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**Impact of Dietary Supplements: Magnesium, Niacin and Vitamin D**

**on Cardiovascular Health**

**Abstract:**

People are encouraged to take dietary supplements for improving cardiovascular health, yet there is a lack of evidence that supports this association. A cross sectional study was conducted to determine the effects of total supplement intake,magnesium, niacin and vitamin D on myocardial infarction and coronary heart disease among U.S. adults. Data from the study population was obtained from the 2013-2014 NHANES data set. Following the adjustment for age, race, sex, smoking, sodium intake, BMI, and prescription for hypertension, vitamin D intake was associated with a decreased odds of coronary heart disease. Apart from this, there was no other association between the exposures and outcomes. These findings highlight the need for a larger sample size, measurement of the temporal relationship, and a better survey design in future studies.

**Introduction/Background:**

Lifestyle choices, such as diet, play a fundamental role in cardiovascular health. Often, people will opt to receive their daily nutrient intake via supplements rather than through a balanced diet. At the core of a balanced diet are foods that are low in sugars and fats, high in minerals, vitamins, and other nutrients.10 In the United States, there appears to be an increase in the use of dietary supplements with approximately half of American adults using supplements .1 Dietary supplements, taken daily, can be used to treat nutritional deficiencies and health disorders. These supplements are advertised as ways to improve cardiovascular health, despite efficacy and safety information of dietary supplements claiming otherwise. Compared to prescribed medications, dietary supplements are not as strictly regulated and are not required to pass rigorous standards before becoming accessible to the public. Surprisingly however, dietary supplements contribute to approximately 23,000 emergency room visits every year in the United States.1

Past studies have been conducted to further assess the relationship between vitamin intake and cardiovascular health. In a prospective cohort-study conducted by Rimm et. al (1993), 51,529 male health professionals completed a detailed questionnaire on their medical history and present diet regimen. In this investigation, it was discovered that vitamin E was protective against coronary disease after adjusting for fiber, smoking, physical activity, and aspirin use. The Israeli Heart Association similarly conducted a comprehensive literature search on nutrition supplements and cardiovascular disease. Unlike the Rimm et. al study, these randomized clinical trials did not support the role of vitamins as a prevention of cardiovascular disease. Furthermore, there was an increased risk of disease among participants with atherosclerosis after taking vitamin A and E. A meta-analysis was conducted using four of the trials in the Israeli Heart Association in which study participants were followed for 1, 5, or 7 years. The meta-analysis reported the effects of vitamin D supplementation on cardiovascular disease. Consequently, a well-established inverse relationship between vitamin D and bone health was discovered. The study found that vitamin D did not have a statistically significant effect on myocardial infarction, stroke, depression or other cardiac and cerebrovascular outcomes. 6

Niacin, also known as vitamin B3, is believed to reduce cholesterol, triglycerides, low density lipoproteins, while increasing high-density lipoproteins. An experimental study funded by the National Heart, Lung and Blood Institute and Abbott Laboratories randomly assigned 3,414 patients with cardiovascular disease to receive either niacin supplements or a placebo. Patients who took niacin were less likely to experience morbidity due to cardiovascular disease. Among patients who had received niacin, no clinical benefit was observed on LDL levels. However, significant improvements in HDL, cholesterol and triglyceride levels were witnessed. 3

In an experimental study conducted by Ceremuzyński et. al, magnesium supplements were shown to regulate the heartbeats of patients with hypomagnesemia. Yet, the effects of magnesium on cardiovascular conditions remain inconclusive.4

Magnesium can be eaten naturally through leafy green vegetables, nuts, avocados, whole grains, legumes, chocolate and seafood. A magnesium rich diet can reduce hypertension and cardiovascular disease and reduce kidney and liver damage.7 The Israeli Heart Association similarly discovered that magnesium supplementation failed to reduce mortality in patients with myocardial infarction.

Although there are studies indicating that niacin, vitamin D, and magnesium can have an effect cardiovascular health, mixed results were found in the studies our group analyzed. We conducted a cross-sectional study to measure the effect of vitamin supplements on overall cardiovascular health. Unlike previous studies that solely focus on participants exposed to a single vitamin, our study measures how a combination of these vitamins may affect cardiovascular health. We predicted a inverse association between dietary supplements and a higher risk of cardiovascular events, specifically myocardial infarction and coronary heart diseases. Our null hypothesis isthat there is no association between niacin, vitamin D, magnesium or total supplements and cardiovascular events. Our alternative hypothesis is that there is an association between niacin, vitamin D, magnesium or total supplements and cardiovascular events.

**Methods:**

**Enrollment and Data Collection**

**Study Population**

The data from the study population was obtained from the National Health and Nutritional Examination Survey (NHANES) 2013- 2014 data set. NHANES is a survey/ physical examination research program that assesses the nutritional and health status of children and adults in the United States. Exposures and disease outcome information were self-reported by the participants through a questionnaire. Our study population includes 212 US men and women, ranging from 20 years old to 80years old. All study participants signed an informed consent form prior to sharing health information through the NHANES.

**Exposures and Outcomes**

The exposures in this study were niacin, vitamin D, magnesium and number of total supplements intake. Niacin, vitamin D, and magnesium were measured in milligrams. Niacin, also known as Vitamin B3, is a crystalline acid that lowers low density lipoproteins (LDL) and triglycerides in the blood.7 Vitamin D is a group of vitamins which aid the metabolism and intestinal absorption of calcium and phosphorous. Vitamin D dietary supplementation is not necessary under normal sunlight exposure because sunlight promotes adequate vitamin D synthesis in the skin.8Magnesium is a mineral that plays a fundamental role in the production of healthy bones, muscle contractions, and nerve signaling in the body.9 Total supplements consumption was measured as the total number of dietary supplements eaten within a 30-day period. All of the exposures were acquired from the Dietary Supplement and Prescription Medication Section (DSQ) of the Sample Person (SP) Questionnaire.

The diseases outcomes measured to assess overall cardiovascular health were myocardial infarction and coronary heart disease.  Myocardial infarction, commonly known as a heart attack, is when blood flow decreases or completely stops flowing to a region of the heart. In the questionnaire, participants were asked whether a doctor or health professional had ever told them that they were having a heart attack.

Coronary heart disease is the buildup of plaque inside the coronary arteries. Individuals with coronary heart disease have a higher risk of having a heart attack. The question asked in the survey was whether a doctor ever told the patients that they had coronary heart disease. The outcome data was acquired through the Medical Conditions section (MCQ) of the questionnaire.Other variables taken into account for confounding were age, race, sex, smoking, sodium intake,  BMI, and prescription for hypertension.

**Statistical Analysis:**

All of the data was analyzed using SAS programming. Prior to analyzing data, we excluded all participants who had missing data for any of the exposures or outcomes. The exposure was measured in either the number of dietary supplements eaten or the mg consumed (ɑ<0.05 for all models). We performed a univariate analysis on Coronary Heart Disease and the total number of vitamin D, niacin, magnesium, and total supplements consumed. Next, we conducted another univariate analysis on myocardial infarction and total number of vitamin D, niacin, magnesium, and total supplements consumed. A covariate analysis was executed using logistic regression in order assess for confounding. We compared the crude odds ratio and the adjusted odds ratio for each potential confounder. Lastly, we made four models to interpret the beta coefficients which were the adjusted log odds ratio.

**Results:**

Prior to adjusting for potential covariates, there were no significant associations between any of the exposures (niacin, magnesium, total supplement, or vitamin D) and either outcome (myocardial infarction and coronary heart disease) (Table 2). This is shown in that all of the 95% confidence intervals for the crude odds ratios include the value of 1 (Table 2).

All the following associations were found after adjusting for potential confounders (Table 3). There is no association between myocardial infarction and total number of supplements taken. The relationship between niacin and myocardial infarction was insignificant. There was also no association found between vitamin D intake and myocardial infarction. There is an insignificant relationship between the amount of magnesium consumed and myocardial infarction (Table 3).

No association was found between the total number of supplements taken and coronary heart disease. There was an insignificant relationship between niacin intake and coronary heart disease. There was no association found between magnesium intake and coronary heart disease. The relationship between vitamin D intake and coronary heart disease was shown to be significant (p= 0.0246, Table 3).

**Discussion**

Although the majority of supplements have not been evaluated for drug-food or drug-drug interactions prior to being accessible to the public, supplements are often advertised for the improvement of cardiovascular health. A few studies have shown that supplements improve cardiovascular health, while other studies have shown that they do not have any effect. 1 The purpose of this cross-sectional study was to determine whether niacin, magnesium, vitamin D, and total supplements improve myocardial infarction and coronary heart disease among the general US population. The only significant association found was between vitamin D intake and coronary heart disease. We concluded that there was no association between niacin, magnesium, or total supplements and coronary heart disease or myocardial infarction.

Although there was an association found between vitamin D supplement intake and coronary heart disease, a large association was not found. Specifically, a high level of vitamin D consumption only decreased the odds for coronary heart disease by only 9%. Overall, our findings indicate that niacin, vitamin D, magnesium and total supplement intake do not have an impact on cardiovascular health (apart from vitamin D and coronary heart disease). This is very useful information because many people who are at high risk of myocardial infarction or coronary heart disease may depend on these supplements on a daily basis in order improve cardiovascular health.

Furthermore, past studies on supplement use and cardiovascular health looked at individual supplements and their effects on the outcome. A major strength of our study is that we not only looked at the impact of individual supplements, but also looked at whether or not a combination of 2 or more supplements had an affect cardiovascular health.

A limitation of our study is that we focused on very few exposures and outcomes. We only looked at the impact of four types of supplements on two cardiovascular  outcomes.  Additionally, we used preexisting data which means that if a participant misinterpreted or left questions unanswered we were unable to reach out to the participants. Due to the cross sectional design of the study, we collected information on exposure data and disease prevalence at a single point in time in order to examine the relationship between the two. The benefits of conducting a cross sectional study design is that we were able to gather data in a relatively short period of time. Furthermore, while doing research on past studies, we did not find a study on supplement intake and disease outcome that was a cross sectional design. However, because the two are simultaneously assessed, a temporal relationship between supplement use and coronary heart disease or myocardial infarctions cannot be studied. Therefore, it is not possible to establish a true cause and effect relationship between the exposure and disease.

Our target population was all US men and women. At first, the sample population included 10,000 participants. After filtering out participants with missing data, our sample size drastically decreased to only 212 participants**.** Because of the relatively small sample size, there may have been a higher variability among the sample size, making the study less representative of the general population.The prevalence of myocardial infarction and coronary heart disease in our study population may not be representative of the prevalence in the entire US population. Furthermore, our study population was made up of the majority of non-Hispanic whites, which does not represent the distribution of the demographics in the United States. This may decrease the generalizability of this study to the targeted population.

The participants were given a survey to fill out in which there could have been responsebias due to the high likelihood that the participants may have not completed all of the questions or may have not answered the questions accurately. The participants may also have inaccurately interpreted the questions on the exposures. All of the questions on supplement intake asked what the total number of supplements taken were within a 30-day period. Some participants may have interpreted this question as the number of supplements taken on a daily basis for all 30 days. Other patients may have interpreted this question as the cumulative number of supplements eaten during a 30-day period. Participants may have also forgotten the supplements that they took over the 30 day period which could have led to recall bias. Furthermore, for some supplements, a serving size can be 2 or more pills. Some participants may have counted the supplements by the number of pills eaten or the number of doses of supplements eaten.

We used guidelines set by the FDA in order to determine the thresholds for normal, low and high vitamin intake. These thresholds are always fluctuating based on recently published studies. While doing research on past studies, we noticed that there has been limited research on what is a tolerable supplement intake level as well as what is a toxic intake level. There is a possibility of misclassification in that we may have inaccurately placed patients who had normal supplement intake levels in the high intake group. This may have been a reason why we did not see an association between the exposure and cardiovascular health.

In the future, it would be interesting to study the impact of other common supplements for cardiovascular health such as fish oil, coenzyme Q10, vitamin A and E. Rather than focusing on only two outcomes, we can measure more disease outcomes such as high blood pressure or arrhythmia.  It would also be important to increase the sample size, which would in turn increase our study power. In order to eliminate response bias among patients we can specify in the question that we are asking for the number of serving sizes of the supplement taken on a daily basis for one month. Furthermore, given that we have more time, we can conduct a prospective cohort study. This would allow us to study the temporal relationship between supplement intake and disease outcome. Also, through a prospective study, we can eliminate some information bias because we will be in contact with the patients rather than looking at past records.

Supplements are heavily advertised for their cardiovascular health benefits. It is important for people to be aware our findings that there was no association between supplements and cardiovascular benefits. Furthermore, I think that people should know that supplements are not an alternative way of receiving nutrients. The best way to receive nutrients is through a healthy well balanced diet.10 I think it would be interesting to study if alternative ways of taking magnesium, niacin, or Vitamin D have an impact on cardiovascular health. Specifically, topical application of vitamins and their effects. Hopefully through future research we will be able to discover more about the benefits and detriments of taking vitamin supplements which will be invaluable to those who frequently use them.

**Citations:**

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**Tables and Figures:**

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|  | **Total (n=212)** |
| **Age (years), mean (sd)** | 59.88 (14.29) |
| **Race/ethnicity, n (%)** |  |
| Non-Hispanic white | 124 (58.49) |
| Non-Hispanic black | 45 (21.23) |
| Hispanic | 28 (13.21) |
| Asian | 12 (5.66) |
| Other | 3 (1.42) |
| **BMI (kg/m2), mean (sd)** | 30.91 (7.66) |
| **Dietary sodium (mg), mean (sd)** | 3388.67 (1546.11) |
| **Antihypertensive treatment (yes/no), n (%)** | 30 (14.15) |
| **Vitamin D (mg), mean (sd)** | 28.27 (49.57) |
| **Niacin (mg), mean (sd)** | 22.74 (30.49) |
| **Magnesium (mg), mean (sd)** | 77.75 (114.95) |
| **Smoking (yes/no), n (%)** | 119 (56.13) |

**Table 1. Demographics of US men and women study participants obtained from NHANES 2013-14.** This table shows the mean and standard deviations (sd) for all qualifiers looked at in the study except for race/ethnicity and smoking.

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| --- | --- | --- |
| **Outcome** | **Supplement** | **Crude Odds Ratio, 95% Confidence Interval** |
| **Myocardial Infarction (MI)** | **\*Total** | 0.49, (0.25-1.95) |
|  | **\*Niacin** | 0.642, (0.199-2.066) |
|  | **\*Vitamin D** | 0.87, (0.302-2.48) |
|  | **\*Magnesium** | 0.81, (0.28-2.32) |
| **Coronary Heart Disease (CHD)** | **Total** | 0.962, (0.38-2.38) |
|  | **\*Niacin** | 0.44, (0.141-1.35) |
|  | **\*Vitamin D** | 3.47, (0.99-12.21) |
|  | **\*Magnesium** | 1.65, (0.58-4.72) |

**Table 2. 95% confidence intervals and Crude Odds Ratio for supplements and MI and CHD Outcomes.** This table shows the crude odds ratios and 95% confidence intervals prior to adjusting for confounders for the association between each exposure and outcome.

**\*** indicates that after the stratification and calculation of percent differences of the crude and adjusted odds ratios, the covariates were determined to be confounders . Our analysis showed no indication of confounders that affected the association between total supplement number and CHD. All variables were still kept in our final logistic regression model due to being well-known risk factors in previous literature.

|  |  |  |  |
| --- | --- | --- | --- |
| **Outcome** | **Supplement** | **P-value** | **Beta** |
| **MI** | **Total** | 0.5918 | 0.021 |
|  | **Niacin** | 0.5755 | 0.021 |
|  | **Vitamin D** | 0.8352 | 0.007 |
|  | **Magnesium** | 0.5999 | 0.019 |
| **CHD** | **Total** | 0.1935 | -0.028 |
|  | **Niacin** | 0.1765 | 0.058 |
|  | **Vitamin D** | **\*0.0246** | -0.092 |
|  | **Magnesium** | 0.3721 | -0.035 |

**Table 3. Effect of Total Supplements, Niacin, Vitamin D, and Magnesium on Myocardial Infarction and Coronary Heart Disease.** These P values are for the relationship for the exposures from our logistic regression models, following the adjustment of potential confounders. Alpha value < 0.05. \***Bold** indicates a significant p-value.