The Association Between Vitamin D, Overweight Status, and Depression: A Retrospective Study

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I was mentored by Mr. Gary J Badger (Biostatistician). He is affiliated with the University of Vermont.

Abstract:

Background: There is a high incidence of vitamin D deficiency in the northeastern region of the United States. There is also a high prevalence of overweight status and depression in the general population. The aim of this study was to assess the relationship between vitamin D deficiency, overweight status, and depression.

Methods: A retrospective analysis was performed on ambulatory patients ≥18 years old who were seen at a local hospital affiliated primary care centers between January 1st, 2016 and December 31st (n=268). The study included both females and non-females. De-identified data was obtained on 25(OH) vitamin D levels, BMI, and PHQ-9 scores. Vitamin D level <20 ng/ml was considered deficient and ≥20 ng/ml was non-deficient. BMI <25 kg/m^2 & ≥25 kg/m^2 represented non-overweight and overweight individuals. PHQ-9 score <10 corresponded to minimal/mild depression and ≥10 corresponded to moderate/severe depression. Patients with prior vitamin D supplementation and conditions leading to vitamin D malabsorption were excluded.

Results: We found a significant association between vitamin D deficiency and overweight status (p= 0.031). We also observed a significant association between vitamin D deficiency and diabetes (p= 0.028). There was no clear association between vitamin D deficiency and hypertension (p= 0.186) or severity of depression (p= 0.405).

Conclusion: These results demonstrate that being overweight may be a risk factor for vitamin D deficiency in the northeastern population of the United States. Our study may form the basis for future prospective analysis assessing the role of vitamin D supplementation in overweight individuals.

Introduction:

Vitamin D is both a dietary nutrient and a hormone our bodies produce. It is a fat-soluble vitamin that has long been known to help the body absorb and retain calcium and phosphorus (*The Nutrition Source*, 2021). There is a high incidence of low vitamin D blood concentrations in the northeastern region of the United States (Huotari, 2008). Further, vitamin D deficiency constitutes as a worldwide epidemiological problem (Duan et al., 2020). In addition, there is a high prevalence of depression and obesity within the general population (Blasco, 2020).

Obese individuals tend to have low plasma levels of 25-OH Vitamin D (Wortsman, 2000). This may be due to their avoidance behavior of sunlight. (Wortsman, 2000). The clearance of Vitamin D is higher possibly with enhanced uptake by the fatty tissue (Wortsman, 2000). It may also be related to higher concentrations of 1-25-(OH)2 D which exerts a negative feedback on the liver production of the active form (Wortsman, 2000). Vitamin D deficiency may increase parathyroid hormone levels and promote a greater inflow of calcium into adipocytes. Another theory is that vitamin D deficiency accelerates the differentiation of preadipocytes into adipocytes. Obesity risk could thus be increased either directly or indirectly. The directly increased risk would

occur by increased adipogenesis and indirectly increased risk by modulated inflammation, oxidative stress, metabolism, or gene regulation (Duan et al., 2020).

Similarly, levels of the active form of vitamin D have been shown to be lower in people with both minor and major depression (Hoogendijk, 2008). Depression is associated with increased morbidity and mortality, because of increased risk for stroke, cardiovascular events, and suicide. It also has economic and social consequences, such as decreased productivity and increased healthcare utilization costs (Menon et al., 2020). The mechanism whereby vitamin D may be associated with mental disorders is not clearly understood. There are vitamin D receptors in the hypothalamus, which may be important in neuroendocrine functioning (Eyles et al., 2005). Some investigators have reported that vitamin D is important for brain development (Eyles et al., 2008). There has also been a proposed modulatory role between depression and inflammation. Vitamin D and depression may by related through an immune-modulatory mechanism (Duan et al., 2020). This research was designed to investigate the relationship between deficiency of vitamin D, obesity, and depression. We proposed that vitamin D deficiency was associated with overweight status and moderate to severe depression in a northeastern population in the United States.

Methods:

This research was approved by the Institutional Review Board of Glens Falls Hospital, Glens Falls, New York, USA. A retrospective study was performed on ambulatory patients seen at Glens Falls Hospital-affiliated primary care centers from January 1st, 2016 to December 31st, 2021. De-identified data was requested on patients 18 years of age or older in whom information was available on 25(OH) vitamin D levels, BMI, and PHQ-9 scores. The study included both

females (n=177) and non-females (n=91). The majority of the study participants were white and non-hispanic (n=233).

The total number of patients screened was 58,243. Three thousand one hundred thirty-eight. patients were less than 18 years old and were excluded. We excluded patients with a diagnosis of chronic pancreatitis (n=46), celiac disease (n=320), Crohn disease (n=357), cystic fibrosis (n=13), and ileocecal resection (n=0). All participants with prior vitamin D supplementation were also excluded (n=15,114). 39,261 adults met all of the inclusion criteria. Of these individuals, 38,993 were excluded sue to missing values on PHQ-9 and/or BMI (32,094 patients missing both BMI and PHQ-9, 40 missing only BMI and 6,859 missing only PHQ-9). Hence, a total of 268 patients were available for analyses.

Patients were stratified according to age, sex, and race. Information on comorbidities including diabetes and hypertension was obtained because these are potential confounding factors (Table 1). Patients were categorized based on BMI: <25 kg/m^2 & ≥ 25 kg/m^2 representing non-overweight and overweight individuals respectively. PHQ-9 score <10 corresponded to minimal/mild depression and ≥ 10 corresponded to moderate/severe depression. This dichotomization of the PHQ-9 has been demonstrated to have good sensitivity (88%) and specificity (88%) for the presence or absence of major depression based on DSM-IV diagnostic criteria. Vitamin D level <20 ng/ml was considered deficient and ≥ 20 ng/ml was non-deficient. Chi square tests were used to examine the associations between demographic characteristics, confounders, and study variables. Odds ratios and their associated 95% confidence intervals were also computed. Statistical analyses were computed using SAS analytics software (SAS Institute, Cary, NC).

Table 1. Characteristics of cohort (N=268)

Characteristic	No. (%) except age
Demographics	
Sex	
Female	177 (66)
Non-Female	91 (34)
Race/Ethnic Origin	
White, Non-hispanic	233 (88)
Other	35 (12)
Age, mean ± SD	43 ± 17
Comorbidities	
Hypertension	
Yes	45 (17)
No	223 (83)
Diabetes	
Yes	46 (17)
No	222 (83)
Study Variables	
Vitamin D Status	
Deficient[a]	96 (36)
Non-Deficient[b]	172 (64)
Overweight[c]	
Yes	132 (49)
No	136 (51)
Depression[d]	
Yes	37 (14)
No	231 (86)

[a] Deficient=Vitamin D <20 ng/ml; [b] Non-deficient=Vitamin D ≥20 ng/ml; [c] Based on BMI Yes=BMI ≥25 kg/m^2, No=BMI <25 kg/m^2; [d] Based on the PHQ-9 scale Yes=Moderate/Severe Depression (PHQ-9 ≥ 10) No=Minimal/Mild Depression (PHQ-9 <10)

Results:

The univariate analyses revealed no significant association between a subject's sex, age, and vitamin D levels. However, these data indicate that females were 30 percent more likely to be vitamin D deficient than males. A 5-year increase in age decreases the odds of being vitamin D deficient by 2 percent (Table 2). The analysis also included comorbidities (Hypertension and Diabetes) and study variables (Overweight Status and Depression). Patients with hypertension had 55 percent higher odds of being vitamin D deficient, this relationship was not significant ($p= 0.186$). In contrast, there was an association between diabetes and vitamin D deficiency. Patients with diabetes were more likely to have low vitamin D levels ($p= 0.028$). If a patient had diabetes, they were about twice as likely to be vitamin D deficient. Finally, there was a significant association between overweight status and vitamin D deficiency ($p= 0.031$). Forty percent of the overweight patients were overweight and vitamin D deficient versus 25 percent who were non-overweight (Figure 1). An overweight patient is nearly twice the odds of being deficient compared to a non-overweight person. A moderate to severely depressed person had 37 percent greater odds of having a vitamin D deficiency than a minimal to mildly depressed person. Nonetheless, we did not find a significant association between vitamin D levels and moderate to severe depression. 37 percent of the patients with moderate to severe depression had vitamin D deficiency versus 30 percent with minimal to mild depression who were vitamin D deficient (Figure 2).

Table 2. Vitamin D Status by Characteristics of Cohort (n=268)

	% Deficient[a] (n)	Odds Ratios (95% CI[b])	p-value[c]
Demographics			
Sex			
Female	38 (67)	1.30 (0.76 to 2.22)	0.333
Non-Female (reference)	32 (29)		
Age (per 5 year increase)	N/A	0.98 (0.92 to 1.06)	0.693
Comorbidities			
Hypertension			
Yes	44 (20)	1.55 (0.81 to 2.96)	0.186
No (reference)	34 (76)		
Diabetes			
Yes	50 (23)	2.04 (1.07 to 3.88)	**0.028**
No (reference)	33 (73)		
Study Variables			
Overweight[d]			
Yes	40 (79)	1.96 (1.06 to 3.63)	**0.031**
No (reference)	25 (17)		
Depression[e]			
Yes	37 (85)	1.37 (0.65 to 2.93)	0.405
No (reference)	30 (11)		

[a] Deficient=Vitamin D <20 ng/ml; [b] CI= Confidence interval; [c] Based on chi-square test; [d] Based on BMI Yes=BMI ≥25 kg/m^2, No=BMI <25 kg/m^2; [e] Based on the PHQ-9 scale, Yes=Moderate/Severe Depression (PHQ-9 ≥ 10) No=Minimal/Mild Depression (PHQ-9 <10)

Figure 1.

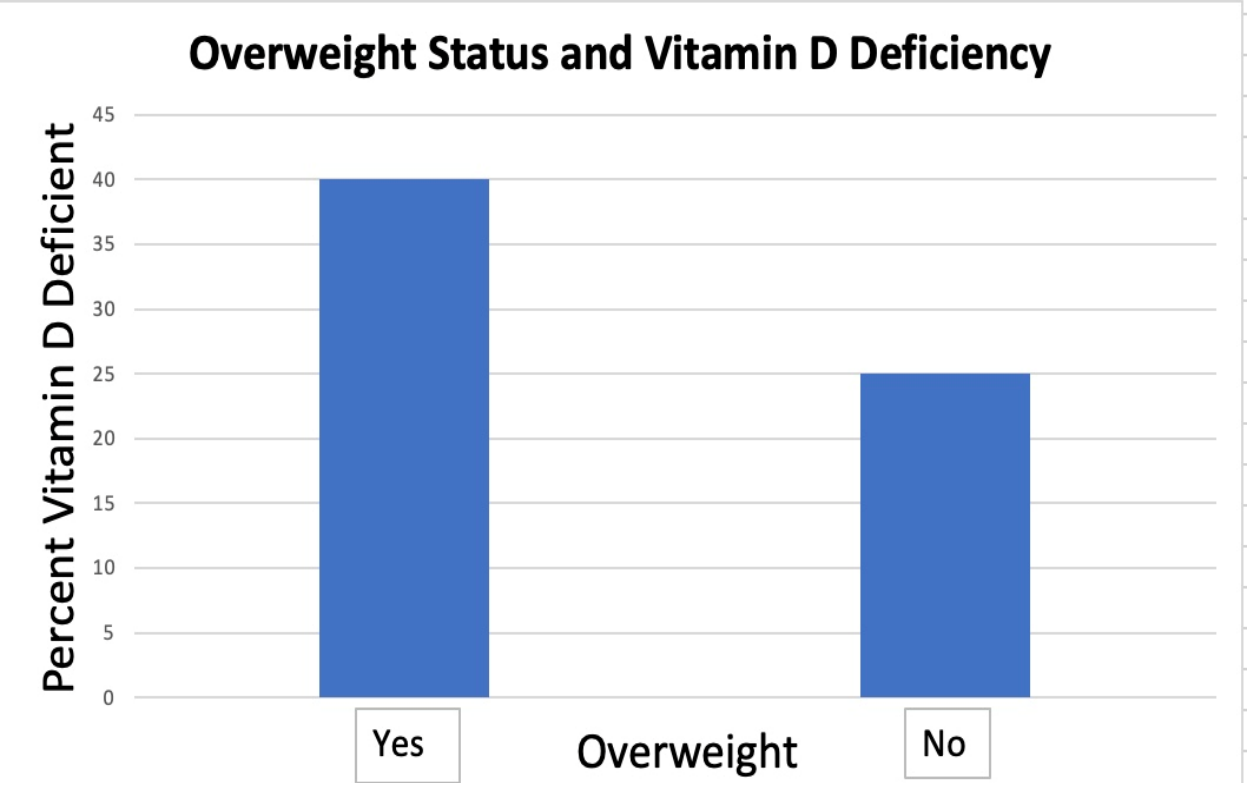
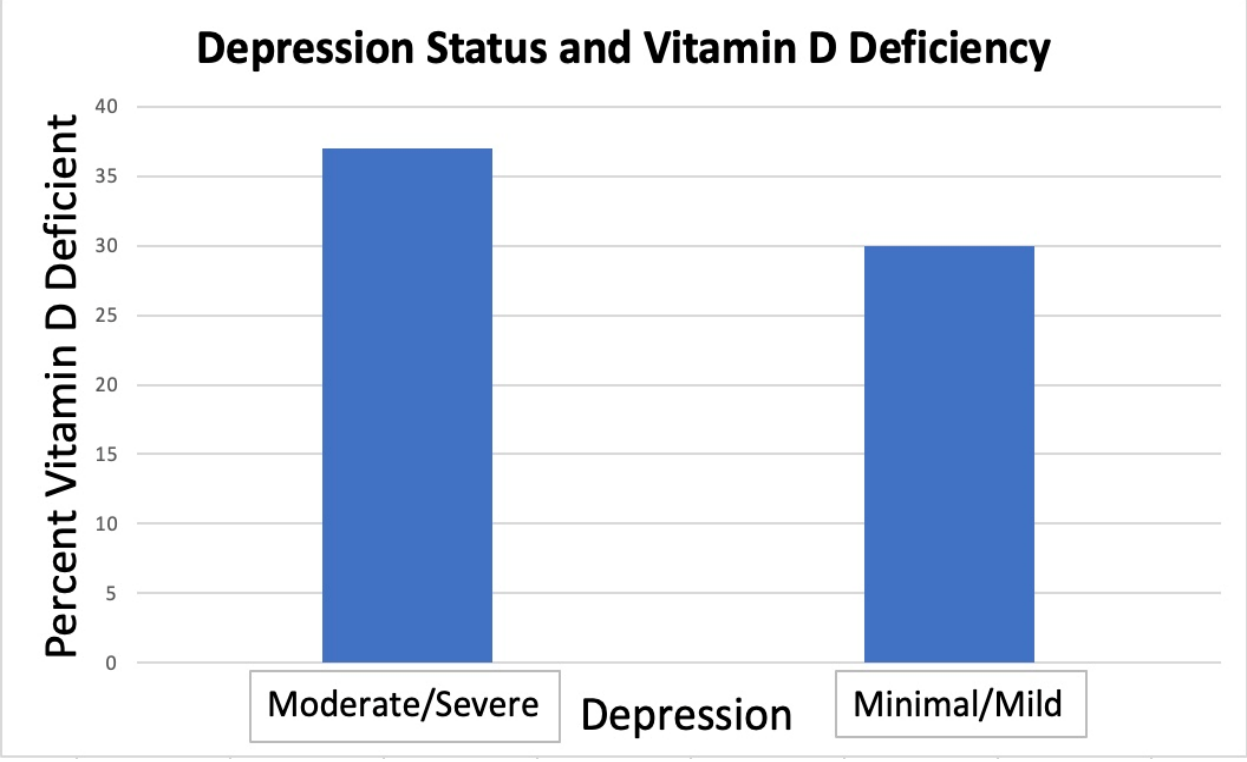


Figure 2.



Investigating the Confound:

It is known that the more excess weight you have, the more resistant your muscle and tissue cells become to your own insulin hormone (Understanding excess weight and its role in type 2 diabetes). It could be postulated that diabetes could disturb the direct relationship shown by the statistically significant p-value for overweight status and vitamin D deficiency. Therefore, an investigation of this potential confound was conducted. Out of those that were not diabetic, 72 percent were overweight. Out of those that were diabetic, 87 percent were overweight (Figure 3). Thus, there were more overweight patients in the diabetic population than in the nondiabetic population. Of those that were non-overweight and nondiabetic, 23 percent were vitamin D deficient. Contrarily, of those that were overweight and nondiabetic, there was an increased percentage, of 37 percent, that were vitamin D deficient (Figure 4). When compared to the non-overweight and nondiabetic group, the overweight and nondiabetic group had double the odds ratio of being vitamin D deficient. Thus, in an isolated population of nondiabetic participants, there was an increased odds of being vitamin D deficient if one was overweight (Table 3). The odds ratio of being vitamin D deficient given someone was overweight and diabetic was 3.43 (Table 3). Out of those that were overweight and diabetic, 50 percent of vitamin D deficient patients were vitamin D deficient (Figure 4). This was the highest percentage of vitamin D deficiency between each of the groups when excluding the non-overweight and diabetic group due to an insufficient sample size of 6. This shows the compounded effect of being both overweight and diabetic when juxtaposed with being neither. The p-value, using the chi-square test, of the combined variable between overweight status and diabetes status was 0.032, thus establishing significance (Table 3).

Figure 3.

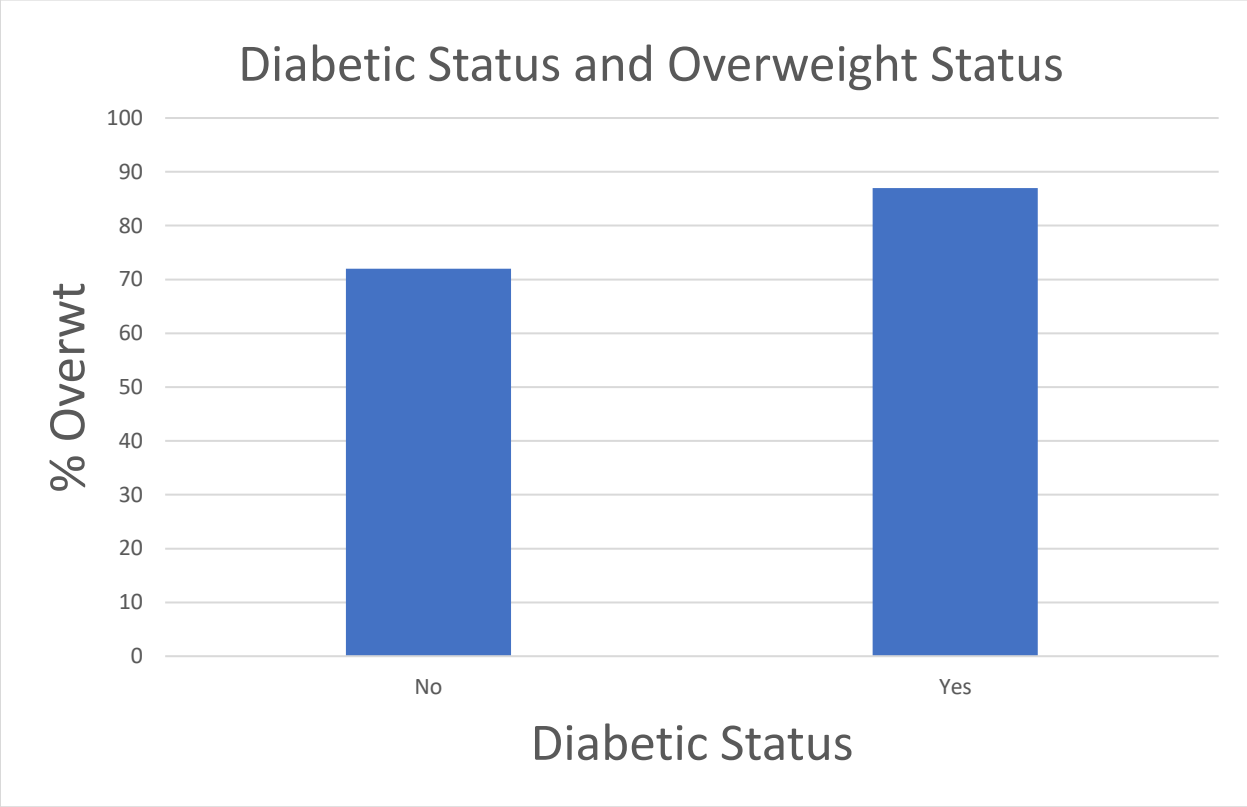

Diabetic Status and Overweight Status
% Overwt
100
90
80
70
60
50
40
30
20
10
0
No
Yes
Diabetic Status

Figure 4.

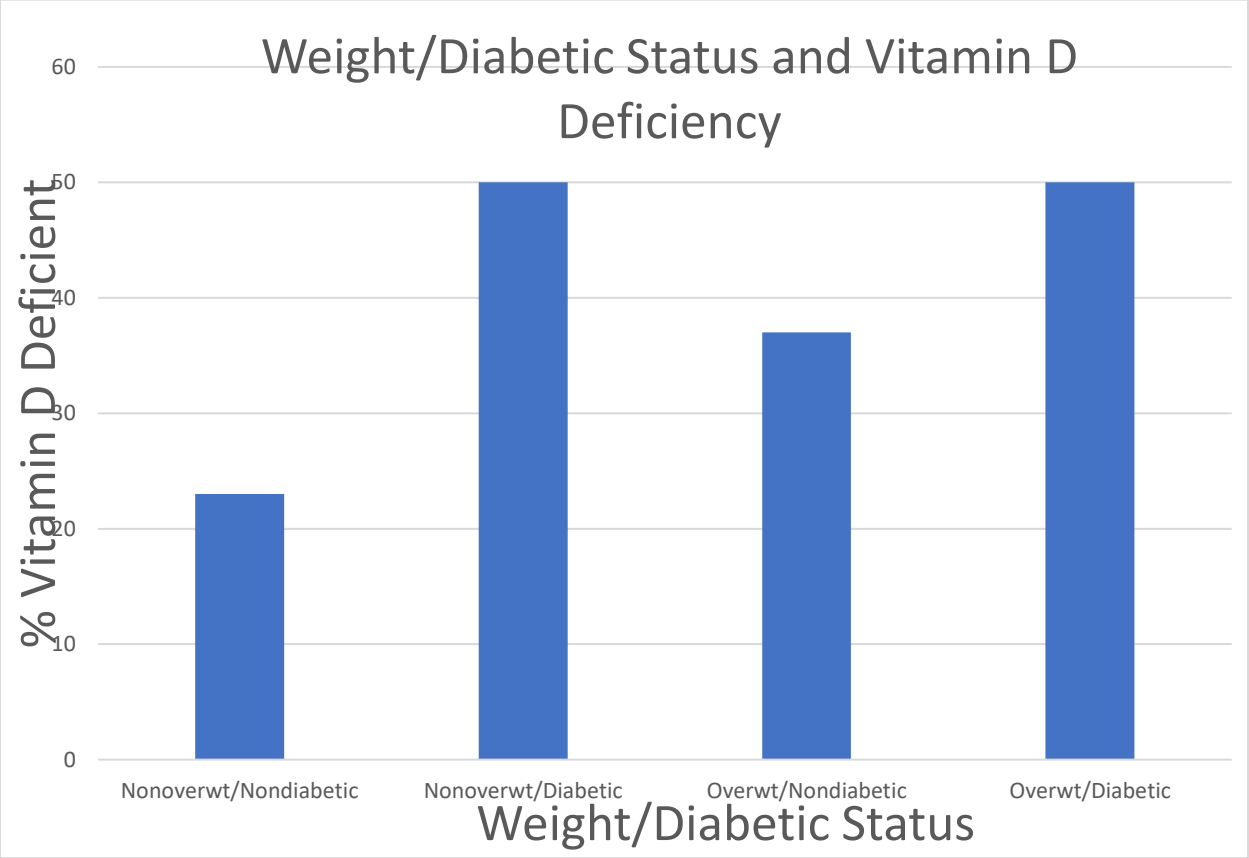


Table 3. Vitamin D Deficiency by Weight/Diabetes

			% Deficient[a] (n)	Odds Ratios (95% CI[b])	p-value[c]
Study Variables					
Overweight[d]	Diabetes				
No	No	(reference)	23 (14)		**0.032**
No	Yes		50 (3)	3.43 (0.62 to 18.9)	
Yes	No		37 (59)	2.00 (1.02 to 3.94)	
Yes	Yes		50 (20)	3.43 (1.45 to 8.10)	

[a] Deficient=Vitamin D <20 ng/ml; [b] CI= Confidence interval; [c] Based on chi-square test; [d] Based on BMI Yes=BMI ≥25 kg/m^2, No=BMI <25 kg/m^2

Discussion:

We found a statistically significant association between vitamin D deficiency and diabetes. In addition, there was a statistically significant association between vitamin D deficiency and overweight status. Eleven percent of the United States population, or 37 million people, have diabetes. There is a close link between obesity and type 2 diabetes. There is a seven times greater risk of diabetes in obese people compared to those of healthy weight, with a threefold increase in risk for overweight people (England, 2014). One possible explanation for our results is that diabetic individuals are more likely to be overweight. Hence, diabetes may be a confounding factor. Nearly half of the adults in the United States (47%, or 116 million) have hypertension (2022). Hypertension prevalence also increased with weight status (normal weight: 31%, overweight: 69%) (Stierman & Afful). Regardless, we did not find a significant association between hypertension and vitamin D deficiency. It is conceivable that several hypertensive individuals in our dataset were not overweight.

The PHQ-9 is a nine-item self-report instrument that was developed for use in medical settings (Kroenke et al., 2001). The questionnaire is administered in doctor's offices during routine checkups and to evaluate mental health. There was no significant association between depression and vitamin D deficiency. A plausible explanation for this is that the individuals who had PHQ-9 scores available had a higher frequency of depression and patients without depression were underrepresented. The lack of representation of minimal to mildly depressed patients may be indicative of a selection bias. It is well known that restricting the range of a variable makes it more difficult to show a relationship with another variables. It was important that the subjects did not have malabsorption of vitamin D and that their levels were naturally produced. The deletion of patients who had a history of Vit D supplements may have filtered out those that originally had

low levels thus creating additional selection bias and taking out some patients in the lower tail of the distribution making it more difficult to find a relationship between your variables of interest. My research will help to facilitate larger-scale studies and potentially encourage screening for low vitamin D in obese and depressed populations.

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