

# The role of body weight in response to vitamin D repletion therapy: a retrospective study



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## ABSTRACT

**Introduction:** In recent years there has been increasing recognition that vitamin D plays an essential role in health maintenance and prevention of disease. Vitamin D is important in cell differentiation and apoptosis, and there are vitamin D receptors in tissues throughout the body, including muscle, brain, breast, prostate, colon and immunoregulatory cells.

Studies show that approximately 36% of otherwise healthy young adults and up to 57% of general medicine inpatients in the United States are either vitamin D insufficient or deficient. Physicians have begun to address this problem with vitamin D supplementation. Obesity is known to be a risk factor for vitamin D insufficiency, partly because vitamin D is fat-soluble and is stored in adipose tissue. In this study we hypothesized that dose response to a standardized vitamin D supplementation regimen would be affected by Body Mass Index.

**Methods:** We did a retrospective review of charts of all patients seen at the Mercy Family Health Center Osteoporosis Clinic between May 2007 and September 2009. Patients with vitamin D deficiency, insufficiency and borderline insufficiency (25-hydroxy vitamin D levels < 38 ng/ml) were treated with 8 weekly doses of vitamin D 2 (ergocalciferol) 50 000 IU. Follow up vitamin D serum levels were obtained at the end of the treatment period. We assumed patients began treatment within one week after the prescription was provided and that patients who returned for repeat vitamin D levels had completed the regimen as prescribed. Patients were included only if repeat vitamin D levels had been obtained within 6 weeks after completion of the regimen. The difference between vitamin D levels before and after treatment was used as an indicator of dose response. Using a linear regression model we accessed the relationship between dose response of vitamin D vs. Body Mass Index (calculated for all patients at the initial visit).

**Results:** There were over 140 charts. Twenty patients met the inclusion criteria. All were female; 16 were African American and 4 were Caucasian; mean age was 63 years; mean BMI was 36, SD=12. Mean vitamin D level before treatment was 20.8 ng/ml. Vitamin D levels increased after treatment in 19 out of 20 patients. In a linear regression model we obtained a slope of -0.54, 95% confidence interval,  $r^2=0.21$ ,  $p<0.0005$  suggesting a negative dose response trend in relation to BMI. Correlation coefficient was -0.460.

**Conclusions:** In our patient group we found a statistically significant inverse relationship between dose response to vitamin D supplementation and BMI. Obese individuals may require higher doses of vitamin D to achieve sufficient serum levels. Based on the results of this pilot study we plan to further investigate this question in a larger prospective trial.



## INTRODUCTION

- Vitamin D plays an essential role in health maintenance and disease prevention. It is important in calcium metabolism, cell differentiation and apoptosis, with vitamin D receptors found throughout the body [1, 2]
- Approximately 36% of otherwise healthy young adults and up to 57% of general medicine inpatients in the United States are either Vitamin D insufficient or deficient. [3]
- Obesity is known to be a risk factor for vitamin D insufficiency. [1,4]
- We hypothesized that dose response to a standardized vitamin D supplementation regimen would be affected by Body Mass Index.

## METHODS

### Study Design

Retrospective review of charts, pilot clinical study

### Patient Population

Patients seen at the Mercy Family Health Center Osteoporosis Clinic between May 2007 and September 2009

### Inclusion Criteria

Vitamin D deficiency, insufficiency and borderline insufficiency (25-hydroxy vitamin D levels < 38 mmol/L)

Treatment with 8 weekly doses of Vitamin D 2 (ergocalciferol) 50 000 IU

Repeat vitamin D levels within 6 weeks after completion of the regimen

### Data Variables

Mathematical difference between vitamin D levels before and after treatment, BMI at the time of initial testing

### Statistics

Linear regression model, ANOVA, analysis of correlation.

Software used: Microsoft Excel

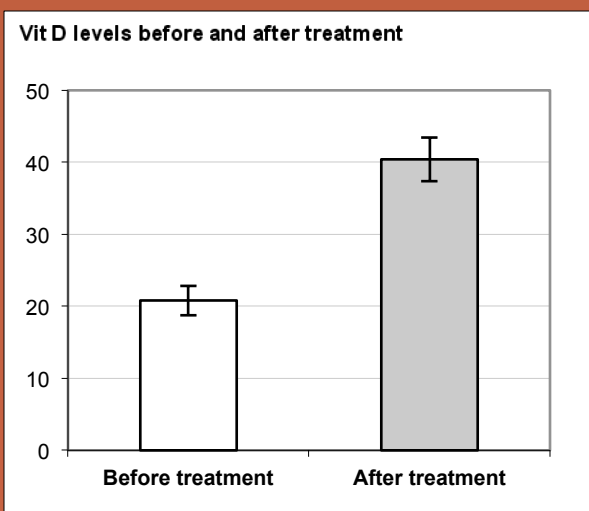
### Assumptions

We assumed patients began treatment within one week after the prescription was provided and that patients who returned for repeat vitamin D levels had completed the regimen as prescribed.

## RESULTS

### Demographics

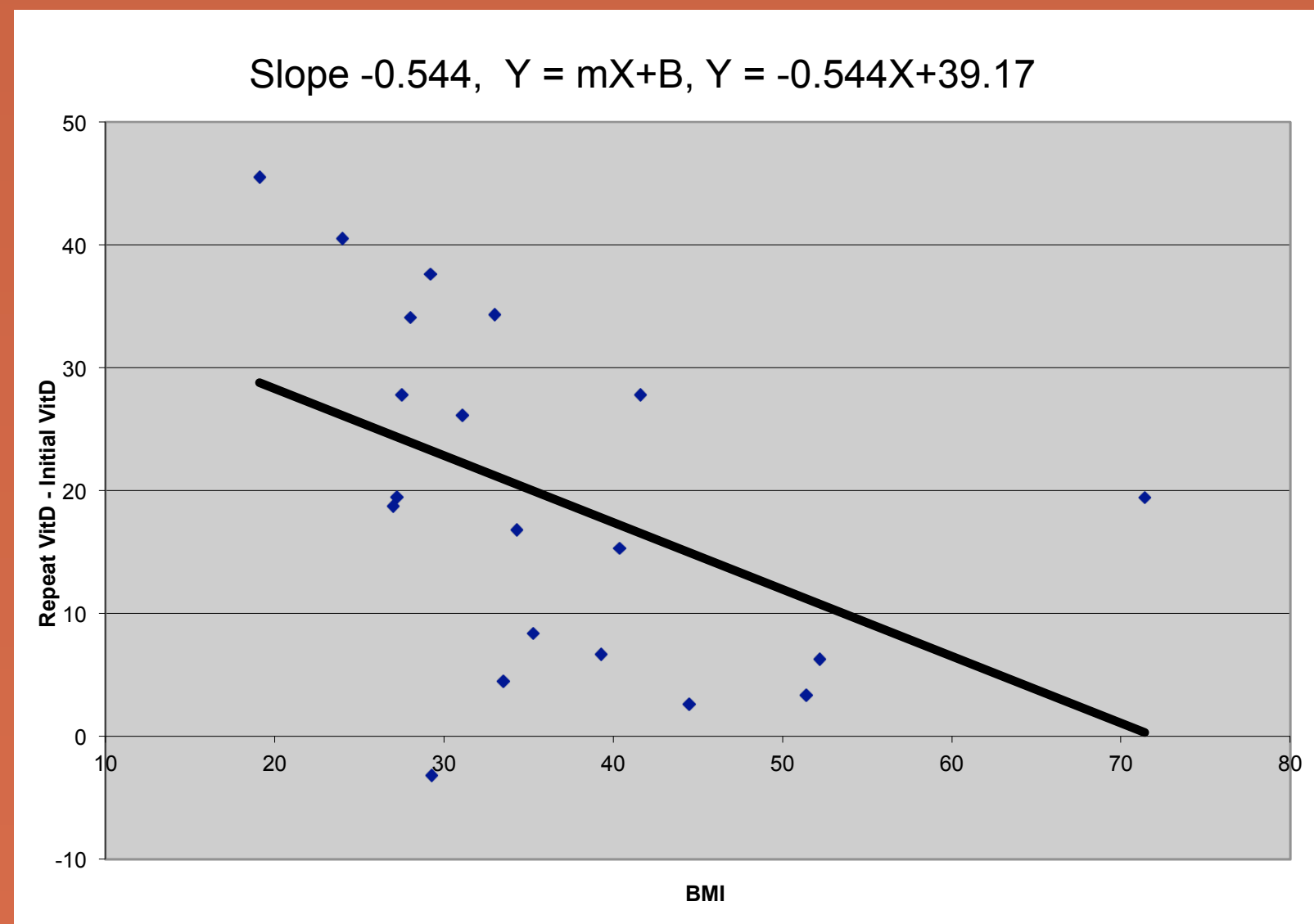
Total number of patients	n=20
Mean Age at the time of initial testing	63 (SD 12)
Sex	100% female
Race	16 African American 4 White
Mean BMI	36 (SD 12)



➤ Vitamin D levels increased after treatment in 19 out of 20 patients:

➤ Mean vitamin D level before treatment was 20.8 ng/ml, after treatment – 41.0 ng/ml

### The relationship between BMI and response to Vitamin D repletion: A linear regression model



	Coefficients	Standard Error	t Stat	P-value	Lower 95%	Upper 95%	Lower 95.0%	Upper 95.0%
Intercept	39.17808939	9.351609276	4.189448921	0.000550984	19.53108738	58.8250914	19.53108738	58.8250914
X Variable 1	-0.54436506	0.24723495	-2.201812732	0.040960334	-1.063786414	-0.024943708	-1.063786414	-0.024943708
Regression Statistics								
Multiple R	0.460634519							
R Square	0.21219416							
Adjusted R Square	0.168416614							
Standard Error	12.95252906							
Observations	20							

➤ In our linear regression model , BMI accounts for 21% of variation in response to vitamin D repletion

➤ Correlation coefficient between Vitamin D repletion levels and BMI was – 0.460.

## DISCUSSION

There have been several studies in recent years regarding vitamin D deficiency in obesity, however the issue of vitamin D repletion in relationship to BMI has not yet been widely addressed.

New investigations are coming out, suggesting that obese individuals may require higher doses of vitamin D to achieve sufficient serum levels [4, 5]. This could potentially change therapeutic approach to vitamin D repletion.

The variation in vitamin D levels is multifactorial , and could depend on age, race, diet, time of year, renal and liver function , medications [1,2]. In our study BMI accounted for 21% in variation of vitamin D response, which is a significant share of the multifactorial array. In the linear regression model, for every increase in BMI of 1 there was a decrease in response to vitamin D repletion by 0.544 ng/ml, confidence interval 95%,  $p<0.001$ . Limitations included small sample size and retrospective study design.

Results of this pilot study are encouraging, and we plan to further investigate this question in a larger prospective trial.



## REFERENCES

1. Holick, MF. Vitamin D Deficiency. NEJM 357;3 266-281, 2007
2. Heaney, RP. Vitamin D in health and Disease. Clin J Am Soc Nephrol 3: 1535-1541, 2008
3. Holick, MF. High prevalence of vitamin D inadequacy and implications for health. Mayo Clin Proc. 81(3):353-73, 2006
4. Rajakumar K, Fernstrom JD, Holick MF, Janosky JE, Greenspan SL. Vitamin D status and response to vitamin D3 in obese vs. non-obese African American children. Obesity16(1): 90-95, 2008
5. Lee P., Greenfield JR, Seibel MJ, Eisman JA, Center JR. Adequacy of vitamin D replacement in severe deficiency is dependent on body mass index. Am J Med 122(11):1058-1060, 2009

Images:

- Vitamin D Metabolism Scheme: adapted from Deeb, KK, Trump, DL & Johnson CS. Vitamin D signaling pathways in cancer: potential for anticancer therapeutics. Nature Reviews Cancer 7 684-700, 2007 © Nature Reviews
- Tabsl. Alengo, gettyimages.com
- Large man and small girl on unbalanced plank. Martin Barraud, gettyimages.com

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