

# Vitamin D deficiency to ill health essay

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**Abbreviations:** CVD, cardiovascular diseases; HF, heart failure; RHI, reactive hyperaemia index; FMD, flow mediated dilation; CRC, colorectal cancer

## Introduction

During the last decade, vitamin D has been linked to a very wide range of diseases with sufficient evidence emerging for fractures, cancer, cardiovascular diseases (CVD) and from altered immune function (Scragg, 2011). Vitamin D is synthesised primarily from skin through the action of UVB sunlight on inactive precursors but can also be obtained from dietary sources. Focusing on both CVD and cancer, being in the top ten causes of death in the world (WHO, 2011), this essay summarises the findings of five papers on the relationship of vitamin D deficiency to both aspects of disease.<sup>1-3</sup>

## Cardiovascular disease

**Vitamin D deficiency is a predictor of reduced survival in patients with heart failure; vitamin d supplementation improves outcome:** Gotsman et al. analysed the data from years 2006 to 2010 for 49,834 members belonging to a health maintenance organisation (HMO) in Israel. Defining optimal and deficient vitamin D 25(OH)D levels as <75nmol/L and <25nmol/L respectively, the team found that the median for the whole cohort was well below optimal levels with prevalence of vitamin D deficiency higher in patients with heart failure (HF). It was also found that treatment with vitamin D supplements for patients with HF, reduced mortality. Due to the large sample size, the team was able to observe population trends of which they also found a definite seasonal variation in vitamin D levels with levels increased in summer and reduced in winter. I chose this study because it allowed 25(OH)D to be singled out as a predictor for mortality in HF.<sup>4-9</sup> This study is limited, however, as it did not include the mortality data nor its incidence and only used single measure of 25(OH)D.

**Vitamin D deficiency is associated with increased il-17 and tnfa levels in patients with chronic heart failure:** milovanovic et al. studied 40 patients to investigate how vitamin D levels affects IL-17 and TNF $\alpha$  status. I chose this study because it showed that even in areas with higher solar radiation, the prevalence of vitamin D deficiency does not change and furthermore, it illustrates a possibly underlying mechanism by which vitamin D deficiency may contribute to the pathogenesis of CVD. The study found significantly lower 25(OH)D with increased TNF $\alpha$  and IL-17 in patients with CHF secondary to hypertension when compared to patients with CHF secondary to coronary disease. Classifying insufficient and deficient 25(OH)D levels as 51 – 74 nmol/l and <50 nmol/l respectively, the study is also found out that 25(OH)D deficient patients had higher New York Heart Association (NYHA) functional classification scores (0 – 3, with 3 being severe limitations in physical activities) being compared to patients who are 25(OH)D insufficient as shown in Figure. Error: Reference source not found Figure NYHA scores in VD deficient and

insufficient CHF patients. NYHA class was determined by observing each patient at rest, dressing, walking and climbing.

**Vitamin D status is associated with arterial stiffness and vascular dysfunction in health humans:** Al Mheid et al. recruited 554 healthy participants and tested their arterial stiffness (AIX), flow-mediated dilation (FMD) and reactive hyperaemia index (RHI) alongside with vitamin D levels. (Al Mheid et al., 2011) Similar to Gotsman et al, the mean 25(OH)D levels was well below optimal levels and 47% of the cohort has vitamin D deficiency after the study defined it as <30ng/ml. It was also seen that a the number of risk factors for CVD increases with a decreasing level of mean 25(OH)D serum levels. Lowered levels of 25(OH)D was found to be independently associated with higher AIX, lower FMD and RHI. I chose this study because it associates vitamin D status with a variety of cardiovascular risk factors and thus allowing potential insight in to the underlying mechanism vitamin D's protective effects.<sup>10-13</sup> This study, however, is also limited because it did not take into account other factors such as physical activity which may account for the observations seen.

## Cancer

**Instrumental variable estimation of the causal effect of plasma 25-hydroxy-vitamin d on colorectal cancer risk: a mendelian randomization analysis:** Theodoratou et al. aimed to 'set out to evaluate the relationship between colorectal cancer (CRC), plasma 25(OH)D levels and genotype at 4 genetic loci tagging genes involved in vitamin D metabolism' by 'aiming to recruiting all incident cases of adenocarcinoma of colorectum presenting to surgical units within Scotland' and drew randomly from a population based register for the controls. (Theodoratou et al., 2012) A total of 2001 cases and 2237 controls were recruited in this way.<sup>14</sup> The authors found that CRC risk was inversely associated with levels of 25(OH)D even after adjustment for age and sex.<sup>15-19</sup> I chose this study as links vitamin D deficiency to another aspect of ill health and also the possible underlying mechanism by which vitamin D deficiency is associated with CRC.

This study, however, is limited in its contribution as it has almost all white people as participants and thus may not be generalizable.

**Vitamin D status at breast cancer diagnosis: correlation with tumor characteristics, disease outcome, and genetic determinants of vitamin d insufficiency:** Hatse et al. in 2012, analysed data on 1800 breast cancer patients from Leuven Multidisciplinary Breast Center in attempt to explore the possible relationship between relapse of breast cancer, survival and tumour characteristics between serum 25(OH) D and if genetic variation in vitamin D-related genes have an effect. The team observed that serum 25(OH)D had an inverse relationship with tumour size but no relation with other tumour characteristics. The team also found that serum 25(OH)D has a similar relationship with the survival rates especially in postmenopausal patients. It is also noteworthy that the team observed marked decrease in 25(OH) D levels with increase in age. The team, however, found that genetic variation of vitamin D pathways plays no role in the pathogenesis of breast cancer. This study was chosen because it able to accurately analyse its study population with the well documented causes of death which led to a further insight on how vitamin D deficiency affects pre and postmenopausal female breast cancer patients.

### Critical summation

Coming to conclusion, all the studies agree that vitamin D deficiency is highly prevalent and contribute to a growing body of evidence towards linking vitamin D deficiency levels and ill health, which in this essay focuses on cardiovascular disease and cancer. Going back to the title, all the articles found an association between vitamin D deficiency and the disease studied though it cannot be concluded that vitamin D deficiency is indeed causative of such diseases. More research is warranted by these to uncover the exact mechanism underlying these associations. Considering the high prevalence of vitamin deficiency and the growing body of evidences that links it to diseases, it may be sufficient to form a basis for population wide intervention. Since vitamin D is mainly and easily acquired through the skin under exposure to UVb sunlight, such recommendation may yet be another reason for an active and health lifestyle.<sup>20-29</sup>

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### Conflicts of interest

Author declares there are no conflicts of interest.

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