Racial Disparity in Blood Pressure: is Vitamin D a Factor?

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BACKGROUND: Higher prevalence of hypertension among African Americans is a key cause of racial disparity in cardiovascular morbidity and mortality. Explanations for the difference in prevalence are incomplete. Emerging data suggest that low vitamin D levels may contribute.
OBJECTIVE: To assess the contribution of vitamin D to racial disparity in blood pressure.
DESIGN: Cross-sectional analysis.
PARTICIPANTS: Adult non-Hispanic Black and White participants from the National Health and Nutrition Examination Survey 2001–2006.
MEASURES: We assessed Black-White differences in systolic blood pressure (SBP) controlling for conventional risk factors, and then additionally, for vitamin D (serum 25[OH]D).
RESULTS: The sample included 1984 and 5156 Black and White participants ages 20 years and older. The mean age-sex adjusted Black-White SBP difference was 5.2 mm Hg. This difference was reduced to 4.0 mm Hg with additional adjustment for socio-demographic characteristics, health status, health care, health behaviors, and biomarkers; adding 25(OH)D reduced the race difference by 26% (95% CI 7–46%) to 2.9 mm Hg. This effect increased to 39% (95% CI 14–65%) when those on antihypertensive medications were excluded. Supplementary analyses that controlled for cardiovascular fitness, percent body fat, physical activity monitoring, skin type and social support yielded consistent results.
CONCLUSION: In cross-sectional analyses, 25(OH)D explains one quarter of the Black-White disparity in SBP. Randomized controlled trials are required to determine whether vitamin D supplementation could reduce racial disparity in BP.

KEY WORDS: vitamin D; blood pressure; African continental ancestry.
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INTRODUCTION

Black Americans have higher age-adjusted blood pressure (BP) than White Americans,[1] yet the causes of this disparity remain uncertain. Previous studies have suggested that diet, obesity, social support, and stress may contribute, but these factors do not seem to fully explain higher Black BP.[2–4] Vitamin D is critical to bone health, but ubiquitous vitamin D receptors and effects on myriads of genes suggest broader clinical effects.[5] Genetic knockout models suggest vascular effects of vitamin D, including vascular endothelium, the renin-angiotensin axis,[6] and vascular smooth muscle including cell proliferation,[7] inflammation,[6] thrombosis,[8] cardiac hypertrophy,[9] and hyperparathyroid hormone secretion.[10] Prospective cohort data suggest low serum vitamin D levels might contribute to cardiovascular disease,[11] in part through elevated BP.[12]

Serum vitamin D levels are largely driven by ultraviolet (UV) synthesis in the skin.[11] Darker skin impedes UV penetration and reduces vitamin D production; this relationship is particularly critical at higher latitudes both because of less intense UV radiation and colder climates leading to less skin exposure.[13] Moreover, cumulative data from comparative anatomy, physiology, and genomics suggest that differences in human skin pigment arose from evolutionary selection pressures involving vitamin D and UV exposure.[14] African ancestry is associated with lower levels; both sunlight and diet result in lower vitamin D levels among persons with stronger African ancestry.[15]

These findings raise the possibility that vitamin D disparities could represent a pathway contributing to racial disparity in BP. To date, there have been few studies addressing this question. Judd et al. reported that serum indicators of vitamin D were associated with BP with attenuation of age-related increases in BP among white, but not Black non-hypertensive adults adjusted for sex, body mass index (BMI), and season.[16] Another study of untreated adults suggested that low serum vitamin D levels explained about half of the Black risk (relative to Whites) in hypertension; this study controlled for age, sex, BMI, and physical activity.[17] These findings are limited by limited control for confounding; vitamin D is associated with many additional aspects of health.[18]

To further evaluate the potential contribution of low serum vitamin D levels to racial differences in BP, we used detailed health information from a current national US sample to control for multiple potential confounders.

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METHODS

Participants

We assessed publicly available data from the National Health and Nutrition Examination Survey (NHANES) conducted from

2001–2006. The overall response rate for the NHANES 2001–2006 examined sample was 77.5%. Our sample included non-Hispanic Black, and non-Hispanic White participants aged 20 years and older, who participated in the baseline examination (n=10,504) and for whom BP and serum vitamin D levels were available. Of these, 659 lacked information on vitamin D, 597 had no systolic BP reading, and 1131 had neither, for an item response rate of 89% (n=9,373). We then excluded participants who had a positive urine pregnancy test result or self-reported being pregnant at exam, (n=480) and those with early renal disease (estimated glomerular filtration rate <60 ml/min using the MDMR equation[19] or urine albumin-to-creatinine ratio [UACR] >30 mg/g) (n=1,782) for a total of 7,140 participants in our analytic sample.

Blood Pressure

BP was measured by physicians trained in assessment using mercury sphygmomanometry and appropriately sized arm cuffs.[20–21] Readings were taken from participants while sitting after five minutes of rest. In determining mean BP, we followed NHANES recommendations. In most instances, the second and third values were averaged. When only two measures were available, we used the second reading to minimize office hypertension. We used systolic BP (SBP) as our outcome because it is more strongly associated with cardiovascular mortality than diastolic BP.[22]

Vitamin D

Serum 25(OH)D was measured using a radioimmunoassay kit (DiaSorin, Stillwater, MN). Although 1,25-dihydroxyvitamin D is the biologically active form of vitamin D, serum 25(OH)D is regarded as the best indicator of vitamin D status in individuals without kidney disease.[22] We grouped vitamin D into quintiles given the potential for non-linear effects.

Race and Ethnicity

We assessed race/ethnicity (Black vs. White) based on self-report. Because our focus was on the difference in SBP between Blacks and Whites, we excluded Hispanics and those of "Other" race to improve the fit and validity of the regression models we used for making the adjusted comparisons of interest. Notably, Hispanics represent a heterogonous group with variable African ancestry.[24]

Control Variables

To address confounding of vitamin D and BP, we assessed a range of variables potentially associated with race, BP, and vitamin D. We grouped covariates into *demographic characteristics*: age (in years), sex (male or female), and race (Black or White); *socioeconomic and social characteristics*: educational level (<high school, high school, > high school), household income at federal poverty (<100%, 100–149%, 150–199%, 200–299%, ≥ 300%), and marital status (married/cohabitating or not); *health and health care*: self rated health (excellent, very good, good, fair, poor), health insurance (insured or not), regular source of care (yes or no), and number of antihypertensive medications currently taking (0, 1, 2, 3 or greater); *behavioral risk factors:* smoking (current, former, never), exposure to smoke (serum cotinine [ng/mL]), BMI (<20, 20–25.5, 25.5–29.9, ≥ 30 kg/m^2), physical activity (about the same, more, or less than most people), alcohol intake (gm/day); dietary nutrients: calcium (gm/day), sodium, and potassium (gm/day); and, *biomarkers:* hemoglobin a1c (%), C reactive protein (mg/L), and serum albumin (g/dl).

We also assessed *additional measures* in supplementary analyses that were collected on selected ages, for selected years. These included cardiovascular fitness assessment based on a submaximal treadmill exercise test (20–49 years, n=1,317),[24] physical activity monitoring based on data from accelerometers (20 years and older, n=2,999),[25] percent body fat based on dual energy absorptiometry (DXA) scanning (20–69 years, n=3,639),[26] social support (can count on anyone when needed for emotional support (40 years and older, n=3,339), and a shortened adaptation of the Fitzpatrick skin type system. This system classifies skin into six ordinal categories based on skin pigment and tanning vs. burning in response to UV exposure (20–59 years, n=4,629).[28]

Statistical Analyses

Analyses were conducted with SUDAAN (version, 10.01) and Stata (v.10.1, College Station, TX), adjusting for the complex survey design of NHANES to yield appropriate design-based population parameter estimates and standard errors. We examined the Black-White differences in SBP using a series of multiple linear regression analyses. The analyses adjusted for demographics, added, in turn, socioeconomic and social characteristics, health and health care, behavioral risk factors, and biomarkers. For each set of covariates, we compared the Black-White differences in SBP without and with adjustment for 25(OH)D. We compared the linear regression coefficient estimates for Blacks from models that excluded and included 25(OH)D using the method of Clogg et al. [28] as a test for the hypothesis that Vitamin D partly accounts for higher Black BP. The percent attenuation was defined as $100 * (\beta_{\text{Model 1}} - \beta_{\text{Model 2}}) / (\beta_{\text{Model 1}})$; where β is the estimated regression coefficient for Black race, and Model 1 excludes and Model 2 includes 25(OH)D.

Because of smaller sample sizes, we trimmed the models for the supplementary analysis. We omitted variables with p values >0.2 and whose omission resulted in less than a 10% change in the race effect on SBP. This resulted in omission of serum cotinine and dietary nutrients. In order to minimize further sample attrition, each variable was added separately and then removed before the next variable was added. This resulted in education and health insurance being removed from the physical activity monitor analysis and poverty, usual source of care and A1C being removed from the cardiovascular fitness analyses.

Sensitivity analyses assessed the contribution of non-linear components of all continuous covariates (by including them as categorical variables or squared terms), examined serum 25(OH)D levels as a continuous variable, and also excluded those taking antihypertensive medications. We conducted an analysis restricted to those with hypertension (systolic >140 and/or

diastolic>90). Finally, we examined models including interactions between 25(OH)D and race. We checked all models for outliers and model fit.

RESULTS

Our final sample included 1,984 and 5,156 non-Hispanic Black and non-Hispanic White participants, respectively, ages 20 and older. Following weighting, this corresponds to 12.2% Blacks within the sample. Table 1 compares the characteristics of these groups. Notably, 61% of Blacks compared to only 11% of Whites had 25(OH)D levels in the lowest quintile, whereas only 2% of Black compared to 25% of Whites had levels in the highest quintiles. Visual inspection of SBP and 25(OH)D levels showed normal distribution of these variables and their error terms and no influential outliers. Explained variance (R^2) for adjusted the models ranged from 20 to 23%. The additional variance explained by 25(OH)D was similar across SBP.

In crude models (no adjustment), participants in the lowest quintile of serum 25(OH)D had SBP that was 5.09 mm Hg higher than those in the highest quintile. In all models, serum 25(OH) D showed statistically significant associations with SBP. In the fully adjusted model, participants in the lowest quintile for 25(OH)D had a mean SBP that was 2.64 mm Hg (95% CIs 2.58-2.70) higher than those in the highest quintile.

Table 2 shows the adjusted effect of serum 25(OH)D on Black-White differences in BP with sequential controls added. The first column shows the difference in BP before adjustment for vitamin D. The second column shows the effect after 25(OH) D was added to the model and the third column shows the percent reduction in the adjusted Black-White BP difference with corresponding 95% confidence intervals (CI).

The attenuation in the Black-White differences varied from 25% to 28% depending on the control variables included. Before any adjustment, the mean difference in BP between Blacks and Whites was 3.3 mm/Hg. In the final model, 25(OH) D accounted for 26% (95% CI 7–46%) of the residual difference in BP between Blacks and Whites. When participants taking BP medications were excluded, the addition of 25(OH)D reduced the effect of race by 39% (95% CI 14–65%).

Results generally consistent in magnitude with the main analysis were observed in supplementary analyses conducted with age subgroups of the sample. In no instance did controlling for the new measure have an appreciable effect on the Black-White difference in SBP (details available from authors). The addition of 25(OH)D to the model resulted in the race disparity being significantly reduced only in the skin type model (32 %; 95% CI 8–57%), the DXA model (48%; 95% CI 22–74%), and social support model (22%; 95% CI 0.1%–43%). In the remaining supplementary models the effects were not statistically significant, though the direction and effect sizes were generally consistent with the presented analyses.

When we restricted the sample to participants with hypertension (N=1,726) and included all covariates, we observed similar results though larger effects. The lowest quintile was associated with statistically significant 6 mm higher SBP. Notably, adjustment for vitamin D status reduced racial differences in mean SBP from a statistically significant 3.2 mm Hg to a non-statistically significant 0.7 mm Hg.

Table 1. Characteristics of Sample by Race

Characteristic	Non-Hispanic Blacks N=1984 Mean or percent (standard error)	Non-Hispanic White N=5156 Mean or percent (standard error)
Systolic blood pressure, mean, mm Hg[a]	124.1 (0.5)	120.8 (0.3)
Demographics		
Age, mean, years[a]	41.8 (0.4)	45.6 (0.3)
Sex [a]		
Male	47.4 (1.0)	51.0 (0.5)
Female	52.7 (1.0)	49.1 (0.5)
SES and Social		
Poverty (%)[a]		
< 100%	21.8 (1.7)	7.9 (0.7)
100–149%	13.9 (1.2)	7.6 (0.6)
150–199%	12.1 (1.1)	8.3 (0.5)
200–299%	17.4 (1.0)	15.3 (0.6)
300% or more	34.8 (1.9)	60.9 1.5)
Education[a]		
Less than high school	26.0 (1.5)	10.8 (0.9)
High school / equivalent	24.8 (1.0)	26.9 (0.8)
More than high school	49.2 (1.4)	62.3 (1.5)
Marital Status[a]		
Married / living as married	47.4 (1.6)	69.7 (0.8)
Single / separated / divorced / widowed	52.6 (1.6)	30.3 (0.8)
Health and Health Care		
Self-rated Health Condition[a]		
Excellent	18.9 (1.1)	22.9 (0.8)
Very Good	25.0 (1.1)	36.2 (0.9)
Good	36.5 (1.1)	29.2 (0.7)
Fair	16.1 (1.2)	9.2 (0.5)
Poor	3.4 (0.5)	2.5 (0.3)
Insurance[a]		
Has health insurance	75.4 (1.2)	85.7 (0.9)
No health insurance	24.6 (1.2)	14.3 (0.9)
Usual source of care		
Yes	86.7 (0.9)	87.2 (0.7)
No	13.3 (0.9)	12.8 (0.7)
Number of BP medications[a]		
0	77.1 (1.1)	79.6 (0.8)
1	12.7 (0.7)	12.5 (0.6)
2	6.4 (0.6)	5.3 (0.3)
3 or more	3.8 (0.5)	2.7 (0.3)
Behavioral		
Body Mass Index (kg/m^2)[a]		
< 20	4.6 (0.6)	5.3 (0.3)
20–<25.5	25.8 (1.3)	33.7 (1.0)
25.5–<30	28.3 (1.0)	30.8 (0.7)
30 +	41.3 (1.4)	30.2 (0.9)
Activity Compared with Others Same Age		
More Active	37.5 (1.3)	37.3 (0.9)
Less Active	21.5 (1.0)	21.0 (0.6)
Same	41.0 (1.1)	41.8 (0.9)
Smoking status[a]		
Current	26.5 (1.5)	26.2 (1.0)
Former	14.2 (0.9)	26.3 (0.8)
Never	59.3 (1.6)	47.5 (1.1)
Serum Cotinine (ng/mL)	81.0 (5.4)	72.1 (3.2)
Alcohol (gm)	4.0 (0.8)	4.2 (0.5)

Table 1. (continued)

Characteristic	Non-Hispanic Blacks N=1984 Mean or percent (standard error)	Non-Hispanic White N=5156 Mean or percent (standard error)
Sodium (mg)	2114.4 (88.6)	2222.0 (55.9)
Potassium (mg)[a]	1602.5 (45.9)	1793.7 (38.6)
Calcium (mg)[a]	466.2 (16.8)	566.4 (16.7)
Biomarkers		
A1c, mean, (%)[a]	5.6 (0.02)	5.4 (0.01)
Albumin, mean, (g/dL)[a]	4.2 (0.01)	4.3 (0.01)
C-Reactive Protein, mean, (mg/dL)[a]	0.5 (0.02)	0.4 (0.01)
Vitamin D (ng/mL)[a]		
1st Quintile (2–15 ng/mL)	60.7 (2.1)	11.0 (0.9)
2nd Quintile (16–20 ng/mL)	20.6 (1.2)	17.8 (0.7)
3 rd Quintile (21–24 ng/mL)	10.0 (1.0)	19.4 (0.7)
4th Quintile (25–30 ng/mL)	6.4 (0.6)	26.3 (0.6)
5th Quintile (31–80 ng/mL)	2.3 (0.3)	25.5 (1.4)
Supplementary Analyses		
Cardiovascular Fitness Level (Treadmill) , mean,	2.2 (0.04)	2.4 (0.03)
Percent body Fat (DXA)	33.2 (0.27)	33.7 (0.23)
Physical Activity Monitor (mean intensity per minute)	337.6 (15.98)	342.7 (9.39)
Skin Type (sun sensitivity)[a]		
Get a severe sunburn with blisters	0.4 (0.1)	3.4 (0.3)
A severe sunburn for a few days with peeling	1.0 (0.3)	13.7 (0.6)
Mildly burned with some tanning	4.2 (0.5)	39.6 (0.9)
Turning darker without a sunburn	28.6 (1.4)	14.6 (0.6)
Nothing would happen in half an hour	65.8 (1.4)	28.8 (1.3)
Social support (Anyone to count for emotional support?) [a]		
Yes	92.9 (1.0)	95.8 (0.4)
No	6.3 (1.0)	3.7 (0.4)
Do not need	0.8 (0.3)	0.6 (0.1)

[a]*Significant difference at the 95% level of confidence*

Other sensitivity analyses revealed consistent findings. These included use of 25(OH)D as a continuous variable, substitution of categorical variables or squared terms for continuous variables (details available from authors). There was no significant interaction between race and 25(OH)D.

DISCUSSION

Given the strong association between Black race and low vitamin D levels and growing evidence that suboptimal vitamin D status may be associated with increased BP, we examined the hypothesis that low serum 25(OH)D levels partly explain racial differences in SBP. Our findings support this hypothesis. In the fully adjusted model, differences in levels explained one quarter of the difference. The effect size was consistent across a variety of covariate controls, suggesting a consistent independent effect of vitamin D. When participants taking BP medications were excluded, the effect of 25(OH)D explained 40% of this disparity.

The finding that vitamin D explains a significant portion of the residual difference in BP between Blacks and Whites is consistent with a previous analysis by Scragg et al. from an earlier sample from NHANES III.[17] Judd et al. reported an inverse association between vitamin D and BP among non-hypertensive Whites, but not among Blacks after adjusting for sex, BMI and season.[16] In contrast to those studies, our study included participants with and without hypertension and controlled for multiple confounders including use of objective measures. Regardless of adjustment, lower serum 25(OH)D levels contributed to disparity in SBP.

BMI is associated with lower vitamin D levels particularly in whites,[29] possibly due sequestering in adipose tissue, decreased sunlight exposure, and disruption of endocrine feedback loops.[30] For this reason, we used objective measures of body fat based on DXA scanning. Including this measure did not appreciably alter our findings. Similarly, differences in diet, particularly calcium, potassium, and sodium have been suggested as potential explanations for racial disparity in hypertension.[31] Yet, dietary differences in these nutrients based on 24-hour dietary recall did not explain racial differences in BP. Vitamin D proved to be among the most powerful and consistent contributors to Black-White differences in BP.

Our findings are consistent with growing evidence that suboptimal vitamin D status is associated with higher BP.[12] While findings from prospective studies regarding the effect of baseline vitamin D on subsequent SBP have been conflicting,[32–34] discrepant findings may reflect differences in control for confounders and statistical power. Some studies may have been too small to detect an effect of the magnitude we observed.

Interventional data are limited. Several small randomized controlled trials of vitamin D supplementation have also yielded conflicting findings.[35] These conflicting findings likely reflect differences in the characteristics of participants, particularly baseline SBP, baseline levels of 25(OH)D, vitamin D doses, and inadequate statistical power. While our study is cross-sectional, it controlled for multiple confounders, was based on a large national sample, and yielded consistent results across different models.

The primary limitation of our findings is that our data are cross-sectional precluding examination of temporal relationships between vitamin D status and BP. While we controlled for many potential confounders across various domains, it remains possible we omitted important confounders. In addition, cross-sectional analyses may not adequately capture cumulative exposure to risk factors over time or effects during critical developmental periods. This applies to factors such as BMI and diet, as well to vitamin D. In addition, dietary recall likely underestimates the effect of diet; 24-hour dietary sodium recall shows low to moderate correlation with 24-hour sodium excretion.[36,38] Other limitations include lack of control for season (not publicly available) and diurnal variation (greater among Whites than Blacks).

Vitamin D did not fully explain the racial difference in BP in the full sample. It is likely that other factors, beyond Vitamin D, such

Table 2. The Adjusted Association of Vitamin D with Black-White Differences in Systolic Blood Pressure (SBP)[a]

Control[b]	Black-White Difference in Mean SBP (mm Hg)		Change in Black-White Difference in SBP Associated with 25(OH)D (95% Confidence Interval)
	Without 25(OH)D (95% Confidence Interval)	With 25(OH)D (95% Confidence Interval)	
None	3.28 (2.31–4.26)	1.69 (0.45–2.93)	67.5% (47.5–87.4)
Age, sex	5.19 (4.28–6.10)	3.91 (2.78–5.03)	24.7% (11.0–38.5)
+SES/Social (% poverty, education and marital status – married/partnered or not)	4.65 (3.63–5.67)	3.32 (2.16–4.48)	28.5% (13.4–43.7)
+Health and health care (self rated health, insurance, regular source of medical care, number of medications)	4.43 (3.42–5.45)	3.19 (2.01–4.36)	28.1% (12.0–44.3)
+ Behavioral risk factors (BMI, physical activity, smoking, cotinine, alcohol, sodium intake, potassium intake, calcium intake)	3.56 (2.50–4.62)	2.56 (1.28–3.84)	28.1% (5.6–50.5)
+Biomarkers (a1c, CRP, albumin)	3.99 (2.91–5.07)	2.94 (1.63–4.24)	26.5% (6.8–46.2)

[a] *Values (differences in SBP in mm Hg) are derived from linear regression models*
[b] *Each of the models sequentially adds the additional controls listed*

as psychosocial stress, medication adherence, and discrimination also contribute to this disparity.[4,38–40] While we were unable to adjust for these factors, we observed similar results following adjustment for social support, a well recognized buffer to psychosocial stress. We observed stronger effects when we excluded participants taking BP medications, suggesting that adherence is unlikely a major confounder. Similarly, we observed stronger effects when we confined the sample to those with hypertension suggesting effects extend to those with clinically relevant SBP.

The association between discrimination and skin color represents a potential confounder. Persons with darker skin (independent of race) have lower educational attainment and experience greater discrimination in the job market.[40–42] However, the relationship between objectively measured skin tone and BP is complex and appears to differ by income.[44–45] Our measure of skin type (i.e. Fitzpatrick score) was relatively crude. It was not significantly associated with SBP, and it attenuated, but did not eliminate the effect of 25(OH)D on the race difference. In summary, our findings are most consistent with the hypothesis that vitamin D represents one piece of the complex puzzle of race and BP. Further study using more refined measures of skin color is needed to tease apart the complex relationship between skin color, psychosocial stress, vitamin D status, and BP.

In contrast to previous studies that excluded persons diagnosed with hypertension[16,17] we included all non-pregnant adults without renal disease with a wider range of SBP. A meta-analysis of 61 prospective studies showed that the proportional difference in the risk vascular-related death associated with a given absolute difference in usual BP is about the same down to at least 115 mm Hg.[21] Hypertension is the most important proximal determinant of disparities in cardiovascular disease.[46] At a population level, seemingly modest Black-White differences in BP represent thousands of excess Black deaths annually from heart disease and stroke.[47] Thus, interventions that appreciably reduce this gap could have a population-wide impact on racial disparities in these outcomes.

Our findings add to the growing body of evidence that low levels of vitamin D among Blacks contribute to cardiovascular disparities. Suboptimal vitamin D has been linked to conditions more prevalent among Blacks including diabetic nephropathy,[48] peripheral vascular disease,[49] kidney disease progressing to renal failure,[50] and cardiovascular mortality.[51] Blacks also have higher rates of endothelial dysfunction and small vessel disease than whites.[52–53] Emerging data suggest that low vitamin D levels are associated with endothelial dysfunction and that correction alleviates this dysfunction.[54–58] A meta-analysis of BP among persons of African ancestry shows a gradient with lowest values among those residing in rural Africa with the greatest UV exposure, intermediate values among those residing in tropical urban areas and less UV exposure due to more indoor work, clothing, and pollution, and the highest rates among persons living in the United States, where UV exposure is the lowest.[59] Together these findings point towards vitamin D deficiency as a potential contributor to higher rates of vascular dysfunction, including hypertension among Blacks living in the United States.

These emerging findings regarding the role of vitamin D in cardiovascular disparities have important implications for addressing racial disparities in cardiovascular morbidity and mortality using a simple downstream intervention.[60] They suggest the possibility of partially mitigating these disparities through oral supplementation with sufficient doses.[61] Thus, there is an urgent need for randomized controlled trials conducted across a range of ages and using various outcomes to rigorously test the hypothesis that vitamin D represents an important contributor to racial disparities in hypertension and cardiovascular conditions.

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