Association of Statin Use With Cataracts
A Propensity Score–Matched Analysis

Jessica Leuschen, MD; Eric M. Mortensen, MD, MSc; Christopher R. Frei, PharmD, MS; Eva A. Mansi, FRCS; Vasudha Panday, MD; Ishak Mansi, MD

IMPORTANCE Cataracts are a main cause of low vision; with the growing elderly population, the incidence of cataracts is likely to increase. Investigators have previously hypothesized that statin antioxidant effects may slow the natural aging process of the lens.

OBJECTIVE To compare the risks for development of cataracts between statin users and nonusers.

DESIGN A propensity score–matched cohort analysis using retrospective data from October 1, 2003, to March 1, 2010. A propensity score–matched cohort of statin users and nonusers was created using 44 variables.

SETTING Database of a military health care system.

PARTICIPANTS Based on medication fills during fiscal year 2005, patients were divided into 2 groups: (1) statin users (received at least a 90-day supply of statin) and (2) nonusers (never received a statin throughout the study). Among 46,249 patients meeting study criteria, we identified 13,626 statin users and 32,623 nonusers.

EXPOSURE Use of statin therapy for more than 90 days.

MAIN OUTCOMES AND MEASURES Primary analysis examined the risks for cataract in the propensity score–matched cohort. Secondary analyses examined the risks for cataract in patients with no comorbidities according to the Charlson Comorbidity Index (patients with no Charlson comorbidity). A sensitivity analysis was conducted to repeat the secondary analysis in patients taking statins for durations of 2, 4, and 6 years.

RESULTS For our primary analysis, we matched 6972 pairs of statin users and nonusers. The risk for cataract was higher among statin users in comparison with nonusers in the propensity score–matched cohort (odds ratio, 1.09; 95% CI, 1.02-1.17). In secondary analyses, after adjusting for identified confounders, the incidence of cataract was higher in statin users in comparison with nonusers (odds ratio, 1.27; 95% CI, 1.15-1.40). Sensitivity analysis confirmed this relationship.

CONCLUSIONS AND RELEVANCE The risk for cataract is increased among statin users as compared with nonusers. The risk-benefit ratio of statin use, specifically for primary prevention, should be carefully weighed, and further studies are warranted.

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Author Affiliations: Wilford Hall Ambulatory Surgery Center, San Antonio, Texas (Leuschen, Panday); San Antonio Military Medical Center, San Antonio, Texas (Mortensen, I. Mansi); University of Texas Southwestern Medical Center, Dallas (Mortensen, I. Mansi); College of Pharmacy, The University of Texas at Austin (Frei); Pharmacotherapy Education and Research Center, School of Medicine, University of Texas Health Science Center, San Antonio, Texas (Frei); Uniformed Services University of the Health Sciences, University of Texas Health Science Center, San Antonio, Texas (Panday); Ramadi Hospital, Alexandria, Egypt (E.A. Mansi).

Corresponding Author: Ishak Mansi, MD, VA North Texas Health System, University of Texas Southwestern, 4500 S Lancaster Rd, Dallas, TX 75216 (ishak.mansi@va.gov).
A ge-related lens opacities (cataracts) are a main cause of low vision and blindness. In addition to being a financial burden that amount to an annual cost of $4.7 billion in the United States, cataracts affect quality of life. With the growing elderly population, the incidence of cataracts is likely to increase. Therefore, understanding and optimizing the modifiable risk factors for developing lens opacities must be a public health priority.

Hydroxymethyl glutaryl coenzyme A reductase inhibitors (statins) are commonly prescribed for prevention of cardiovascular disease. Investigators have previously hypothesized that statins’ antioxidant and anti-inflammatory effects on the lens may slow the aging process of the lens nucleus and epithelium. Observational studies have reported conflicting results; some studies have demonstrated increased risk for cataract in association with statin use, while others have demonstrated decreased risk. The wider use of statins in primary prevention is heavily debated.

The objective of this study was to compare the risks for cataract development between statin users and nonusers within a military health care system where patients have equal access and standards of health care.

Methods

This study was approved by the institutional review board at the Brooke Army Medical Center. This study was exempt from obtaining informed consent from patients because it was an observational study on preexisting data.

This was a retrospective cohort study of all adult patients enrolled in the San Antonio Military Multi-Market Area as Tricare Prime or Plus. Using the Military Health System Management Analysis and Reporting Tool, we retrieved medical encounters data and medication fill histories. The Military Health System Management Analysis and Reporting Tool is a powerful tool that has been used in health care administration, use, and outcomes research. The data include the full spectrum of clinical care regardless of point-of-service location or affiliation:

1. Outpatient electronic medical record system, which contains all outpatient service activities. Health care providers document outpatient encounter details and close encounters by determining visit codes and billing level.
2. Inpatient electronic medical record system, which is used to document all inpatient service activities. Professional coders record the diagnosis and procedure codes based on notes and discharge summaries.
3. Medical benefit claims data, which contain services and medications from health care providers outside the military facilities.
4. Laboratory data, which include all laboratory results performed within the military system.
5. Pharmacy Data Transaction Service, which includes the medication issue date, strength, dosage form, and days of supply for all medications dispensed at or outside of military facilities. Although it is possible that medications may be purchased outside of Tricare, this is unlikely since those costs would be unnecessarily out-of-pocket expenses for Tricare beneficiaries.

Patient Selection

Patient selection and inclusion and exclusion criteria were published in detail previously. All study subjects were enrolled in the system throughout the study. The study duration was divided into 2 periods: (1) the baseline period was used to identify patients’ baseline characteristics (October 1, 2003, to September 30, 2005) and (2) the follow-up period was used to identify the occurrence of outcome events (October 1, 2005, to March 1, 2010).

We identified 2 groups of patients: (1) statin users were patients who received and filled a statin medication prescription for at least 90 days in the period from October 1, 2004, to September 30, 2005 (fiscal year 2005). Patients who received statins for fewer than 90 days were excluded from the study. And (2) nonusers were patients who did not receive a statin at any time throughout the study from October 1, 2003, to March 1, 2010.

Inclusion Criteria

The study included all patients who met the following criteria: (1) were aged 30 to 85 years old, (2) were enrolled in Tricare Prime or Plus in the San Antonio Multi-Market Area, and (3) had at least 1 outpatient visit during the baseline period and 1 outpatient visit during the follow-up period.

Exclusion Criteria

Exclusion criteria included body trauma and burn patients (based on International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] codes): codes for burn patients were those identified by the Agency for Healthcare Research and Quality–Clinical Classifications Software, category 240; trauma codes were compiled from the ICD-9 manual and previous publications. Also excluded were patients who newly started treatment with statins after September 30, 2005 (end of baseline; the purpose of this exclusion was to allow for creating 2 treatment groups with equal periods of follow-up) and patients who did not receive at least 1 prescription medication during the study baseline.

Outcome Measures

An event was defined as the occurrence of an ICD-9-CM code during follow-up in either the inpatient or outpatient setting consistent with a cataract diagnosis. Cataracts were defined using ICD-9-CM codes for cataracts as identified by Agency for Healthcare Research and Quality–Clinical Classifications Software, category 86. We also used the following prespecified diagnosis subgroups for cataracts: (1) the cataract subgroup included presenile, senile, and traumatic cataracts (eTable in Supplement) and (2) the cataract 2 subgroup included cataracts secondary to ocular disorders, systemic diseases, diabetes mellitus, radiation, and others (eTable in Supplement).

Data Analysis

Details of all patients who met the study criteria were previously published. We described patients’ comorbidities using the Deyo et al adaptation method of the Charlson Co-
mo mortality Index (CCI). A propensity score–matched cohort of statin users and nonusers was created using 44 variables that were expected to increase the likelihood for receiving statins (eg, diabetes mellitus, ischemic heart disease, cerebrovascular diseases, peripheral vascular diseases, and smoking\textsuperscript{28}) and increase the risk for cataract (eg, excessive alcohol use, obesity, smoking, glaucoma, severe refractory disorders, and corticosteroid administration\textsuperscript{27}). The variables used to create the propensity score were age, sex, 17 comorbid conditions as defined by the Deyo method (Table 1), total CCI score,\textsuperscript{25} obesity, alcohol dependence/abuse, illicit drug use, cigarette smoking, glaucoma (eTable in Supplement), vision defects/blindness (eTable in Supplement), health care use (number of outpatient visits and inpatient admissions during baseline and follow-up), and the use of 14 medication groups (Table 1).\textsuperscript{28}

### Propensity Score Matching

We used logistic regression analysis to create the propensity score and test the balance of covariates in our models using the routines developed by Becker and Ichino.\textsuperscript{29} We then used the routine developed by Leuven and Sianesi\textsuperscript{30} to perform nearest-number matching with a caliper of 0.001.

### Primary Analysis

In this analysis, we estimated the risk for cataract in relation to statin use in the propensity score–matched cohort.

In the secondary analysis, we created a prespecified subgroup of patients in which patients with any CCI comorbidity according to the Deyo et al\textsuperscript{25} method were excluded (patients with no Charlson comorbidities). Hence, all statin users and nonusers in secondary analysis had a CCI score of 0.

We then used logistic regression analysis to examine the risk for outcome. Covariates included in each secondary analysis were statin use, age, sex, obesity, smoking, alcohol use, illicit drug use, glaucoma, vision defects/blindness, number of all admissions, number of all outpatient visits, and use of different classes of medications as listed in Table 1 in the baseline period.

### Sensitivity Analysis

In this analysis of patients with no Charlson comorbidity included 33,513 patients (6113 statin users and 27,400 nonusers). Table 3 describes patient baseline characteristics in this cohort.

After adjusting for the identified confounders, statin use was associated with higher adjusted OR for any cataract and cataract 1 (presenile, senile, and traumatic cataract), but not for cataract 2 (cataract secondary to ocular disorders, systemic diseases, diabetes mellitus, radiation, etc) (Table 4). We also repeated the analysis using backward stepwise technique to maximize the value of $R^2$. The final model identified statin use as an independent predictor of cataract (adjusted OR, 1.43; 95% CI, 1.32-1.53; Nagelkerke $R^2 = 0.52$). We also repeated the analysis with no Charlson comorbidity included 33,513 patients (6113 statin users and 27,400 nonusers). Table 3 describes patient baseline characteristics in this cohort.

After adjusting for the identified confounders, statin use was associated with higher adjusted OR for any cataract and cataract 1 (presenile, senile, and traumatic cataract), but not for cataract 2 (cataract secondary to ocular disorders, systemic diseases, diabetes mellitus, radiation, etc) (Table 4). We also repeated the analysis using backward stepwise elimination technique to maximize the value of $R^2$. The final model identified statin use as an independent predictor of cataract (adjusted OR, 1.42; 95% CI, 1.32-1.52; Nagelkerke $R^2 = 0.52$). Cumulative simvastatin years was significantly related to increased cataract risk (OR, 1.001; $P < .001$), but not to the maximum dose of statin used in simvastatin-equivalent doses (OR, 0.99; $P = .33$).

For our secondary analysis, the cohort of patients with no Charlson comorbidity included 33,513 patients (6113 statin users and 27,400 nonusers). Table 3 describes patient baseline characteristics in this cohort.

After adjusting for the identified confounders, statin use was associated with higher adjusted OR for any cataract and cataract 1 (presenile, senile, and traumatic cataract), but not for cataract 2 (cataract secondary to ocular disorders, systemic diseases, diabetes mellitus, radiation, etc) (Table 4). We also repeated the analysis using backward stepwise technique to maximize the value of $R^2$. The final model identified statin use as an independent predictor of cataract (adjusted OR, 1.43; 95% CI, 1.32-1.53; Nagelkerke $R^2 = 0.52$). Cumulative simvastatin years was significantly related to increased cataract risk (adjusted OR, 1.001; $P < .001$), but not to the maximum dose of statin used in simvastatin-equivalent doses (adjusted OR, 0.99; $P = .46$).

We examined the relationship between cataract and both LDL cholesterol and high-density lipoprotein cholesterol by restricting the cohort to statin nonusers and introducing both...
### Table 1. Characteristics of Statin Users and Nonusers in Propensity Score–Matched Cohorts

<table>
<thead>
<tr>
<th></th>
<th>Statin Users (n = 6972)</th>
<th>Nonusers (n = 6972)</th>
<th>P Value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>56.5 (12.5)</td>
<td>56.8 (12.2)</td>
<td>.19</td>
</tr>
<tr>
<td>Male</td>
<td>3769 (54.1)</td>
<td>3778 (54.2)</td>
<td>.88</td>
</tr>
<tr>
<td>Comorbidities at baseline&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>59 (0.8)</td>
<td>66 (0.9)</td>
<td>.53</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>130 (1.9)</td>
<td>130 (1.9)</td>
<td>&gt; .99</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>136 (2)</td>
<td>142 (2)</td>
<td>.76</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>153 (2.2)</td>
<td>146 (2.1)</td>
<td>.73</td>
</tr>
<tr>
<td>Dementia</td>
<td>29 (0.4)</td>
<td>29 (0.4)</td>
<td>&gt; .99</td>
</tr>
<tr>
<td>Chronic obstructive lung disease</td>
<td>817 (11.7)</td>
<td>835 (12)</td>
<td>.66</td>
</tr>
<tr>
<td>Rheumatologic diseases</td>
<td>157 (2.3)</td>
<td>170 (2.4)</td>
<td>.47</td>
</tr>
<tr>
<td>Peptic ulcer disease</td>
<td>99 (1.4)</td>
<td>102 (1.5)</td>
<td>.89</td>
</tr>
<tr>
<td>Mild liver disease</td>
<td>30 (0.4)</td>
<td>30 (0.4)</td>
<td>&gt; .99</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>699 (10)</td>
<td>680 (9.8)</td>
<td>.61</td>
</tr>
<tr>
<td>Diabetes mellitus with complications</td>
<td>182 (2.6)</td>
<td>162 (2.3)</td>
<td>.28</td>
</tr>
<tr>
<td>Hemiplegia/paraplegia</td>
<td>9 (0.1)</td>
<td>9 (0.1)</td>
<td>&gt; .99</td>
</tr>
<tr>
<td>Renal disease</td>
<td>96 (1.4)</td>
<td>91 (1.3)</td>
<td>.77</td>
</tr>
<tr>
<td>Malignancy</td>
<td>438 (6.3)</td>
<td>435 (6.2)</td>
<td>.92</td>
</tr>
<tr>
<td>Liver disease (moderate/severe)</td>
<td>4 (0.1)</td>
<td>4 (0.1)</td>
<td>&gt; .99</td>
</tr>
<tr>
<td>Metastatic neoplasm</td>
<td>24 (0.3)</td>
<td>20 (0.3)</td>
<td>.55</td>
</tr>
<tr>
<td>HIV</td>
<td>7 (0.2)</td>
<td>9 (0.1)</td>
<td>.63</td>
</tr>
<tr>
<td>Charlson Comorbidity Index total score, mean (SD)</td>
<td>0.59 (1.1)</td>
<td>0.57 (1.15)</td>
<td>.42</td>
</tr>
<tr>
<td>No. of outpatient visits during baseline, mean (SD)</td>
<td>32.3 (31.8)</td>
<td>32.2 (31.3)</td>
<td>.72</td>
</tr>
<tr>
<td>No. of inpatient admissions during baseline, mean (SD)</td>
<td>0.27 (0.8)</td>
<td>0.27 (0.7)</td>
<td>.95</td>
</tr>
<tr>
<td>No. of outpatient visits during follow-up, mean (SD)</td>
<td>89.5 (84.2)</td>
<td>88.4 (115)</td>
<td>.50</td>
</tr>
<tr>
<td>No. of inpatient admissions during follow-up, mean (SD)</td>
<td>0.8 (1.8)</td>
<td>0.8 (1.9)</td>
<td>.81</td>
</tr>
<tr>
<td>Obesity</td>
<td>1066 (15.3)</td>
<td>1059 (15.2)</td>
<td>.89</td>
</tr>
<tr>
<td>Illicit drug use</td>
<td>11 (0.2)</td>
<td>10 (0.1)</td>
<td>.83</td>
</tr>
<tr>
<td>Alcohol abuse/dependence</td>
<td>72 (1)</td>
<td>60 (0.9)</td>
<td>.30</td>
</tr>
<tr>
<td>Smoking</td>
<td>565 (8.1)</td>
<td>581 (8.3)</td>
<td>.62</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>681 (9.8)</td>
<td>684 (9.8)</td>
<td>.96</td>
</tr>
<tr>
<td>Vision defect/blindness</td>
<td>3073 (44.1)</td>
<td>3096 (44.4)</td>
<td>.71</td>
</tr>
<tr>
<td>Medications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta blocker</td>
<td>1274 (18.3)</td>
<td>1275 (18.3)</td>
<td>.98</td>
</tr>
<tr>
<td>Diuretic</td>
<td>1934 (27.7)</td>
<td>1950 (28)</td>
<td>.76</td>
</tr>
<tr>
<td>Calcium channel blocker</td>
<td>1105 (15.8)</td>
<td>1086 (15.6)</td>
<td>.68</td>
</tr>
<tr>
<td>Nonstatin lipid-lowering drugs</td>
<td>520 (7.5)</td>
<td>483 (6.9)</td>
<td>.23</td>
</tr>
<tr>
<td>ACE inhibitor/ARB</td>
<td>2444 (35.1)</td>
<td>2427 (34.8)</td>
<td>.76</td>
</tr>
<tr>
<td>Oral hypoglycemic</td>
<td>321 (4.6)</td>
<td>297 (4.3)</td>
<td>.32</td>
</tr>
<tr>
<td>Cytochrome p450&lt;sup&gt;c&lt;/sup&gt;</td>
<td>465 (6.7)</td>
<td>461 (6.6)</td>
<td>.89</td>
</tr>
<tr>
<td>Aspirin</td>
<td>2169 (31.1)</td>
<td>2147 (30.8)</td>
<td>.69</td>
</tr>
<tr>
<td>NSAID</td>
<td>3998 (57.3)</td>
<td>3993 (57.3)</td>
<td>.93</td>
</tr>
<tr>
<td>SSRI</td>
<td>1167 (16.7)</td>
<td>1191 (17.1)</td>
<td>.60</td>
</tr>
<tr>
<td>Systemic corticosteroid</td>
<td>272 (3.9)</td>
<td>270 (3.9)</td>
<td>.93</td>
</tr>
<tr>
<td>Antipsychotic</td>
<td>89 (1.3)</td>
<td>94 (1.3)</td>
<td>.71</td>
</tr>
<tr>
<td>Sedatives</td>
<td>1377 (19.8)</td>
<td>1370 (19.7)</td>
<td>.88</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td>13 (0.2)</td>
<td>20 (0.3)</td>
<td>.23</td>
</tr>
</tbody>
</table>

Abbreviations: ACE/ARB, angiotensin-converting enzyme/angiotensin-receptor blocker; HIV, human immunodeficiency virus; NSAID, nonsteroidal anti-inflammatory drug; SSRI, selective serotonin reuptake inhibitors.  
<sup>a</sup> Calculated using χ<sup>2</sup> test for categorical variables and t test for continuous variables.  
<sup>b</sup> Diagnosis is based on ICD-9-CM codes as identified in the Deyo method for applying the Charlson comorbidity score.  
<sup>c</sup> Cytochrome p450 medications that inhibit the cytochrome p450 system as identified in a recent Food and Drug Administration warning.
parameters into our regression model. Mean LDL cholesterol level was inversely related to risk for cataract (adjusted OR, 0.997; \( P = .009 \)); mean high-density lipoprotein cholesterol was not (adjusted OR, 1.002; \( P = .16 \)). Introducing mean LDL cholesterol in a logistic regression model of patients with no Charlson comorbidities continued to demonstrate that statin use was independently associated with an increased adjusted OR for cataract (Table 4). Sensitivity analysis demonstrated consistent results in all subgroups of statin users for 2, 4, or 6 years (Table 4).

### Discussion

In this study, statin use was associated with a higher incidence of cataract diagnosis in the propensity score–matched cohort and in all the secondary and sensitivity analyses.

Cataract development may be induced by oxidative stress; statins’ bidirectional effects on oxidation processes, including a possible mitochondrial effect, can potentially increase risk for cataract. Previous studies hypothesized that the inhibition of cholesterol biosynthesis by statin medications prevents proper epithelial cell development within the crystalline lens, which requires high cholesterol to maintain its transparency. Increased rates of cataract among animals and humans with hereditary cholesterol deficiency have been noted. Administration of atorvastatin was noted to induce cataract in the lens structure of Wistar rats.

Several observational studies investigating the association of statin therapy with cataracts have produced conflicting results, with some reporting a protective effect, a negative effect, no effect, and an inconsistent effect. Recently, several studies found that statin use was associated with increased risk for cataract. In a prospective cohort study, the outcomes of 225,922 new statin users were compared with 1,778,770 nonusers. The adjusted hazard ratio (HR) for cataract in statin users compared with nonusers was 1.32 (95% CI, 1.26-1.37) in men. This adverse effect was similar across various types of statins.

### Table 2. Unadjusted Risk for Cataracts in Statin Users Compared With Nonusers After Propensity Score Matching

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Statin Users</th>
<th>Nonusers</th>
<th>Odds Ratio (95% CI)</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cataract</td>
<td>2477 (35.5)</td>
<td>2337 (33.5)</td>
<td>1.09 (1.02-1.17)</td>
<td>.01</td>
</tr>
<tr>
<td>Cataract 1</td>
<td>2131 (30.6)</td>
<td>2031 (29.1)</td>
<td>1.07 (1.00-1.15)</td>
<td>.06</td>
</tr>
<tr>
<td>Cataract 2</td>
<td>1233 (17.7)</td>
<td>1188 (17.0)</td>
<td>1.05 (0.96-1.14)</td>
<td>.31</td>
</tr>
</tbody>
</table>

### Table 3. Selected Characteristics of Statin Users and Nonusers Among Patients With No Charlson Comorbidities

<table>
<thead>
<tr>
<th>No. (%)</th>
<th>Statin Users (n = 6113)</th>
<th>Nonusers (n = 27400)</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>56.6 (12.2)</td>
<td>43.6 (10.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Male</td>
<td>3707 (60.6)</td>
<td>12,246 (44.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Obesity</td>
<td>901 (14.7)</td>
<td>2520 (9.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Alcohol abuse/dependence</td>
<td>48 (0.8)</td>
<td>153 (0.6)</td>
<td>.04</td>
</tr>
<tr>
<td>Smoking</td>
<td>477 (7.8)</td>
<td>1401 (5.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>527 (8.6)</td>
<td>1050 (3.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Vision defect/blindness</td>
<td>2613 (42.7)</td>
<td>11,048 (40.3)</td>
<td>.001</td>
</tr>
</tbody>
</table>

### Abbreviations

- ACE/ARB, angiotensin-converting enzyme/angiotensin-receptor blocker
- HDL, high-density lipoprotein
- LDL, low-density lipoprotein

### Notes

- No-comorbidity cohort is defined as patients who have a Charlson Comorbidity Index of 0 according to the Deyo et al method.
- Calculated using \( \chi^2 \) test for categorical variables and \( t \) test for continuous variables.
- Cytochrome p450 medications that inhibit the cytochrome p450 system as identified in a recent Food and Drug Administration warning.
- There were 2207 missing values among statin users and 15,143 among the nonusers.
other retrospective study of 6336 patients, statin use was associated with nuclear sclerosis and posterior subcapsular cataract.37

Conversely, in a prospective, observational study including 1299 patients, the OR of nuclear cataract was lower in statin users (0.40; 95% CI, 0.18-0.90), after excluding smokers and diabetics and adjusting for potential confounders.36 In another population-based cohort study including 3654 elderly participants, statin use was protective for any cataract (adjusted HR, 0.52; 95% CI, 0.29-0.93).35

Furthermore, several studies have found no effect or inconsistent effect of statins on the cataract development. In a case-control analysis involving 13 982 patients who underwent cataract extraction and 34 049 control subjects, long-term statin use (>5 years) was protective against cataract surgery, but short-term statin use (<5 years) was associated with an increased rate of cataract extraction.9 In another case-control analysis, 7405 cases and 28 327 control subjects were matched by age, sex, practice type, calendar time, and duration of medical history in the database.40 Long-term use of statins was not associated with an increased cataract risk (adjusted OR, 0.9; 95% CI, 0.5-1.6), but concomitant use of simvastatin and erythromycin was associated with an increased risk for cataract.40 Moreover, a controlled, double-blind study randomized 621 individuals to receive simvastatin or matching placebo. After 18 months, there were no significant differences between the treatment groups in the refractive condition of the eye or in the incidence of cataract.41

An important consideration in observational studies is the presence of baseline confounders that may mask an actual relationship or falsely demonstrate the presence of relationship. Adherence to statins may be a marker for a healthy user bias that may result in false association of statin use with better outcomes. In a large prospective cohort study, statin-adherent patients had a lower adjusted risk ratio for motor vehicle and workplace accidents in comparison to nonadherent patients.42 Several risk factors for cardiovascular disease (eg, older age, diabetes mellitus, and smoking), which constitute indications for statin therapy, are also risk factors for development of cataract. Hence, adequate description of baseline characteristics and adjustment for these potential confounders is necessary.

To our knowledge, ours is the first study to use a propensity score-matched analysis to adjust for baseline confounders in statin users and nonusers. The propensity score-matched cohorts were equally balanced between the 2 treatment groups. This study also is one of the largest studies in the literature, comprising more than 45 000 patients followed up longitudinally within the same health care system. Additionally, all patients in this study received health care in a relatively homogenous health care system (military health care), with similar insurance coverage (Tricare Prime or Plus) and similar access to care and medication coverage. This consistency partially minimizes bias resulting from differences because of health care accessibility and use.

Limitations of this study included its retrospective observational design, such as the presence of unidentified confounders and the difficulty in adjusting for these confounders. Propensity score matching offers a strong tool to adjust for confounders, and we were successful in creating balanced cohorts. However, the presence of yet unidentified baseline confounders cannot be absolutely ascertained. Measurement inadequacies for covariates, residual confounding, omitted variable bias, and potential for interaction effects are all factors that could continue to confound results. Moreover, successful propensity score matching of individual baseline...
Association of Statin Use With Cataracts  

ORIGINAL INVESTIGATION RESEARCH

Statistical analysis:
Panday, I.Mansi.

Correction:
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employees of the US government. This work was

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data on visual impairment in the year 2002. Bull

2. Salm M, Belys K, Sloan FA. Trends in cost of

3. Brenner MH, Curbow B, Javitt JC, Legro MW,
Sommer A. Vision change and quality of life in the
elderly: response to cataract surgery and treatment
of other chronic ocular conditions. Arch

http://one.aao.org/CE/PracticeGuidelines/PPP


6. Fong DS, Poon KY. Recent statin use and cataract

7. Hippisley-Cox J, Coupland C. Unintended effects
of statins in men and women in England and Wales:
population based cohort study using the QResearch

8. Cenedella RJ. Cholesterol and cataracts. Surv

V. Persistence with statins and incident cataract:
a population-based historical cohort study. Ann

therapy for healthy men identified as “increased

11. Redberg RF, Katz MH. Healthy men should not

12. Kugler J. Military Health System Patient Centered
Medical Home guide: Tricare–Office of the
Chief Medical Officer, Department of Defense. June 2011.
http://www.tricare.mil/mta/ccm/download
/MHSCPMCHGuide.pdf.

13. Tricare Management Activity. M2 functional

14. Luhman S, Lehr E, Hefflin C, Saund N. Interface
Control Document Describing the Case Management
Exchange from BEA to MDR and M2 Baseline.
DHSS Program Management. August 18, 2008 edition. Falls

15. Enwold L, Brinton LA, McGlynn KA, Zahn SH,
Potter JF, Zhu K. Oral contraceptive use among
women in the military and the general US population.

16. Moncz C. Outpatient Workload (RVU) Predictors:
Age, Gender & Beneficiary Category. Baltimore, MD:
US Army Medical Department Center and School,
2008.

17. Gantt CJ, Neely JA, Villafana IA, Chun CS,
Gharabaghi SM. Analysis of weight and associated
health consequences of the active duty staff at a
major Naval medical center. Mil Med.

18. George SZ, Childs JD, Teyhen DS, et al. Brief
psychosocial education, not core stabilization,
reduced incidence of low back pain: results from the
Prevention of Low Back Pain in the Military (POLM)

19. Elmitwalli T, Otterpohl R. Grey water treatment
in upflow anaerobic sludge blanket (UASB) reactor
at different temperatures. Water Sci Technol.
2011;64(3):610-617.

20. Mansi I, Frei CR, Pugh MJ, Mortensen EM.
Psychologic diseases and statin use: a propensity

Clinical Classifications Software (CCS) for ICD-9-CM.
http://www.hcup-us.ahrq.gov/toolssoftware/ccs

22. Elikhauser A, Steiner C, Harris DR, Coffey RM.
Comorbidity measures for use with administrative

assessments based on patient report: results from the
Veterans Health Study. J Ambul Care Manage.

24. Mansi I, Frei CR, Pugh J, Malikis U, Mortensen
EM. Statins and musculoskeletal conditions,
arthropathies, and injuries. JAMA Intern Med.

25. Deyo RA, Cherkin DC, Ciol MA. Adapting a
clinical comorbidity index for use with ICD-9-CM

26. Grundy SM, Cleeman JI, Merz CN, et al; Coordinating Committee of the National
Cholesterol Education Program. Implications of recent clinical trials for the National Cholesterol
Education Program Adult Treatment Panel III

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Study concept and design: Mortensen, Frei, E. A.
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Acquisition of data: I. Mansi.

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most statin users received statin prescriptions for prolonged
periods (mean cumulative use of 1695 days), which suggests
actual compliance with their statin prescription.

In conclusion, this study found statin use to be associ-
ated with an increased risk for cataract. Efforts to curtail pre-
ventable causes of cataracts entail further studies, including
prospective observational studies/registries or randomized
clinical trials, to confirm or refute these findings. Such stud-
ies should include regular ophthalmologic examinations and
objective assessment tools rather than relying on patient sur-
evies or administrative data. Weighing the benefit-risk ratio
of statin use, specifically for primary prevention, should be care-
fully considered.

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of statin use, specifically for primary prevention, should be care-
fully considered.


**OPHTHALMIC IMAGES**

Dehisced Corneal Button With No Evidence of a Ruptured Globe

Katherine M. Whipple, MD; Jeffrey E. Lee, MD; Alex S. Huang, MD, PhD; Stuart I. Brown, MD

**A**

An 87-year-old woman presented to our hospital complaining that her 20-year-old corneal transplant (penetrating keratoplasty) had “popped off” during dinner. A dehisced corneal button, hinged at the 6-o’clock position, was present (A). There was no globe rupture owing to a transparent membrane beneath the corneal graft (B).