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The Impact of Vitamin D Supplementation on Hypertension: A Literature Review

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Abstract

Introduction

Hypertension is one of the most common chronic diseases, and its prevalence continues to rise. Studies have shown that the prevalence of hypertension among adults aged 30–79 is 32% in women and 34% in men, less than half of treated individuals achieve effective blood pressure control. As a result, global rates of hypertension control remain low, at only 23% (range 20–27) for women and 18% (range 16–21) for men with hypertension. Behavioral and environmental risk factors for the development of hypertension are extensively described in the literature. Among the lesser-known factors contributing to the increased incidence of hypertension is vitamin D deficiency. Vitamin D, primarily known for its role in calcium and phosphate metabolism, has been implicated as one of the factors influencing cardiovascular function. Vitamin D deficiency has become a global issue, particularly in regions with limited sunlight exposure.

Aim of the study

The objective of this review is to analyze the current literature regarding the impact of vitamin D supplementation on blood pressure levels.

Materials and Methods
This review incorporates literature from the PubMed database, which was searched using the keywords "hypertension" and "vitamin D." Randomized controlled trials published between 2020 and 2024 were included.

Results
The literature review reveals various aspects of the relationship between vitamin D supplementation and blood pressure regulation. Hypertension remains one of the most prevalent chronic diseases, with its frequency consistently rising. Despite the development of new treatment methods, many patients still fail to achieve effective blood pressure control, posing a significant challenge to healthcare. Increasing evidence suggests that vitamin D may play a role in regulating blood pressure, which is particularly relevant given the widespread deficiency of this vitamin in global populations. Vitamin D deficiency is a common issue affecting a substantial portion of society, making the topic of supplementation and its potential effects even more urgent.

Conclusion
There is evidence to suggest potential benefits of vitamin D supplementation on blood pressure regulation, although the study results are inconclusive and do not yet support definitive clinical recommendations. Further research is necessary to determine the optimal dosages, duration of supplementation, and target serum 25(OH)D levels for achieving the blood pressure-lowering effects of vitamin D.

Keywords: hypertension, vitamin D deficiency.

1. Introduction:

The well-known role of vitamin D is the regulation of calcium-phosphate metabolism and bone health. However, it is important to recognize that its significance extends beyond the musculoskeletal system. The literature describes a connection between the level of vitamin D and its metabolites with the functioning of the cardiovascular system, especially regarding its impact on the development of hypertension. Vitamin D deficiency is highly prevalent worldwide. Several factors contributing to low vitamin D levels in the body have been identified, including air pollution, higher geographical latitude, seasonal variations, sedentary lifestyle, and dietary habits.[1]

[1] Arabi A, El Rassi R, El-Hajj Fuleihan G. Hypovitaminosis D in developing countries-prevalence, risk factors and outcomes. Nat Rev Endocrinol. 2010 Oct;6(10):550-61. doi: 10.1038/nrendo.2010.146. PMID: 20852586.

Studies indicate that vitamin D deficiency may influence the development of hypertension through various biological mechanisms. The relationship between low vitamin D levels and increased arterial stiffness has been described in newly diagnosed hypertensive patients.[2] One mechanism involves the effect of vitamin D on the renin-angiotensin-aldosterone system (RAAS), a key regulator of blood pressure. Vitamin D has been shown to reduce the activity of this system, which normally causes vasoconstriction and sodium retention, ultimately raising blood pressure. Therefore, vitamin D deficiency leads to increased RAAS activity and, consequently, a higher risk of hypertension. Numerous studies also report the anti-inflammatory and antioxidant properties of vitamin D, which support endothelial function.[3] Inflammation and oxidative stress negatively impact blood vessels, contributing to increased arterial stiffness, which in turn raises blood pressure. Thanks to its properties, optimal vitamin D levels may counteract these destructive processes, serving as a protective factor against hypertension, atherosclerosis, and other cardiovascular diseases.

Research has shown an increased risk of hypertension among populations exposed to seasonal variations in vitamin D levels. A linear increase in blood pressure has been observed with increasing distance from the equator.[4] Furthermore, blood pressure tends to be higher in the winter months, when UV exposure is lower, compared to summer. This phenomenon supports the potential impact of vitamin D on blood pressure regulation mechanisms.

Hypertension remains a significant challenge for clinicians worldwide, contributing to one of the leading causes of premature mortality. Studies indicate that in 2010, 31.1% of adults globally suffered from hypertension.[5] Despite the development of new therapeutic methods, a substantial number of patients remain resistant to treatment. Resistant hypertension is defined as high blood pressure that does not normalize despite optimal treatment with at least three antihypertensive medications, including a diuretic. Studies have shown that the prevalence of resistant hypertension in the hypertensive population between 1991 and 2017 was 10.3%. Given the substantial economic costs associated with treating hypertension and its serious health consequences, such as an increased risk of cardiovascular diseases, strokes, and chronic kidney diseases, intensive research efforts are essential. Further studies should focus on a better understanding of the mechanisms behind this condition, identifying risk factors, and exploring new therapeutic possibilities.[6]

2. Purpose:

The aim of this study was to provide a review of the latest scientific works and summarize the current knowledge on the impact of vitamin D deficiency on hypertension.

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[2] Cakal S, Çakal B, Karaca O. Association of vitamin D deficiency with arterial stiffness in newly diagnosed hypertension. Blood Press Monit. 2021 Apr 1;26(2):113-117. doi: 10.1097/MBP.0000000000000497. PMID: 33234810.]

[3] Della Nera G, Sabatino L, Gaggini M, Gorini F, Vassalle C. Vitamin D Determinants, Status, and Antioxidant/Anti-inflammatory-Related Effects in Cardiovascular Risk and Disease: Not the Last Word in the Controversy. Antioxidants (Basel). 2023 Apr 18;12(4):948. doi: 10.3390/antiox12040948. PMID: 37107323; PMCID: PMC10135791.

[4] Rostand SG. Ultraviolet light may contribute to geographic and racial blood pressure differences. Hypertension. 1997 Aug;30(2 Pt 1):150-6. doi: 10.1161/01.hyp.30.2.150. PMID: 9260973.

[5] Mills KT, Bundy JD, Kelly TN, Reed JE, Kearney PM, Reynolds K, Chen J, He J. Global Disparities of Hypertension Prevalence and Control: A Systematic Analysis of Population-Based Studies From 90 Countries. Circulation. 2016 Aug 9;134(6):441-50. doi: 10.1161/CIRCULATIONAHA.115.018912. PMID: 27502908; PMCID: PMC4979614.

[6] Noubiap JJ, Nansseu JR, Nyaga UF, Sime PS, Francis I, Bigna JJ. Global prevalence of resistant hypertension: a meta-analysis of data from 3.2 million patients. Heart. 2019 Jan;105(2):98-105. doi: 10.1136/heartjnl-2018-313599. Epub 2018 Aug 7. PMID: 30087099.

3. Materials and Methods

3.1.Literature Search

In November 2024, a literature review was conducted using the PubMed database. The following keywords were used for the search: “hypertension,” “vitamin D.” Only studies published between 2020 and 2024 were included. The search identified a total of 32 randomized controlled trials (RCTs) with control groups.

3.2. Selection Criteria

The inclusion criteria for the studies selected for this review were: (1) peer-reviewed journals, (2) RCTs, (3) studies investigating the effect of vitamin D levels on blood pressure values. The exclusion criteria included: (1) non-RCT studies, (2) studies involving participants younger than 18 years old.

4. Results

The characteristics of the studies included in the research are presented in the table below.

First author, publication date, study type	Number of participants, age	Duration of the study	Inclusion criteria	Intervention group	Control group
Papakonstantinou E., 2024 Apr 28, RCT [7]	53; 18-70	8 weeks	Body mass index (BMI) > 25 kg/m², age 18–70 years, and hyperglycemia (fasting glucose level > 100 mg/dL) and/or hyperlipidemia (total cholesterol > 200 mg/dL, LDL-C > 100 mg/dL, HDL-C < 40 mg/dL for men and <50 mg/dL for women,	Consumption of 250 ml of the assigned orange juice (Aspis SA Hellenic Juice Industry, Argos-Korinthos, Greece) daily, 30 minutes before lunch, with the orange juice fortified with 2000 IU of vitamin D3 and 108 cfu/ml of probiotics.	Consumption of 250 ml of the assigned orange juice (Aspis SA Hellenic Juice Industry, Argos-Korinthos, Greece) daily, 30 minutes before lunch, with the orange juice not fortified.

[7] Papakonstantinou E, Zacharodimos N, Georgiopoulos G, Athanasaki C, Bothou DL, Tsitsou S, Lympaki F, Vitsou-Anastasiou S, Papadopoulou OS, Delialis D, Alexopoulos EC, Petsiou E, Keramida K, Doulgeraki AI, Patsopoulou IM, Nychas GE, Tassou CC. Two-Month Consumption of Orange Juice Enriched with Vitamin D3 and Probiotics Decreases Body Weight, Insulin Resistance, Blood Lipids, and Arterial Blood Pressure in High-Cardiometabolic-Risk Patients on a Westernized Type Diet: Results from a Randomized Clinical Trial. Nutrients. 2024 Apr 28;16(9):1331. doi: 10.3390/nu16091331. PMID: 38732578; PMCID: PMC11085203.

			triglycerides > 150 mg/dL) and/or hypertension (systolic blood pressure > 130 mmHg or diastolic blood pressure > 80 mmHg).		
Theiler-Schwetz V, 2022 Mar 24, RCT[8]	188; 18,8-86	8 weeks	Adults aged 18 years or older, with hypertension and serum 25(OH)D levels <30 ng/ml.	Receiving 2800 IU of vitamin D3 (Oleovit D3, Fresenius Kabi Austria, Graz, Austria).	Placebo (coconut oil).
Subramanian A, 2021 Jan, RCT[9]	1257; >18	6 months	Pregnant women who were generally in good health; aged 18 years or older; between 17-24 weeks of pregnancy based on the recalled date of the last menstrual period (LMP) and ultrasound; and had a singleton pregnancy.	Administration of one of three doses of vitamin D during pregnancy: low (4200 IU/week), medium (16800 IU/week), or high (28000 IU/week); calcium supplements (500 mg/day) and iron and folic acid (66 mg iron/day; 350 µg folic acid/day) throughout the intervention period.	Placebo, calcium supplements (500 mg/day), as well as iron and folic acid (66 mg of iron/day; 350 µg of folic acid/day) throughout the entire study period.
Zelzer S, 2024	505; 61,2 ±	8 weeks	Patients with	Supplementatio	Placebo.

[8] Theiler-Schwetz V, Trummer C, Grübler MR, Keppel MH, Zittermann A, Tomaschitz A, Karras SN, März W, Pilz S, Gängler S. Effects of Vitamin D Supplementation on 24-Hour Blood Pressure in Patients with Low 25-Hydroxyvitamin D Levels: A Randomized Controlled Trial. Nutrients. 2022 Mar 24;14(7):1360. doi: 10.3390/nu14071360. PMID: 35405973; PMCID: PMC9003372.

[9] Subramanian A, Korsiak J, Murphy KE, Al Mahmud A, Roth DE, Gernand AD. Effect of vitamin D supplementation during pregnancy on mid-to-late gestational blood pressure in a randomized controlled trial in Bangladesh. J Hypertens. 2021 Jan;39(1):135-142. doi: 10.1097/HJH.0000000000002609. PMID: 32773651; PMCID: PMC7752208.

Mar 14, RCT[10]	10,6		hypertension and 25(OH)D levels below 75 nmol/L.	n with 2,800IU of vitamin D daily for 8 weeks.	
Sheikh V, 2020 Oct, RCT[11]	208; 26-84	8 weeks	Age between 18 and 75 years, with systolic blood pressure of 140 mmHg or higher or diastolic blood pressure of 90 mmHg or higher, and vitamin D deficiency or insufficiency.	Vitamin D (calciferol) administration based on serum vitamin D levels. Patients with serum vitamin D levels below 20 ng/mL received 50,000 IU of vitamin D weekly for two months. Patients with serum vitamin D levels between 20 and 30 ng/mL received 1,000 IU of vitamin D weekly for two months.	Placebo.
de Paula TP, 2020 Nov 12, RCT[12]	127; 65 ± 9	8 weeks	Outpatients with type 2 diabetes mellitus (HbA1c 6.5–10%), hypertension (office systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg, or undergoing	Administration of vitamin D at a dose of 100,000 IU of cholecalciferol (25(OH)D).	Placebo.

[10] Zelzer S, Meinitzer A, Enko D, Keppel MH, Herrmann M, Theiler-Schwetz V, Trummer C, Schmitt L, Tomaschitz A, Sadoghi P, Dierkes J, Pludowski P, Zittermann A, März W, Pilz S. Classification of Vitamin D Status Based on Vitamin D Metabolism: A Randomized Controlled Trial in Hypertensive Patients. Nutrients. 2024 Mar 14;16(6):839. doi: 10.3390/nu16060839. PMID: 38542750; PMCID: PMC10975656

[11] Sheikh V, Mozaianimonfared A, Gharakhani M, Poorolajal J, Ph D. Effect of vitamin D supplementation versus placebo on essential hypertension in patients with vitamin D deficiency: a double-blind randomized clinical trial. J Clin Hypertens (Greenwich). 2020 Oct;22(10):1867-1873. doi: 10.1111/jch.13926. Epub 2020 Sep 20. PMID: 32951301; PMCID: PMC8030057.

[12] de Paula TP, Moreira JSR, Sperb LF, Muller MEP, Steemburgo T, Viana LV. Efficacy of single-dose cholecalciferol in the blood pressure of patients with type 2 diabetes, hypertension and hypovitaminoses D. Sci Rep. 2020 Nov 12;10(1):19611. doi: 10.1038/s41598-020-76646-6. PMID: 33184328; PMCID: PMC7665034.

			antihypertensive treatment), and vitamin D deficiency (serum 25(OH)D concentration below 20 ng/mL or 50 nmol/L).		
Abderhalden LA, 2020 Sep 1, RCT[13]	273; >60	24 months	Adults aged ≥60 years who underwent planned unilateral knee replacement surgery due to severe knee osteoarthritis, with no planned bilateral knee replacement within the next 2 years.	Taking a single capsule of vitamin D 2000 IU/day, calcium supplementation of 500 mg/day (calcium carbonate).	Supplementation of 800 IU of vitamin D3 per day, supplementation of 500 mg of calcium per day (calcium carbonate).

Table 1. Characteristics of the analyzed articles

Papakonstantinou's team analyzed the effect of consuming vitamin D and probiotic-enriched orange juice on blood pressure values. The study included 53 overweight or obese adults following a Western-style diet. The participants, who were receiving antihypertensive and lipid-lowering treatments (irbesartan, manidipine, amlodipine, ramipril, nebivolol, and candesartan), were divided into two groups. One group received an intervention consisting of 2000 IU of vitamin D3 and 108 cfu/ml of probiotics per serving of orange juice (OJ). Peripheral systolic (SBP) and diastolic (DBP) blood pressure measurements were taken before and every two weeks throughout the study. At the end of the study, peripheral SBP was significantly reduced in both groups, with a more pronounced reduction in DBP in the intervention group. However, central systolic and diastolic blood pressures did not show significant changes.

The Theiler-Schwetz V team assessed the impact of vitamin D supplementation on 24-hour blood pressure in patients with low serum 25-hydroxyvitamin D. The study involved patients aged over 18 with diagnosed hypertension and low vitamin D levels (serum 25(OH)D <30 ng/ml). One hundred patients in the intervention group received 2800 IU of vitamin D3 daily for eight weeks. A placebo was administered to the control group. No significant effects on 24-hour systolic and diastolic blood pressure were observed for patients whose final serum

[13] Abderhalden LA, Meyer S, Dawson-Hughes B, Orav EJ, Meyer U, de Godoi Rezende Costa Molino C, Theiler R, Stähelin HB, Ruschitzka F, Egli A, Forman JP, Willett WC, Bischoff-Ferrari HA. Effect of daily 2000 IU versus 800 IU vitamin D on blood pressure among adults age 60 years and older: a randomized clinical trial. Am J Clin Nutr. 2020 Sep 1;112(3):527-537. doi: 10.1093/ajcn/nqaa145. PMID: 32542307.

25(OH)D levels remained below 20 ng/ml. However, exploratory analysis of the entire cohort showed a marginally significant trend toward an association between achieved 25(OH)D levels and 24-hour systolic blood pressure.

Hypertension is a common condition in pregnant women. Subramanian's team studied the effects of vitamin D supplementation during pregnancy on blood pressure in the mid and late stages of pregnancy. The study included 1298 healthy pregnant women aged 17 to 24 weeks, excluding those with pre-existing hypertension. Participants were divided into three groups receiving low (4200 IU/week), medium (16800 IU/week), or high (28000 IU/week) doses of vitamin D, while the control group received a placebo. Additionally, all participants received calcium (500 mg/day), iron (66 mg/day), and folic acid (350 μg/day) supplements throughout the intervention. The study found no significant effect on systolic or diastolic blood pressure in women with low vitamin D and low blood pressure by the end of pregnancy. However, in the 36th week of pregnancy, systolic and diastolic pressures were about 2 mmHg higher in women who received the highest dose of vitamin D compared to the placebo group. This result contrasts with earlier reports[14][15][16]suggesting that vitamin D supplementation during pregnancy lowers blood pressure.
The differences observed in the results may potentially be attributed to discrepancies in baseline vitamin D levels among the participants, variations in the timing of supplementation initiation during pregnancy, and differences in the duration of the intervention. This issue warrants further investigation and presents an interesting direction for future research.
In Zelzer S.'s study, the researchers aimed to assess whether patients with functional vitamin D deficiency experienced benefits from vitamin D supplementation in terms of bone metabolism and cardiovascular risk. The primary objective of the initial analysis was to evaluate whether supplementation with 2900 IU of vitamin D daily for 2 months significantly reduced systolic blood pressure (SBP) compared to placebo. The study involved 505 hypertensive patients with serum 25(OH)D levels below 75 nmol/L. The intervention group received 2800 IU of vitamin D daily for 8 weeks, while the control group received a placebo. The results of this randomized controlled trial (RCT) indicated that vitamin D supplementation had no significant impact on 24-hour blood pressure reduction, both systolic and diastolic. Any observed changes could have been incidental or related to other factors independent of supplementation. Further studies on larger patient cohorts are necessary to confirm or exclude potential benefits of vitamin D in hypertension therapy.

Sheikh V.'s team published a study analyzing the impact of vitamin D supplementation compared to placebo on primary hypertension in patients with vitamin D deficiency. The study included 208 participants aged 18 to 75 years with systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg and vitamin D deficiency. The intervention group

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[14] Asemi Z, Samimi M, Tabassi Z, Shakeri H, Esmaillzadeh A. Vitamin D supplementation affects serum high-sensitivity C-reactive protein, insulin resistance, and biomarkers of oxidative stress in pregnant women. *J Nutr* 2013; 143:1432–1438.

[15] Asemi Z, Samimi M, Siavashani MA, Mazloomi M, Tabassi Z, Karamali M, et al. Calcium-vitamin D co-supplementation affects metabolic profiles, but not pregnancy outcomes, in healthy pregnant women. *Int J Prev Med* 2016; 7:49.

[16] Zerofsky MS, Jacoby BN, Pedersen TL, Stephensen CB. Daily cholecalciferol supplementation during pregnancy alters markers of regulatory immunity, inflammation, and clinical outcomes in a randomized controlled trial. *J Nutr* 2016; 146:2388–2397.

received vitamin D supplementation based on their serum vitamin D levels: 50,000 IU/week for 2 months for those with serum vitamin D <20 ng/ml, and 1000 IU/week for 2 months for those with levels between 20-30 ng/ml. The control group received a placebo pearl for 2 months. Both groups also received routine antihypertensive medications. Prior to supplementation, systolic blood pressure was slightly higher in the intervention group compared to the control group. However, after the intervention, SBP significantly decreased in the intervention group compared to the control group. No noticeable effect on diastolic blood pressure was observed following vitamin D supplementation.

De Paula and colleagues undertook an analysis of the effectiveness of a single dose of cholecalciferol on blood pressure in patients with type 2 diabetes, hypertension, and vitamin D deficiency. The study included outpatients with type 2 diabetes (HbA1c 6.5–10%), hypertension (office systolic blood pressure ≥140 mm Hg or diastolic ≥90 mm Hg, or ongoing antihypertensive treatment), and vitamin D deficiency (serum 25(OH)D levels below 20 ng/mL or 50 nmol/L). Participants were divided into two groups: the placebo group (capsules containing microcrystalline cellulose) and the intervention group, which received 100,000 IU of cholecalciferol (25(OH)D). At the end of the study, results showed that diastolic blood pressure (DBP) decreased in the intervention group, with a similar trend observed in systolic blood pressure (SBP) [−8 (−10; −2) vs. −2 (−5; 2) mm Hg; P = 0.07] compared to the placebo group. Significant differences in ambulatory blood pressure monitoring (ABPM) values were found favoring the intervention group [−7.5 (−12; −0.5) vs. −1 (−6; 5) mm Hg, P = 0.02], during the day [−7 (−13; −2) vs. −1 (−5; 6) mm Hg; P = 0.007], and at night [−7.0 (−17; 1) vs. 3 (−3; 10) mm Hg; P = 0.009]. In the intervention group, significant reductions in diastolic blood pressure were observed both in the 24-hour measurement [−3.5 (−6; −0.8) vs. −1 (−3; 3.5) mm Hg; P = 0.04] and during the daytime [−5.0 (−7.5; −0.8) vs. 0.0 (−4; 2) mm Hg; P = 0.01].

Abderhalden LA's research team evaluated the impact of supplementation with two different doses of vitamin D on blood pressure values in a population of patients over 60 years of age. The study included patients aged over 60 who had undergone unilateral knee arthroplasty and had no plans for bilateral knee replacement within the next 24 months. Participants were randomly assigned to two groups: one group received 2000 IU of vitamin D3 daily (123 patients), and the other received 800 IU (127 patients). Additionally, each participant received calcium supplementation at 500 mg per day. The intervention lasted for 24 months. The secondary outcome of the study was to assess changes in blood pressure values among the participants undergoing supplementation. The two-year supplementation with 2000 IU of vitamin D daily did not provide significant benefits or harms in lowering blood pressure compared to the standard dose of 800 IU daily in individuals aged 60 and older following total knee replacement. Both groups demonstrated a similar, significant decrease in systolic and diastolic blood pressure during the day, at night, and in 24-hour measurements.

Post hoc analyses showed that the 2000 IU dose was more effective in reducing systolic blood pressure variability, leading to a reduction of nearly 0.5 mm Hg, corresponding to a 4.4% decrease. Additionally, observations suggested that an optimal serum 25(OH)D concentration of approximately 28.7 ng/ml might be associated with the greatest reduction in blood pressure, regardless of the dose of vitamin D administered.

5. Discussion and Summary

The literature review indicates that the impact of vitamin D supplementation on blood pressure (BP) values is complex, with results varying depending on the studied population, the doses of vitamin D administered, initial vitamin D levels, and the duration of the intervention. However, a noticeable trend emerges suggesting an improvement in BP among patients whose serum vitamin D levels reach an optimal range. Short-term supplementation, particularly at moderate doses, seems to offer limited benefits in terms of influencing blood pressure values. Long-term interventions with higher doses of vitamin D may be more effective in stabilizing BP.

In cases where patients with baseline vitamin D deficiency underwent supplementation, a more pronounced positive effect on BP values was observed, with a more significant reduction in systolic blood pressure (SBP). This suggests that targeted supplementation may offer potential benefits for those with insufficient vitamin D levels. The results varied across different study groups, including individuals with hypertension, pregnant women, patients with diabetes, and older adults. It appears that the response to vitamin D supplementation might be influenced by comorbid conditions and concurrent medications.

It is important to note that the studies employed different methods for measuring blood pressure, including 24-hour measurements and standard office measurements (usually repeated three times). The methods used to collect data may not have fully captured the changes in the studied variables. Several studies also indicated that the effect of vitamin D is partially dependent on the achieved level of 25(OH)D in the serum. Therefore, monitoring vitamin D levels during supplementation may be as important as the dosage itself. While there is evidence suggesting potential benefits of vitamin D supplementation in regulating blood pressure, the results remain inconclusive and do not yet allow for definitive clinical recommendations. Further studies are necessary to determine optimal vitamin D doses, the duration of supplementation, and target serum 25(OH)D levels to achieve BP-lowering benefits.

Disclosure

Authors Contribution

Larysa Bielecka is the sole author of this work. The author was responsible for:

- the conception and design of the study,
- conducting the research,
- data analysis and interpretation,
- writing the manuscript.

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Conflicts of Interest

The author declares no conflict of interest.

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