- Our observations that the bioavailability of 900 µg 25(OH)D<sub>3</sub> was not different between malabsorptive patients and healthy adults support that the more water-soluble 25(OH)D<sub>3</sub> can be absorbed directly into the portal system.
- Orally administered 25(OH)D<sub>3</sub> would be a good choice for treatment of vitamin D deficiency in malabsorptive patients.
- Further studies should be conducted to evaluate the bioavailability of 25(OH)D in a larger number of patients with other malabsorptive conditions.

ANTICANCER RESEARCH 40: 551-556 (2020)

doi:10.21873/anticanres.13984

# **The Effect of Various Doses of Oral Vitamin D<sub>3</sub> Supplementation on Gut Microbiota in Healthy Adults: A Randomized, Double-blinded, Dose-response Study**

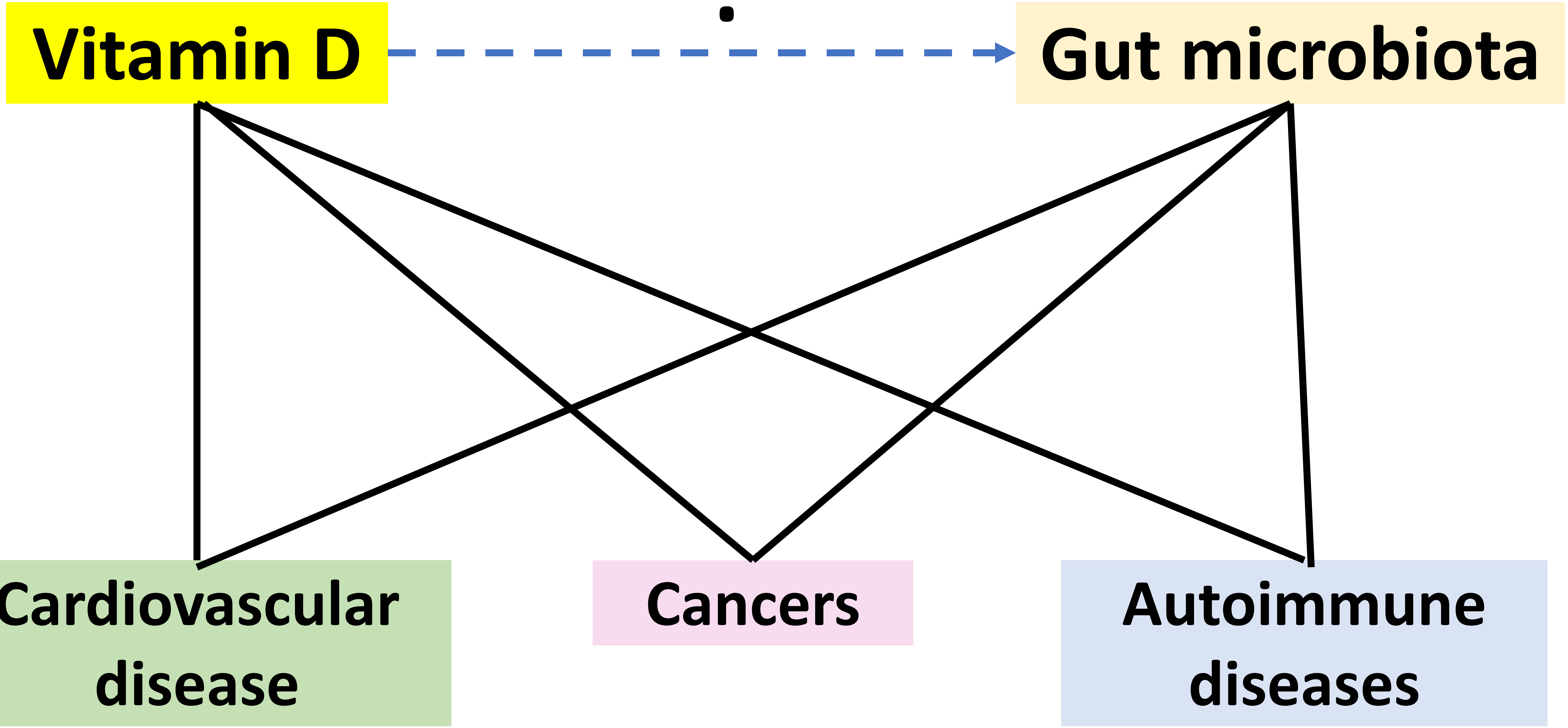
NIPITH CHAROENNGAM, ARASH SHIRVANI, TYLER A. KALAJIAN, ANJELI SONG and MICHAEL F. HOLICK

*Department of Medicine, Section of Endocrinology, Nutrition, and Diabetes, Vitamin D,  
Skin and Bone Research Laboratory, Boston University Medical Center, Boston, MA, U.S.A.*

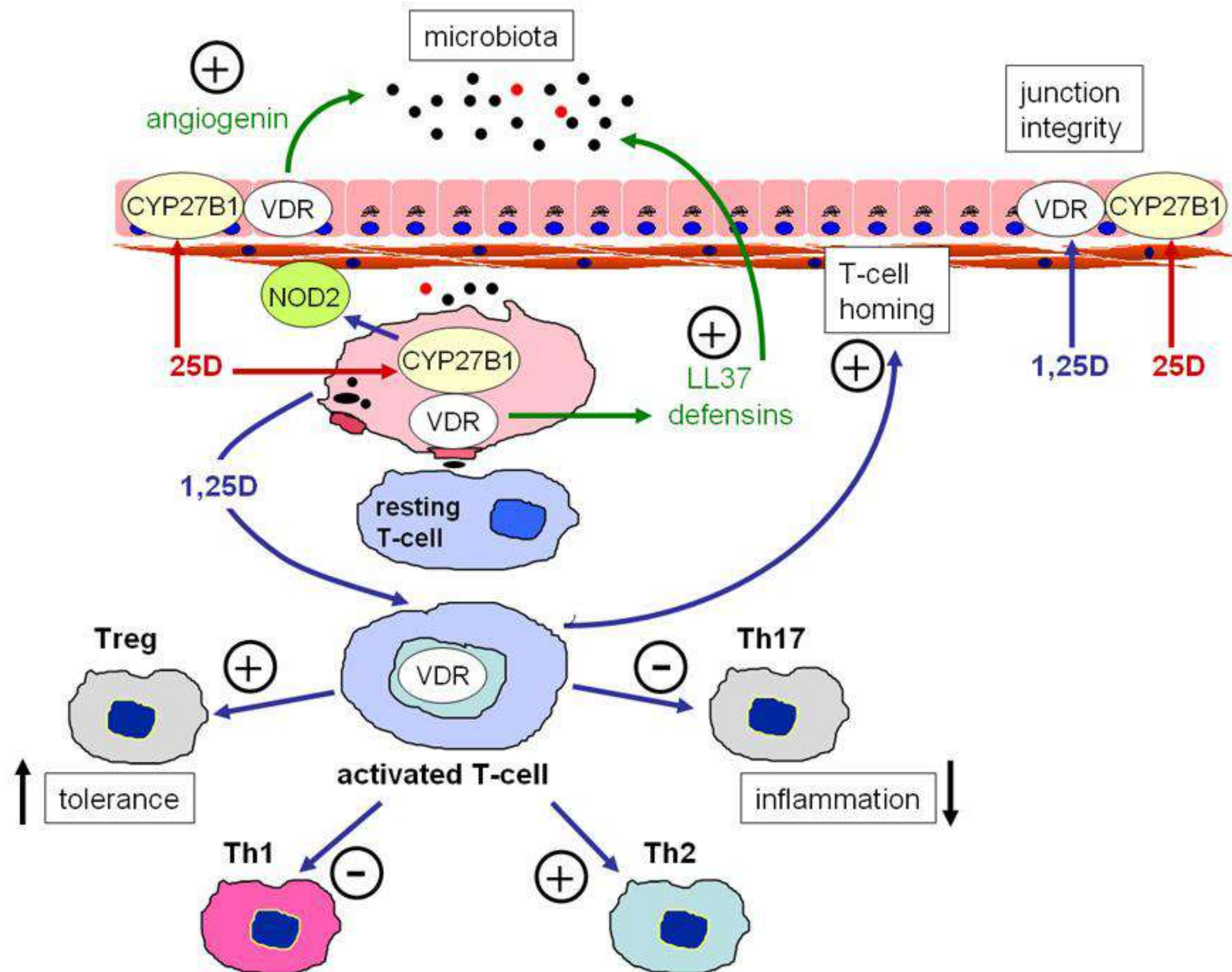


**The Effect of Various Doses of Oral Vitamin D<sub>3</sub> Supplementation on Gut Microbiota in Healthy Adults:  
A Randomized, Double-blinded, Dose-response Study**

?



# The Effect of Various Doses of Oral Vitamin D<sub>3</sub> Supplementation on Gut Microbiota in Healthy Adults: A Randomized, Double-blinded, Dose-response Study



# The Effect of Various Doses of Oral Vitamin D<sub>3</sub> Supplementation on Gut Microbiota in Healthy Adults: A Randomized, Double-blinded, Dose-response Study

[www.nature.com/scientificreports](http://www.nature.com/scientificreports)

**SCIENTIFIC  
REPORTS**  
nature research

OPEN

## Disassociation of Vitamin D's Calcemic Activity and Non-calcemic Genomic Activity and Individual Responsiveness: A Randomized Controlled Double-Blind Clinical Trial

Arash Shirvani , Tyler Arek Kalajian, Anjeli Song & Michael F. Holick\*

The aims of this randomized controlled double-blind clinical trial were to assess the impact of vitamin D supplementation on calcium metabolism and non-calcemic broad gene expression by relating them to the individual's responsiveness to varying doses of vitamin D<sub>3</sub>. Thirty healthy adults were randomized to receive 600, 4,000 or 10,000 IU/d of vitamin D<sub>3</sub> for 6 months. Circulating parathyroid hormone (PTH), 25(OH)D, calcium and peripheral white blood cells broad gene expression were evaluated. We observed a dose-dependent increase in 25(OH)D concentrations, decreased PTH and no change in serum calcium. A plateau in PTH levels was achieved at 16 weeks in the 4000 and 10,000 IU/d groups. There was a dose-dependent 25(OH)D alteration in broad gene expression with 162, 320 and 1289 genes up- or down-regulated in their white blood cells, respectively. Our results clearly indicated that there is an individual's responsiveness on broad gene expression to varying doses of vitamin D<sub>3</sub>. Vitamin D<sub>3</sub> supplementation at 10,000 IU/d produced genomic alterations several fold higher than 4,000 IU/d even without further changes in PTH levels. Our findings may help explain why there are some inconsistency in the results of different vitamin D's clinical trials.

# The Effect of Various Doses of Oral Vitamin D<sub>3</sub> Supplementation on Gut Microbiota in Healthy Adults: A Randomized, Double-blinded, Dose-response Study

## *The Effect of Various Doses of Oral Vitamin D<sub>3</sub> Supplementation on Gut Microbiota in Healthy Adults: A Randomized, Double-blinded, Dose-response Study*

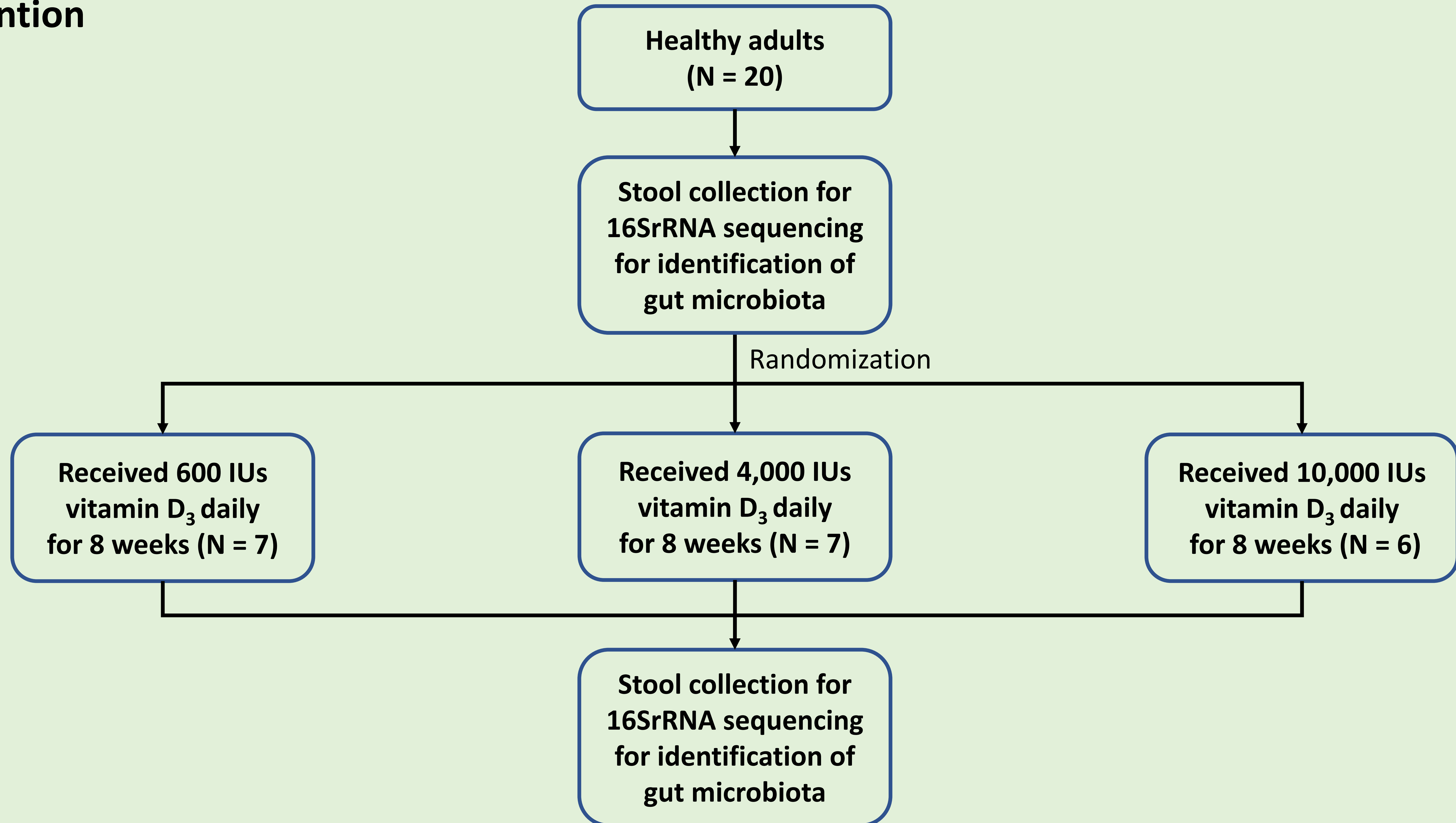
**Study design:** Randomized, double-blinded, dose-response pilot study

**Subjects:** 20 healthy adults with vitamin D insufficiency or deficiency

- Age ≥18 years old (healthy or with a history of intestinal malabsorption)
- No conditions affecting vitamin D absorption and metabolism
- BMI <30 kg/m<sup>2</sup>
- Vitamin D deficiency/insufficiency defined by serum total 25(OH)D <30 ng/mL
- Not taking vitamin D supplement ≥ 600 IUs/d
- Not pregnant
- No contraindications to oral vitamin D
- No direct exposure to artificial UVB or solar radiation during the past month for >8 hours

# The Effect of Various Doses of Oral Vitamin D<sub>3</sub> Supplementation on Gut Microbiota in Healthy Adults: A Randomized, Double-blinded, Dose-response Study

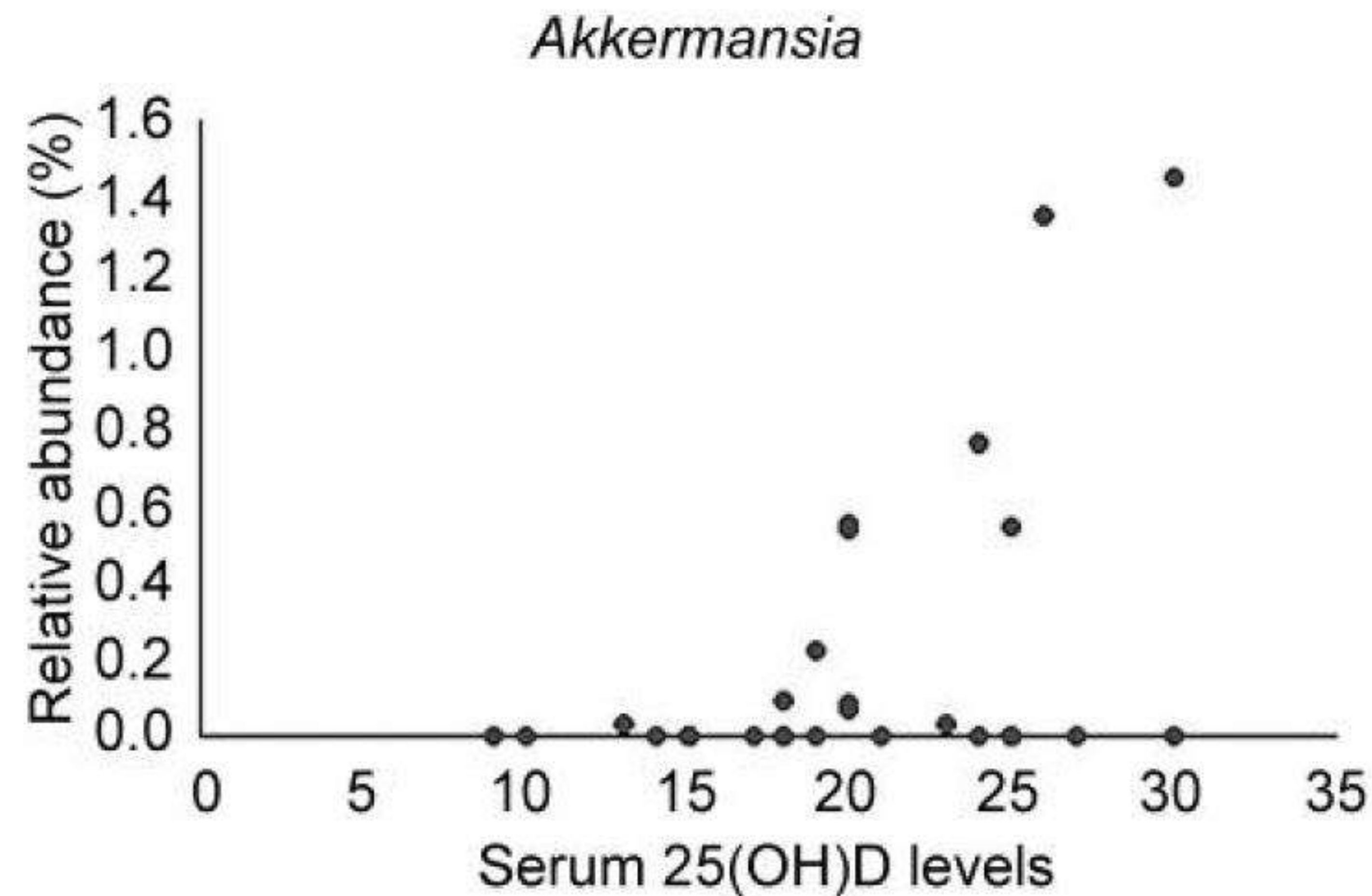
## Intervention



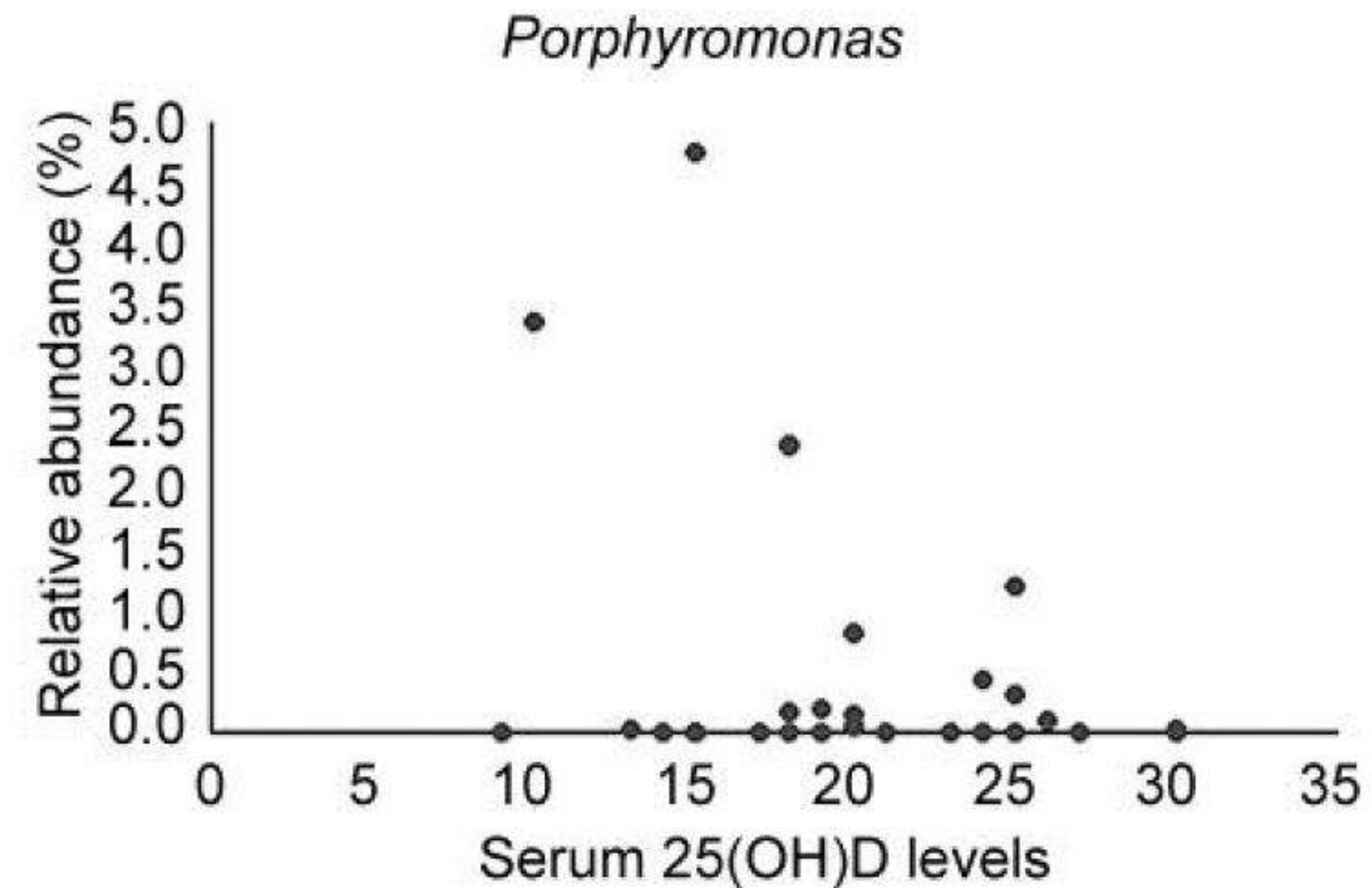
# The Effect of Various Doses of Oral Vitamin D<sub>3</sub> Supplementation on Gut Microbiota in Healthy Adults: A Randomized, Double-blinded, Dose-response Study

## Results

Relative abundance of *Akkermansia* and *Porphyromonas* of the participants at various levels of serum 25(OH)D at baseline of the study



$R = 0.684, p = 0.001$



$R = -0.435, p = 0.043$



# The Effect of Various Doses of Oral Vitamin D<sub>3</sub> Supplementation on Gut Microbiota in Healthy Adults: A Randomized, Double-blinded, Dose-response Study

*Mini Review*

## A next-generation beneficial microbe: *Akkermansia muciniphila*

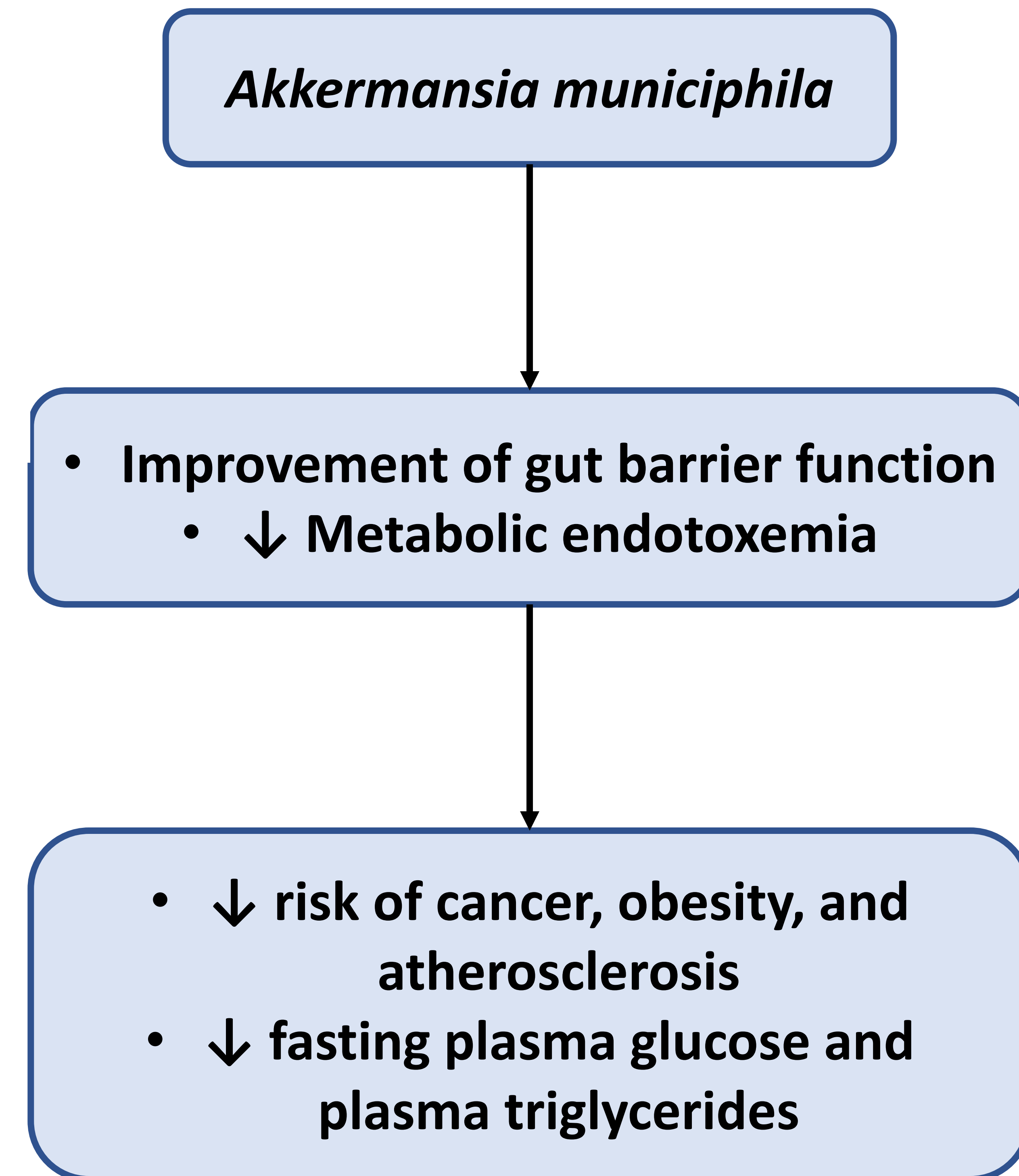
Yuji Naito,<sup>1,2,\*</sup> Kazuhiko Uchiyama<sup>1</sup> and Tomohisa Takagi<sup>1</sup>

<sup>1</sup>Molecular Gastroenterology and Hepatology and <sup>2</sup>Department of Endoscopy and Ultrasound Medicine, University Hospital, Kyoto Prefectural University of Medicine, 465 Kajji-cho, Kamigyo-ku, Kyoto 602-8566, Japan

(Received 11 May, 2018; Accepted 13 May, 2018; Published online 20 June, 2018)

There have been many reports on the roles of intestinal flora and intestinal environment in health promotion and disease prevention. Beneficial bacteria such as *Bifidobacterium* and lactic acid-producing bacteria have been shown to improve the intestinal environment, and yield a good effect on metabolism, immunity and nerve response. In this review, in addition to these beneficial bacteria, we introduced *Akkermansia muciniphila* as a next-generation beneficial microbe. Several reports indicate that *Akkermansia muciniphila* affects glucose metabolism, lipid metabolism, and intestinal immunity, and that certain food ingredients such as polyphenols may increase the abundance of *Akkermansia muciniphila* in the gut.

**Key Words:** *Akkermansia muciniphila*, diabetes, polyphenols, cancer immunotherapy



# The Effect of Various Doses of Oral Vitamin D<sub>3</sub> Supplementation on Gut Microbiota in Healthy Adults: A Randomized, Double-blinded, Dose-response Study



Journal of  
**PERIODONTAL RESEARCH**

J Periodont Res 2016; 51: 359-365  
All rights reserved

© 2015 John Wiley & Sons A/S.  
Published by John Wiley & Sons Ltd

JOURNAL OF PERIODONTAL RESEARCH  
doi:10.1111/jre.12315

Medicina 2018, 54, 45

4 of 8

Vitamin D inhibits the growth of and virulence factor gene expression by *Porphyromonas gingivalis* and blocks activation of the nuclear factor kappa B transcription factor in monocytes

**D. Grenier<sup>1</sup>, M.-P. Morin<sup>1</sup>, J. Fournier-Larente<sup>1</sup>, H. Chen<sup>2</sup>**  
<sup>1</sup>Oral Ecology Research Group, Faculty of Dentistry, Université Laval, Quebec City, QC, Canada and <sup>2</sup>Department of Stomatology, Hubei University of Science and Technology, Xianning, Hubei, China

Grenier D, Morin M-P, Fournier-Larente J, Chen H. Vitamin D inhibits the growth of and virulence factor gene expression by *Porphyromonas gingivalis* and blocks activation of the nuclear factor kappa B transcription factor in monocytes. J Periodont Res 2016; 51: 359-365. © 2015 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd

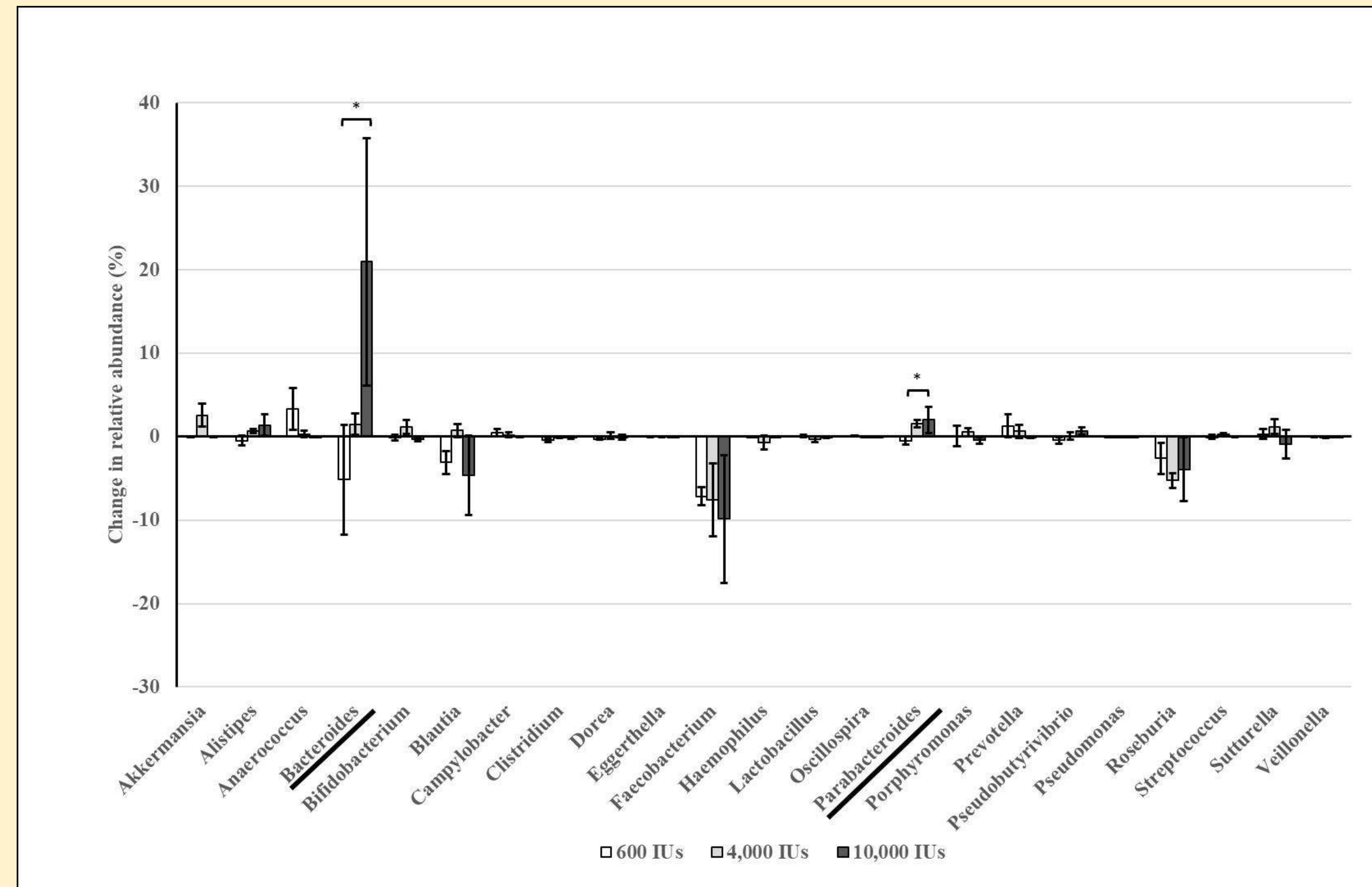
**Table 1.** The relationship between 25-hydroxyvitamin D<sub>3</sub> (25(OH)D<sub>3</sub>) concentrations in the plasma and periodontal diseases.

Authors, Year of Publication	Study Design	Sample Size	Outcome Measure	Outcome Measurement	Results
Dietrich et al., 2004 [13]	cross-sectional	11 202	Periodontitis	attachment level	decreased concentration is associated with changed (poor) periodontal condition
Dietrich et al., 2005 [14]	cross-sectional	6 700	Gingivitis	level of gingival inflammation (bleeding index)	decreased concentration is associated with gingival inflammation and higher bleeding index
Borggess et al., 2011 [15]	case-control	123 cases, 123 controls	PD in pregnant women	probing depth, bleeding index	women with vitamin D deficiency in the plasma (<75 nmol/L) are more prone to chronic periodontitis during pregnancy
Zhou et al., 2012 [16]	case-control	193 cases, 181 controls	PD and chronic obstructive pneumonia	pockets depth, periodontal attachment level, gingival bleeding index, teeth number	decreased concentration is associated with poor periodontal condition
Teles et al., 2012 [11]	exploratory	56	Chronic periodontitis	bleeding index, probing depth, periodontal attachment level, teeth number	decreased concentration is associated with poor periodontal condition
Antonoglou et al., 2013 [17]	comprehensive	80	Chronic periodontitis with type 1 diabetes	amount of plaque, probing depth, attachment level	authors did not find correlation between 25(OH)D <sub>3</sub> concentration in the plasma and chronic periodontitis
Millen et al., 2013 [18]	multi-center	920	Chronic periodontitis in postmenopausal age	X-ray, attachment level, probing depth, bleeding index	decreased concentration is associated with chronic periodontitis increased concentration is associated with gingival bleeding
Liu et al., 2009 [19]	preliminary	178	Aggressive periodontitis	probing depth, attachment level, bleeding index	increased concentration is associated with aggressive periodontitis
Zhang et al., 2013 [20]	case-control	44 cases, 32 controls	Generalized aggressive periodontitis	probing depth, attachment level, bleeding index	increased concentration is associated with generalized aggressive periodontitis

# The Effect of Various Doses of Oral Vitamin D<sub>3</sub> Supplementation on Gut Microbiota in Healthy Adults: A Randomized, Double-blinded, Dose-response Study

## Results

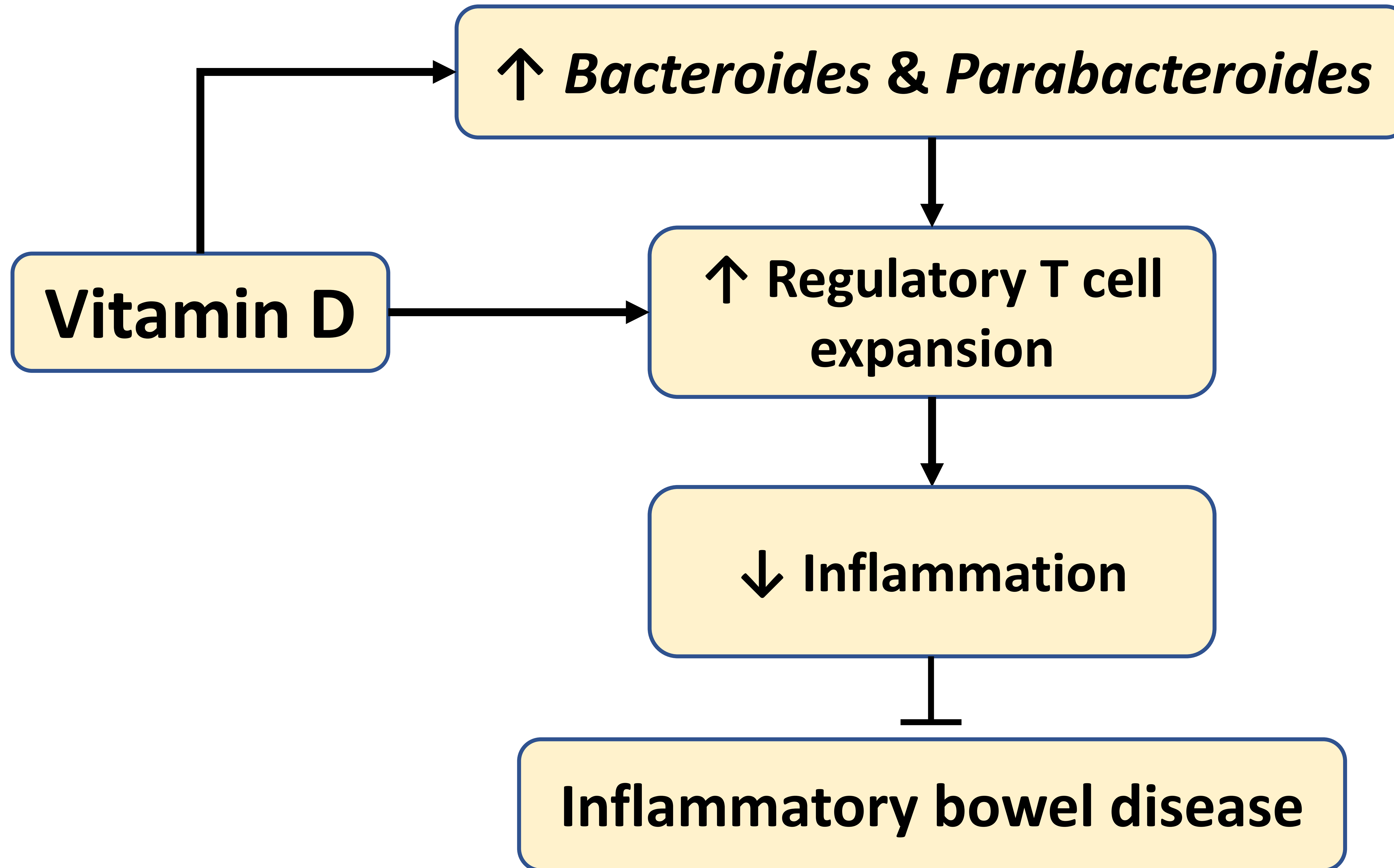
Changes in relative abundance of clinically relevant bacterial genera in participants receiving various doses of vitamin D<sub>3</sub> for 8 weeks



Data are expressed  
as mean ± SEM

Dose-dependent increase in relative abundance of *Bacteroides* and *Parabacteroides*

# The Effect of Various Doses of Oral Vitamin D<sub>3</sub> Supplementation on Gut Microbiota in Healthy Adults: A Randomized, Double-blinded, Dose-response Study



# The Effect of Various Doses of Oral Vitamin D<sub>3</sub> Supplementation on Gut Microbiota in Healthy Adults: A Randomized, Double-blinded, Dose-response Study

Systematic Review and Meta-Analysis

Medicine®

OPEN

## Efficacy of vitamin D in treatment of inflammatory bowel disease

### A meta-analysis

Jinzhong Li, MD<sup>a</sup>, Ning Chen, MD<sup>b</sup>, Dan Wang, MD<sup>a</sup>, Jie Zhang, PhD<sup>b</sup>, Xiaobing Gong, PhD<sup>a,\*</sup>

#### Abstract

**Background:** Vitamin D (VitD) deficiency is prevalent in patient with inflammatory bowel disease (IBD). Recent studies have found that VitD can induce and maintain IBD remission through antibiosis, anti-inflammatory, and repair of intestinal mucosal barriers, thus improving the patient's disease activity and quality-of-life. The purpose of this meta-analysis is to evaluate the therapeutic effect and safety of VitD in the treatment of IBD.

**Methods:** Published randomized controlled trials (RCTs) were included from electronic databases (PubMed, Embase, Cochrane library, Web of Science, and so forth). Cochrane handbook was applied to evaluate the methodological quality. The levels of 25(OH)D<sub>3</sub>, relapse rate, inflammation index, and adverse events were compared between the experimental group and the control group (placebo group). All statistical analyses were directed by Revman 5.3 software and statistical significance was defined as  $P < .05$ .

**Results:** Eighteen RCTs involved 908 patients were included. Meta-analysis showed that VitD improved the 25(OH)D<sub>3</sub> levels more significantly than the control group (ng/mL, weighted mean deviation [WMD]=7.85, 95% CI (5.52, 10.18),  $P < .000001$ ), and compared with lower doses, there were significant differences increasing 25(OH)D<sub>3</sub> levels (WMD=11.19, 95% CI [4.73, 17.65],  $P = .0007$ ) in high-dose VitD treatment while there was no significant difference in the adverse events between 2 groups (WMD=1.56, 95% CI [0.74, 3.29],  $P = .24$ ). VitD reduced the relapse rate more significantly than the control group, but there were no significant differences between the low-dose and high-dose vitamin D treatment. The erythrocyte sedimentation rate (ESR) and high-sensitivity C-reactive protein (hsCRP) of the VitD and the control group showed no statistically significant difference (ESR [mm/h]: WMD=-0.22, 95% CI [-5.73, 5.29],  $P = .94$ ; hsCRP (mg/dL): WMD=-0.53, 95% CI [-1.68, 0.62],  $P = .37$ ).

**Conclusions:** The treatment of VitD in patients with IBD can improve the level of 25(OH)D<sub>3</sub> and control the relapse rate of the disease, whose clinical curative effect is more accurate. Thus VitD should be recommended for the treatment of IBD, at least as an adjunctive treatment.

**Abbreviations:** CD = Crohn disease, DCs = dendritic cells, ESR = erythrocyte sedimentation rate, hsCRP = high-sensitivity C-reactive protein, IBD = inflammatory bowel disease, NF- $\kappa$ B = nuclear factor kappa B, NOD2 = nucleotide-binding oligomerization domain protein 2, RCTs = randomized controlled trials, TNF- $\alpha$  = tumor necrosis factor- $\alpha$ , UC = ulcerative disease, VDR = vitamin D receptor, VitD = Vitamin D.

**Keywords:** Crohn disease, inflammatory bowel disease, meta-analysis, systematic review, ulcerative colitis



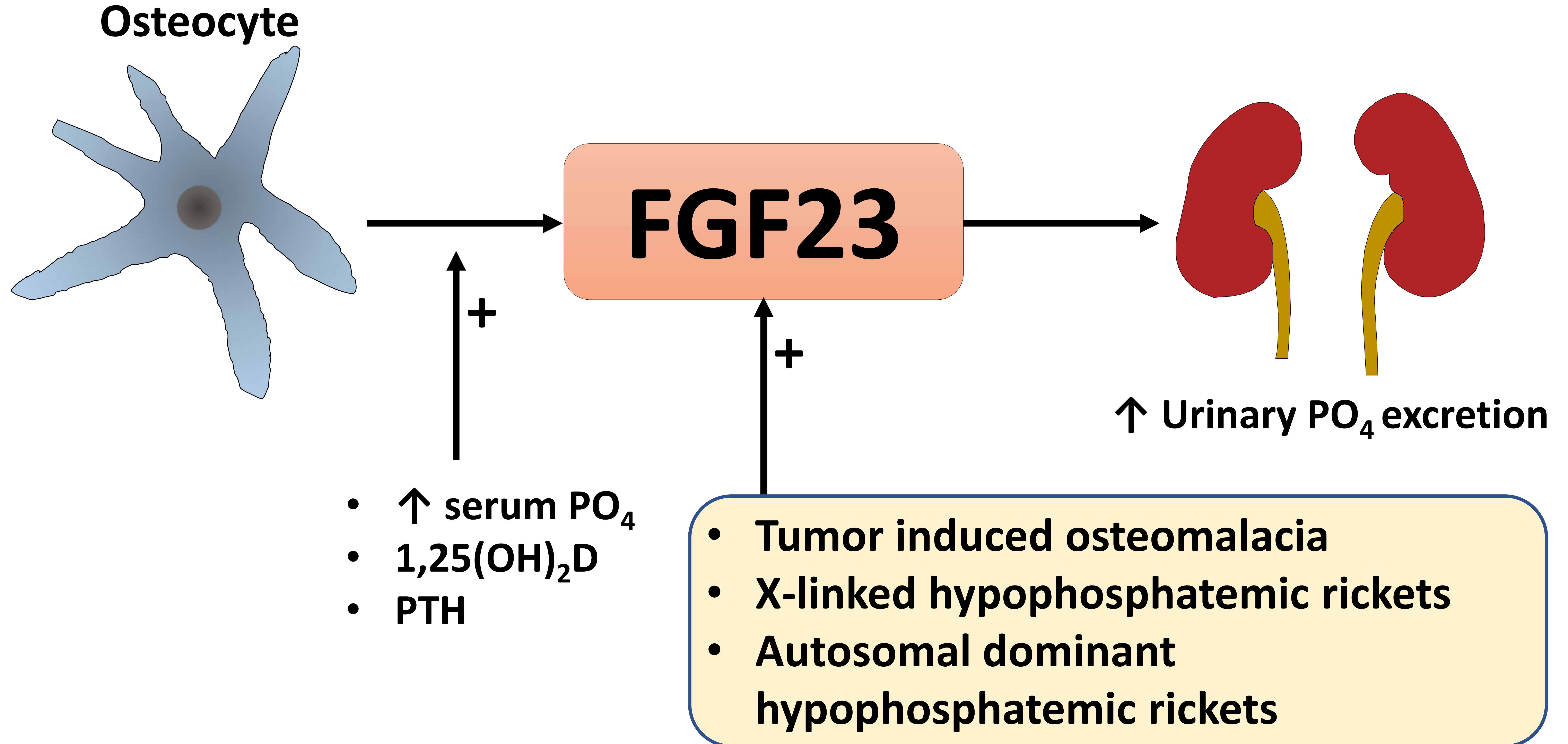
# Oral vitamin D<sub>3</sub> supplementation increases serum fibroblast growth factor 23 concentration in vitamin D-deficient patients: a systematic review and meta-analysis

N. Charoenngam<sup>1,2</sup> • P. Rujirachun<sup>3</sup> • M.F. Holick<sup>2</sup> • P. Ungprasert<sup>4</sup>

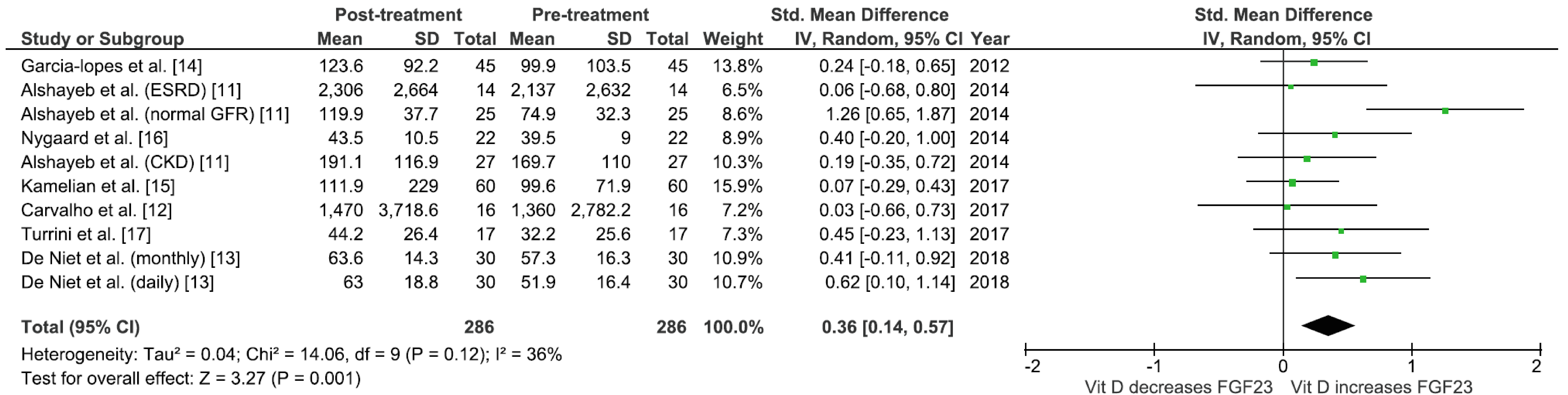
Received: 21 April 2019 / Accepted: 18 July 2019

© International Osteoporosis Foundation and National Osteoporosis Foundation 2019

# Oral vitamin D<sub>3</sub> supplementation increases serum fibroblast growth factor 23 concentration in vitamin D-deficient patients: a systematic review and meta-analysis



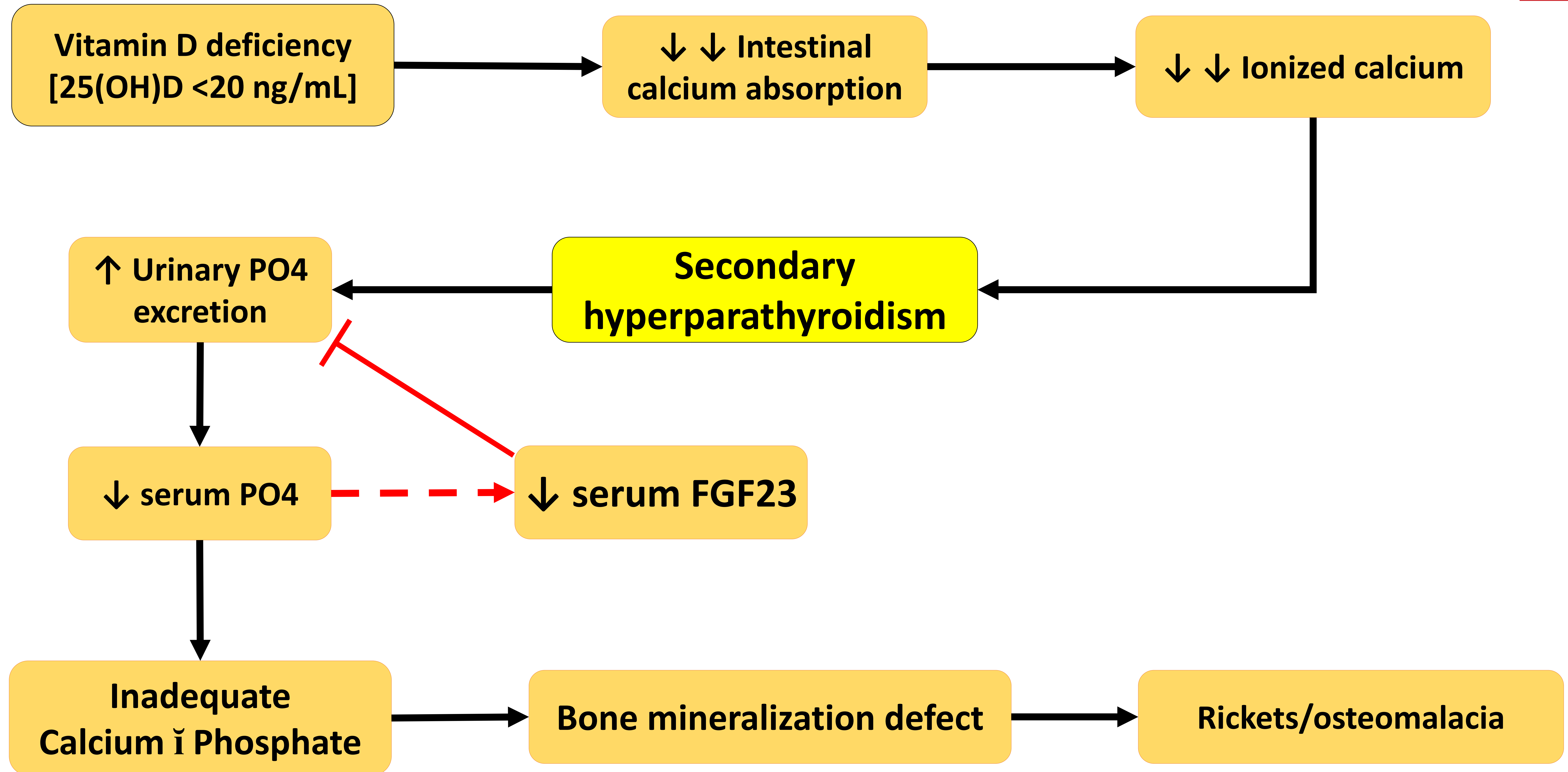
# Oral vitamin D<sub>3</sub> supplementation increases serum fibroblast growth factor 23 concentration in vitamin D-deficient patients: a systematic review and meta-analysis



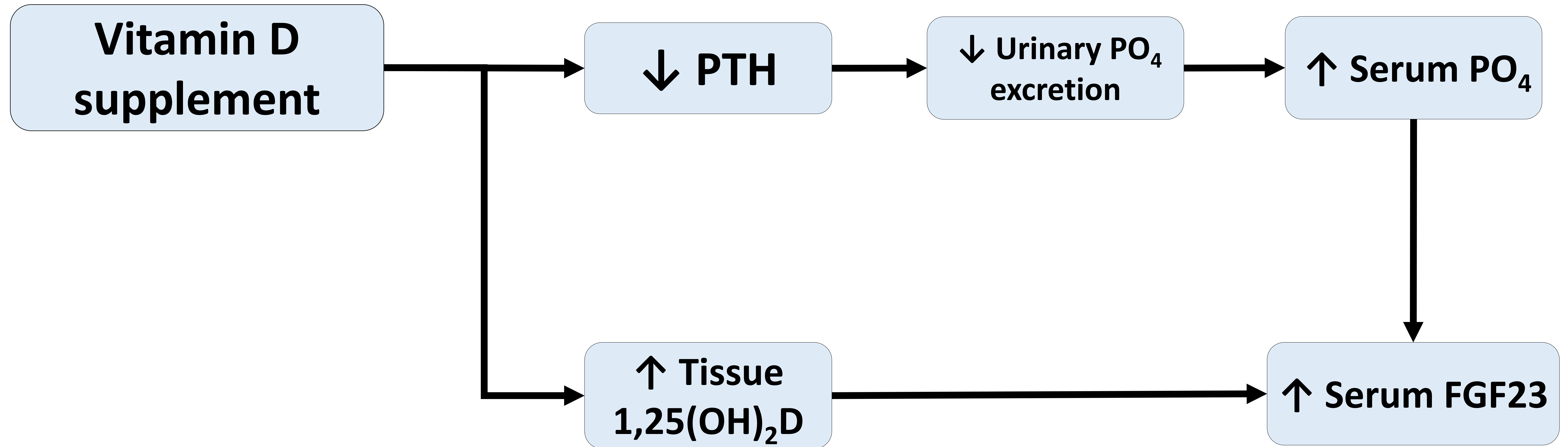
**Fig. 2** Forest plot of the meta-analysis of change in serum intact FGF23 concentration after oral vitamin D<sub>3</sub> supplementation in vitamin D-deficient patients



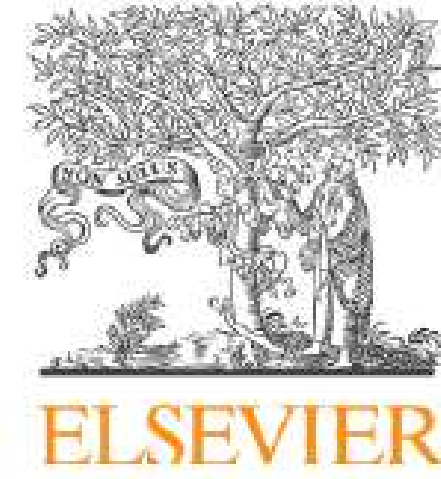
# Oral vitamin D<sub>3</sub> supplementation increases serum fibroblast growth factor 23 concentration in vitamin D-deficient patients: a systematic review and meta-analysis



# Oral vitamin D<sub>3</sub> supplementation increases serum fibroblast growth factor 23 concentration in vitamin D-deficient patients: a systematic review and meta-analysis



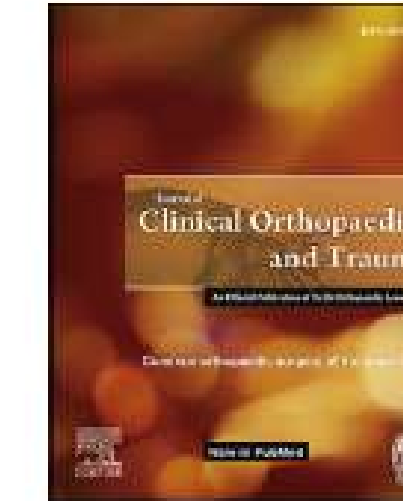
# Reviews



Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Journal of Clinical Orthopaedics and Trauma

journal homepage: [www.elsevier.com/locate/jcot](http://www.elsevier.com/locate/jcot)



## Vitamin D for skeletal and non-skeletal health: What we should know

Nipith Charoenngam<sup>a, b, \*</sup>, Arash Shirvani<sup>a</sup>, Michael F. Holick<sup>a</sup>

<sup>a</sup> Department of Medicine, Section of Endocrinology, Nutrition, and Diabetes, Vitamin D, Skin and Bone Research Laboratory, Boston University Medical Center, Boston, MA, USA

<sup>b</sup> Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

### ARTICLE INFO

#### Article history:

Received 31 May 2019  
Received in revised form  
12 July 2019  
Accepted 13 July 2019  
Available online xxx

Keywords:  
Vitamin D

### ABSTRACT

Vitamin D plays an essential role in regulating calcium and phosphate metabolism and maintaining a healthy mineralized skeleton. Humans obtain vitamin D from sunlight exposure, dietary foods and supplements. There are two forms of vitamin D: vitamin D<sub>3</sub> and vitamin D<sub>2</sub>. Vitamin D<sub>3</sub> is synthesized endogenously in the skin and found naturally in oily fish and cod liver oil. Vitamin D<sub>2</sub> is synthesized from ergosterol and found in yeast and mushrooms. Once vitamin D enters the circulation it is converted by 25-hydroxylase in the liver to 25-hydroxyvitamin D [25(OH)D], which is further converted by the 25-hydroxyvitamin D-1 $\alpha$ -hydroxylase in the kidneys to the active form, 1,25-dihydroxyvitamin D [1,25(OH)<sub>2</sub>D]. 1,25(OH)<sub>2</sub>D binds to its nuclear vitamin D receptor to exert its physiologic functions. These functions include: promotion of intestinal calcium and phosphate absorption, renal tubular calcium reabsorption, and calcium mobilization from bone. The Endocrine Society's Clinical Practice Guideline defines vitamin D deficiency, insufficiency, and sufficiency as serum concentrations of 25(OH)D of <20 ng/mL, 21–29 ng/mL, and 30–100 ng/mL, respectively. Vitamin D deficiency is a major global public health problem in all age groups. It is estimated that 1 billion people worldwide have vitamin D deficiency or insufficiency. This pandemic of vitamin D deficiency and insufficiency is attributed to a modern lifestyle and environmental factors that restrict sunlight exposure, which is essential for endogenous synthesis of vitamin D in the skin. Vitamin D deficiency is the most common cause of rickets and osteomalacia, and can exacerbate osteoporosis. It is also associated with chronic musculoskeletal pain, muscle weakness, and an increased risk of falling. In addition, several observational studies observed the association between robust levels of serum 25(OH)D in the range of 40–60 ng/mL with decreased mortality and risk of development of several types of chronic diseases. Therefore, vitamin D-deficient patients should be treated with vitamin D<sub>2</sub> or vitamin D<sub>3</sub> supplementation to achieve an optimal level of serum 25(OH)D. Screening of vitamin D deficiency by measuring serum 25(OH)D is recommended in individuals at risk such as patients with diseases affecting vitamin D metabolism and absorption, osteoporosis, and older adults with a history of falls or nontraumatic fracture. It is important to know if a laboratory assay measures total 25(OH)D or only 25(OH)D<sub>3</sub>. Using assays that measure only 25(OH)D<sub>3</sub> could underestimate total levels of 25(OH)D and may mislead physicians who treat patients with vitamin D<sub>2</sub> supplementation.

# Reviews

## REVIEW



## The ongoing D-lemma of vitamin D supplementation for nonskeletal health and bone health

*Nipith Charoenngam<sup>a,b</sup>, Arash Shirvani<sup>a</sup>, and Michael F. Holick<sup>a</sup>*

### **Purpose of review**

The goal of this review is to give some perspective on the results and conclusions of three recent randomized controlled vitamin D intervention studies that have challenged the health benefit of vitamin D supplementation for reducing risk for cardiovascular disease, cancer, all-cause mortality and type 2 diabetes and improving bone health.

### **Recent findings**

Vitamin D supplementation to adults who were vitamin D sufficient or insufficient did not reduce risk for developing cardiovascular disease, cancer, type 2 diabetes nor increases bone mineral density (BMD). Patients who were vitamin D deficient with cancer and received vitamin D reduced risk for mortality by 25% and prediabetic adults who were vitamin D deficient and received vitamin D reduced their risk of developing type 2 diabetes by 62%. Older adults receiving 4000 and 10 000 IUs of vitamin D<sub>3</sub> daily for 3 years had reduced radial BMD but had no change in either total hip areal bone density or bone strength in the radius and tibia.

### **Summary**

Caution is needed when evaluating results and conclusions from randomized controlled trials that investigate health benefits of vitamin D; most studies suggest health benefits when vitamin D supplementation is provided to vitamin D deficient populations and little benefit when given to populations that are vitamin D sufficient/insufficient.

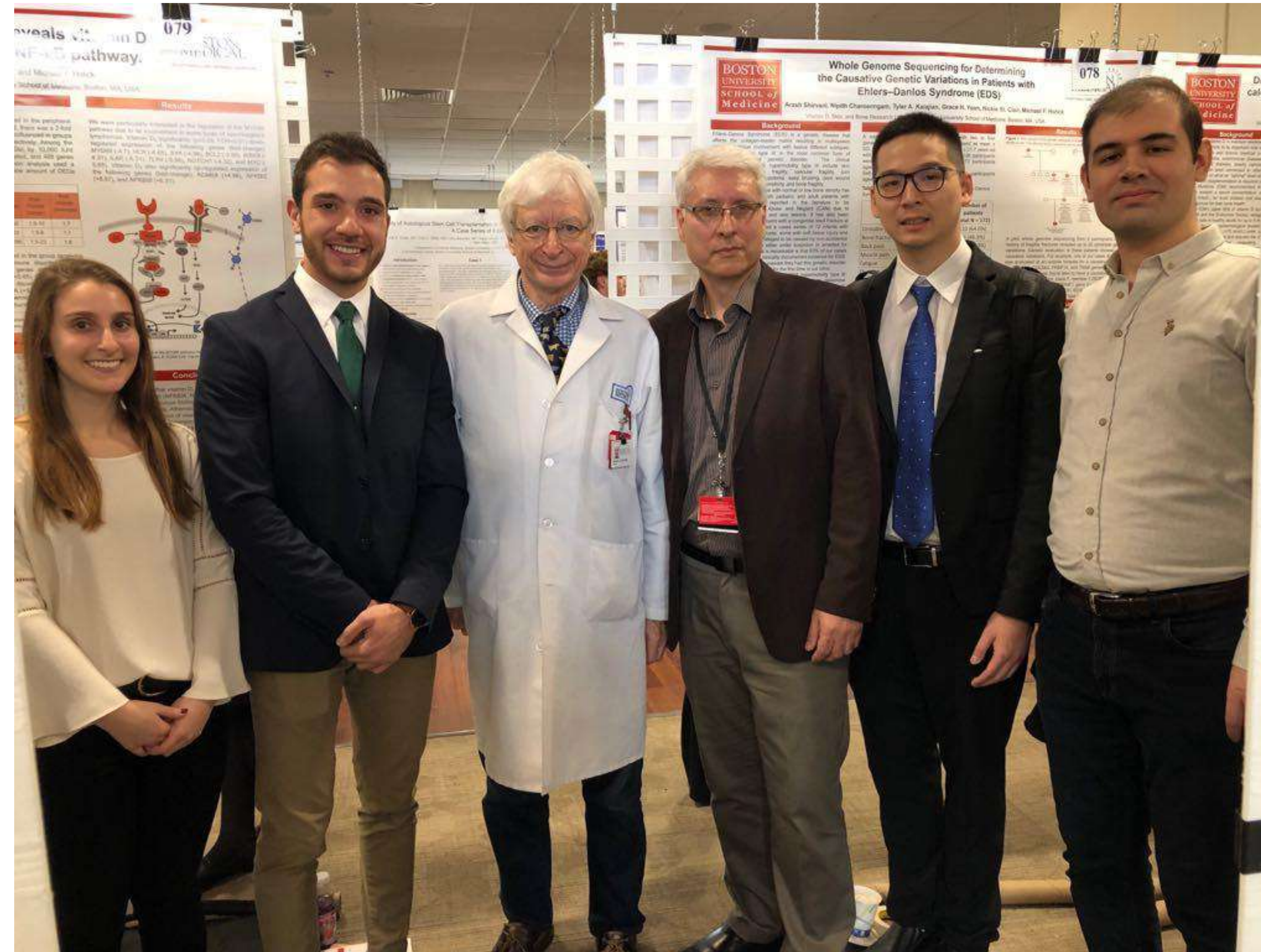
### **Keywords**

25-hydroxyvitamin D, bone health, D2d, VITAL, vitamin D

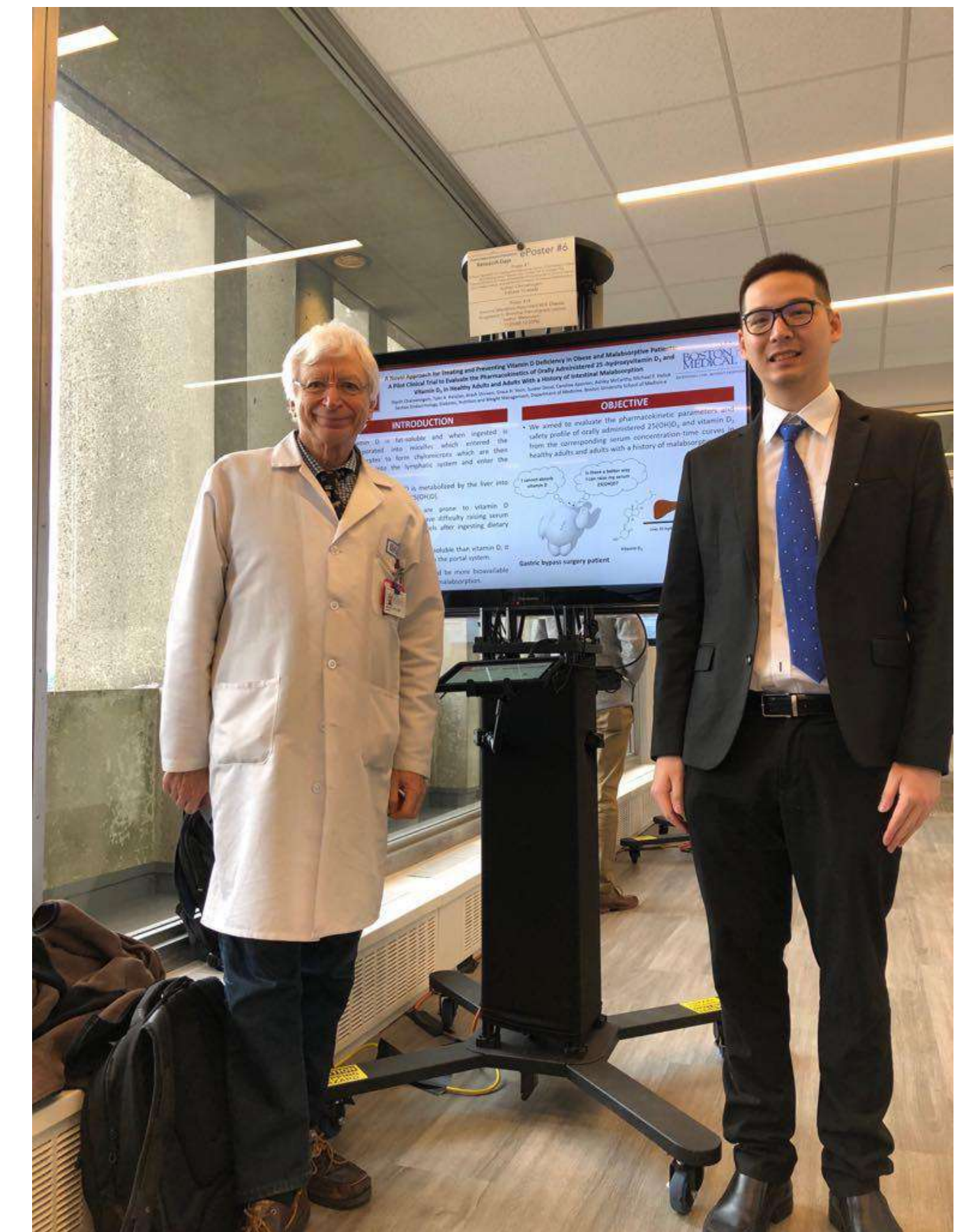
# Research presentation



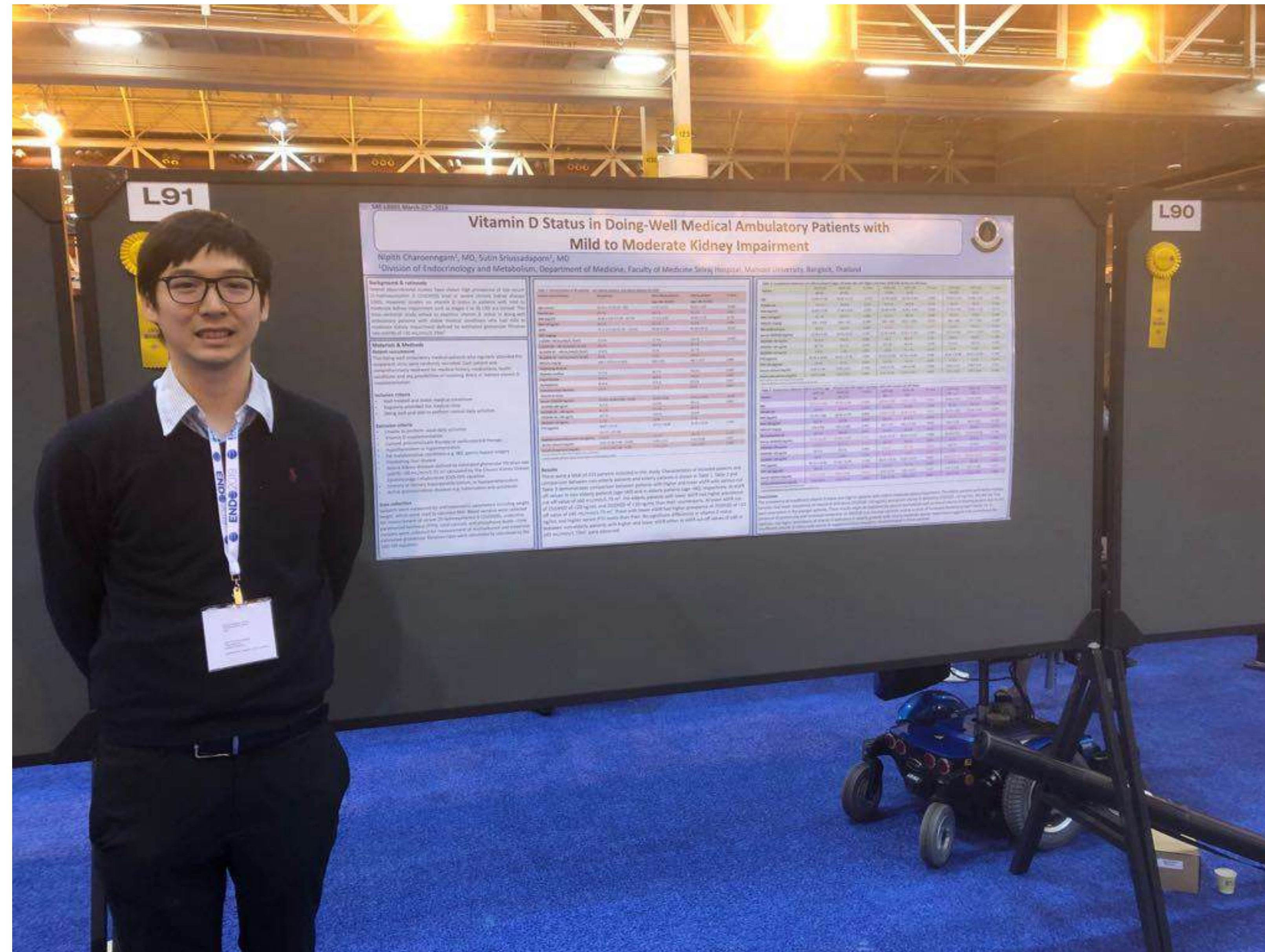
*Oral-Blitz presentation BUSM*



*Poster presentation BUSM*



# Research presentation



*Poster presentation ENDO 2019*

# Research presentation



October 17 & 18, 2019 | Portsmouth Harbor Events, 100 Deer St., Portsmouth, NH

**Lawrence Raisz Memorial**

**New England  
Bone Club 2018**

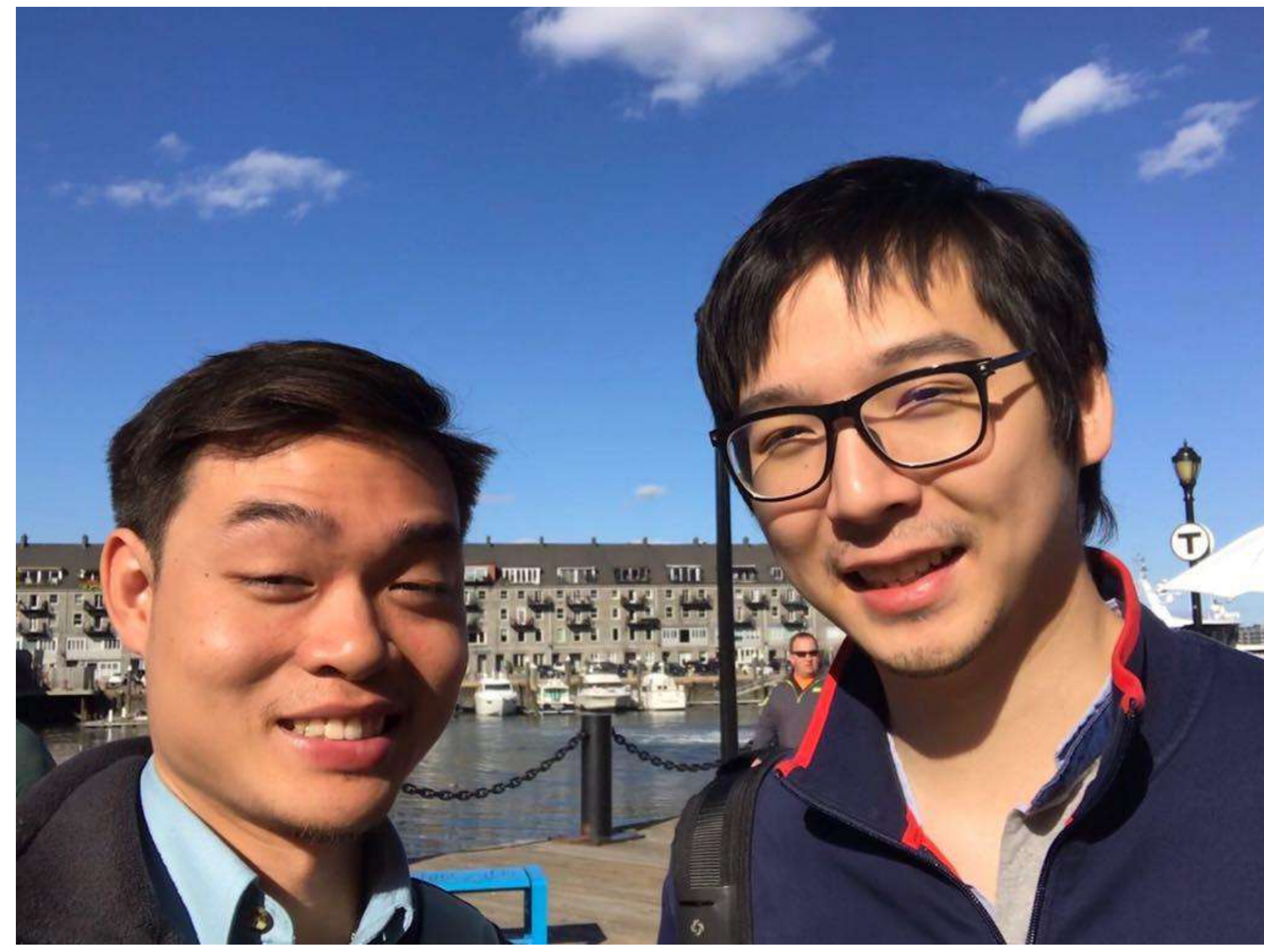
October 17 & 18, 2019



A program of  
Maine Medical Center Research Institute | Southern NH Area Health Education Center |  
Exeter Hospital | Northern New England Translational Research

*Oral presentation NE Bone club 2019*

# Meetings with friends in Boston







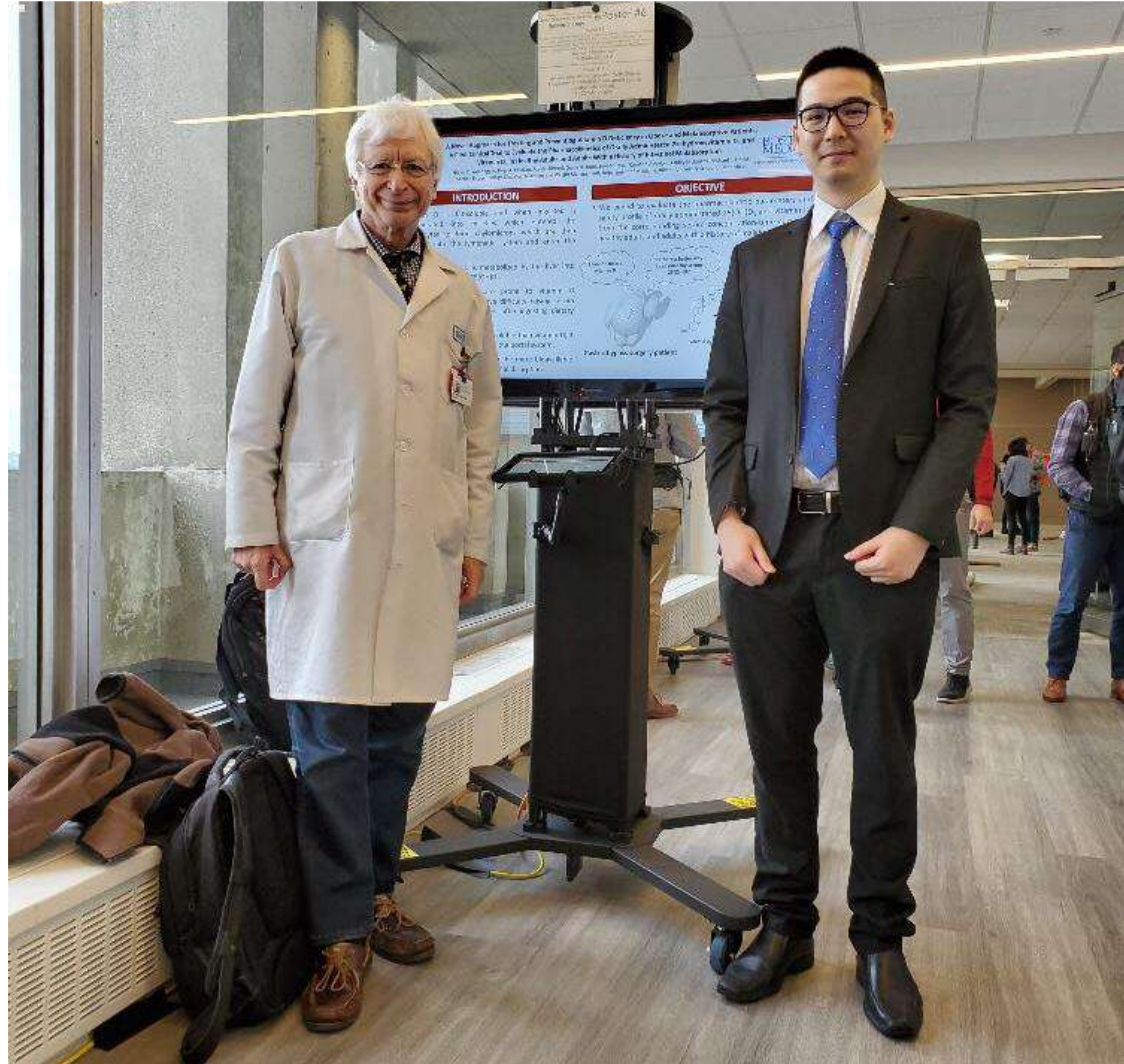
# My Siriraj Mentors











THANK YOU

