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## Association of Vitamin D Deficiency and Age-Related Macular Degeneration in Medicare Beneficiaries

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Several studies have found an association between vitamin D deficiency and age-related macular degeneration (AMD).<sup>1-4</sup> Vitamin D has been shown to have immunomodulatory and antiangiogenic properties, suggesting a biologically plausible role in the pathogenesis of AMD.<sup>5</sup> This study examines the possible association of vitamin D deficiency and subsequent incidence of first diagnosis of nonneovascular and neovascular AMD in a cohort of Medicare beneficiaries. To our knowledge, this is the first study to evaluate incidence rather than prevalence of AMD in a large sample of vitamin D-deficient patients.

### Methods

For this retrospective, longitudinal cohort analysis, Medicare 5% claims files were used to identify beneficiaries diagnosed as having vitamin D deficiency. This study was approved by the Duke University Institutional Review Board.

We composed a sample of individuals diagnosed as having vitamin D deficiency (International Classification of Diseases, Ninth Revision codes 268.0-268.9) from 2004 through 2006. To identify other comorbidities, we used a 5-year look-back period. We excluded individuals with any AMD diagnosis prior to vitamin D deficiency diagnosis and individuals who had not seen an ophthalmologist or optometrist within the look-back and follow-up periods.

Using propensity score matching, we created a control group without vitamin D deficiency matched on age, sex, race, and Charlson Comorbidity Index score. We computed average treatment effects on the treated individuals using propensity score matching for the whole sample and stratified by race. However, our sample size was inadequate to account for some additional covariates that have been associated with onset of AMD. Therefore, we also used a Cox proportional hazards model to calculate adjusted time to AMD.

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**Author Contributions:** Dr Sloan had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Financial Disclosure:** None reported.

## Results

Between 2004 and 2006, 6966 beneficiaries in the Medicare 5% sample were diagnosed as having vitamin D deficiency. To assess possible racial disparities in diagnosis of vitamin D deficiency, we examined age at first diagnosis of vitamin D deficiency. Black beneficiaries tended to be diagnosed at a younger age compared with white beneficiaries. Rates of first diagnoses of non-neovascular and neovascular AMD during the 3-year follow-up were not significantly different in the vitamin D–deficient and matched groups (**Table 1**). Because black individuals are more likely to have vitamin D deficiency but less likely to have AMD, we stratified the results by race to reduce residual confounding. This subgroup analysis showed lower incidence rates of both types of AMD in the black cohort but no differences by vitamin D status.

After adjusting for additional demographic factors and systemic comorbidities using a Cox proportional hazards model, associations between vitamin D deficiency and first diagnosis of nonneovascular and neovascular AMD were not statistically significant (**Table 2**).

## Comment

Our findings conflict with several previously published studies,<sup>1-4</sup> although Golan et al<sup>6</sup> also found no association between vitamin D levels and AMD. One possible explanation is that the cross-sectional study design and use of prevalent cases in earlier studies does not allow assessment of whether vitamin D deficiency predated development of AMD, whereas our study design looking at incident cases of AMD required that vitamin D deficiency occurred first. While we cannot draw conclusions regarding causality, the measurement of incident rather than prevalent cases provides information on the risk of developing AMD rather than just a measure of how widespread AMD is in this population.

One weakness of the study is that claims data do not contain laboratory findings; thus, we do not know beneficiaries' exact serum vitamin D levels. We were not able to adjust for family history of AMD or complement factor H polymorphisms. We also found a low prevalence of vitamin D deficiency (1.3% in 2006) compared with previous studies.

Although more research is needed, our study did not find a statistically significant association between vitamin D deficiency and subsequent diagnosis of either non-neovascular or neovascular AMD.

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**Table 1**

Rates of First Diagnosis of Nonneovascular and Neovascular Age-Related Macular Degeneration in Matched Groups

Diagnosis	%		P Value
	Vitamin D Deficient	Non-Vitamin D Deficient	
Whole sample (n = 13 932)			
Nonneovascular AMD	8.90	9.14	.62
Neovascular AMD	1.34	1.29	.82
White (n = 11 726)			
Nonneovascular AMD	9.79	9.57	.68
Neovascular AMD	1.50	1.35	.48
Black (n = 1604)			
Nonneovascular AMD	4.24	3.37	.36
Neovascular AMD	0.37	0.37	>.99

Abbreviation: AMD, age-related macular degeneration.

**Table 2**

Cox Proportional Hazards Model Results for First Diagnosis of Age-Related Macular Degeneration During Follow-up in Matched Vitamin D– and Non–Vitamin D–Deficient Groups

Variable	Hazard Ratio (95% CI)	
	Nonneovascular AMD	Neovascular AMD
Vitamin D deficiency	1.023 (0.904-1.157)	1.058 (0.770-1.453)
Age	1.044 (1.033-1.056) <sup>a</sup>	1.039 (1.010-1.069) <sup>a</sup>
Male	0.793 (0.681-0.924) <sup>a</sup>	1.173 (0.824-1.672)
Black	0.472 (0.360-0.620) <sup>a</sup>	0.273 (0.111-0.670) <sup>a</sup>
Other race	0.708 (0.497-1.008)	0.832 (0.366-1.889)
Congestive heart failure	0.946 (0.809-1.105)	0.745 (0.499-1.111)
Stroke	0.942 (0.776-1.143)	0.987 (0.579-1.685)
Hypertension	1.043 (0.854-1.274)	0.974 (0.591-1.605)
Ischemic heart disease	1.119 (0.971-1.289)	1.349 (0.934-1.948)
Cerebrovascular disease	1.124 (0.964-1.311)	0.701 (0.465-1.056)
Hyperlipidemia	1.278 (1.075-1.519) <sup>a</sup>	0.983 (0.645-1.497)
History of smoking counseling	1.216 (1.018-1.453) <sup>a</sup>	1.499 (0.976-1.081)
Charlson Comorbidity Index score	0.976 (0.955-0.998) <sup>a</sup>	1.027 (0.976-1.081)

Abbreviation: AMD, age-related macular degeneration.

<sup>a</sup>Values are statistically significant at  $P < .05$ .