Statin Use and the Incidence of Advanced Age-related Macular Degeneration in the Complications of Age-related Macular Degeneration Prevention Trial

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Objective: To evaluate the impact of statin use on the incidence of advanced age-related macular degeneration (AMD) and its components, choroidal neovascularization (CNV) and geographic atrophy (GA), among patients with bilateral large drusen.

Design: Cohort study within a multicenter, randomized, clinical trial.

Participants: Patients enrolled in the Complications of Age-related Macular Degeneration Prevention Trial (CAPT).

Methods: Eligibility criteria for the clinical trial required that participants have ≥10 large (>125 μm) drusen and visual acuity ≥20/40 in each eye. Patients scheduled for their final CAPT visit after May 2005 were interviewed on their history of use of cholesterol-lowering medications, including statins. Trained readers identified CNV and end point GA (>1 Macular Photocoagulation Study disc area of GA) based on review of fluorescein angiograms and fundus photographs taken at annual follow-up visits and when patients reported symptoms. The risk ratio for participants developing CNV or developing GA associated with statin use was estimated with time-dependent Cox proportional hazards models.

Main Outcome Measures: Development of advanced AMD, CNV, and end point GA.

Results: Among 764 patients eligible for the interview, 744 (97.4%) patients completed the interview on medication use. Statin use was reported by 296 (39.8%) of those interviewed, with the majority, 187 (63.2%) of the 296, beginning use after enrollment in CAPT. Among 744 patients, advanced AMD developed in 332 (22.5%) eyes of 242 (32.5%) patients, CNV in 222 (15%) eyes of 176 (23.7%) patients, and GA in 114 (7.7%) eyes of 80 (10.8%) patients. With adjustment for other risk factors, the estimated risk ratio for eyes (95% confidence interval) associated with statin use was 1.15 (0.87–1.52) for advanced AMD, 1.35 (0.99–1.83) for CNV, and 0.80 (0.46–1.39) for GA.

Conclusions: The CAPT data are not consistent with a strong protective effect (risk ratio, ≤0.85) of statins on the development of advanced AMD among patients with bilateral large drusen.

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In 2001, Hall et al[1] reported that the prevalence of age-related macular degeneration (AMD) was markedly lower (1 in 27 [3.7%]) among members of a birth cohort who reported using statins (hydroxymethyl glutaryl coenzyme A reductase inhibitors) than in those who did not use statins (76 of 352 [21.6%]). Because the many effects of statins include actions on processes implicated in the pathogenesis of AMD, specifically inflammation and angiogenesis, a protective effect of statins is biologically plausible.[2]

Several other investigators have evaluated the relationship between statin use and AMD through case-control, cross-sectional, and prospective follow-up studies with various methods for defining the drug used (any cholesterol-lowering drug or statins only), ascertaining drug use (patient interview, filled prescriptions, or medical records), ascertaining presence of AMD (photograph grading or medical record review), and defining AMD (early only, late only, early and late combined, choroidal neovascularization [CNV] only, and geographic atrophy [GA] only).[3–11] In 2004, van Leeuwen et al[12] pooled the data on incident early AMD and use of cholesterol-lowering drugs from population-based, prospective studies in the United States, The Netherlands, and Australia and found no association (odds ratio, 1.0; 95% confidence interval [CI], 0.6–1.6).[12] In 2007, Chuo et al[13] published results of a meta-analysis of 7 observational studies, published in 2006 or before, of statin use and early or late AMD and obtained a pooled relative risk of 0.70 (95% CI, 0.48–1.03).[13] They concluded that statins "do not appear to lower the risk of developing AMD, although clinically significant effects cannot be excluded."

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After the meta-analysis, published data from the cross-sectional Women's Health Initiative Sight Examination and the prospective Beaver Dam Eye Study of incident AMD yielded statistically nonsignificant relative risks near 1.0, whereas the prospective Blue Mountain Study yielded relative risks of 0.33 (95% CI, 0.13–0.84) for incident soft indistinct drusen, 0.54 (95% CI, 0.26–1.11) of incident early AMD, and 0.52 (95% CI, 0.26–1.04) for early and late AMD combined.[14–16] These later studies had larger proportions of patients taking statins, presumably for longer duration, than the studies reported previously.

Thus, results to date have been inconsistent in supporting a protective effect of statins on development of AMD at any stage, yet not conclusive in ruling out clinically significant effects. The Complications of Age-Related Macular Degeneration Prevention Trial (CAPT) provides the opportunity to examine the effect of statins in a large group of patients at relatively high risk of progressing from having bilateral drusen to advanced AMD. In CAPT, AMD status was documented photographically for a period of 5–6 years and the period of statin use, if any, was ascertained through patient interview at the end of follow-up. Results of the clinical trial indicated no beneficial or harmful effect of CAPT laser treatment on visual acuity or the incidence of advanced AMD.[17]

Methods

Study Population

Details of the design and methods for CAPT study have been published previously.[17–19] Only the major features of CAPT relevant to the evaluation of statin use as a risk factor for advanced AMD are described here. Between May 1999 and March 2001, 1052 patients were enrolled through 22 clinical centers in the United States. The institutional review board associated with each center approved the study, and written informed consent was obtained from each patient. The CAPT eligibility criteria specified that each eye have $\geq$10 drusen $\geq$125 μm in diameter and visual acuity $\geq$20/40. Neither eye was to have evidence of CNV, serous pigment epithelial detachment, GA within 500 μm of the foveal center or $>$1 Macular Photocoagulation Study disc area in size, or other ocular conditions likely to compromise visual acuity or contraindicate application of laser treatment. Both eyes of the patients were enrolled into the CAPT; 1 eye of each patient was selected randomly for laser treatment, and the contralateral eye was assigned to observation. Patients had to be $\geq$50 years old and free of conditions that would likely preclude 5 years of follow-up.

Study Procedures

During the initial visit, patients provided information on demographic characteristics, history of diabetes mellitus, history of cigarette smoking, current use of aspirin, and current use of antihypertensive medications. Blood pressure was measured once while the patient was sitting. Stereoscopic color fundus photographs were taken of each eye and fluorescein angiography with frames from each eye was performed. During follow-up, stereoscopic color photographs of each eye and angiograms were taken annually and color photographs also were taken at 6 months. Angiograms also were taken when patients reported symptoms between annual visits. Follow-up was scheduled for either 5 or 6 years, depending on the date of enrollment.

Beginning in May 2005, patients who were completing their final CAPT visit were interviewed on their history of use of cholesterol-lowering medications including statins, bile acid sequestrants, and nicotinic acid. Patients reporting medication use were asked the starting year and ending year of their use for each cholesterol-lowering medication.

Baseline photographic images were graded by trained readers in the CAPT Reading Center using a system that incorporated methods from the Wisconsin Age-Related Maculopathy Grading System and the International Classification and Grading System for Age-Related Maculopathy and Age-Related Macular Degeneration.[20,21] Fundus features described in the grading included number of drusen, largest drusen size, percent of area covered by drusen, drusen confluence, predominant drusen size, percent of retinal area within 3000 μm of the foveal center covered by drusen, focal hyperpigmentation, and retinal pigment epithelium (RPE) depigmentation.

Determination of Choroidal Neovascularization, End Point Geographic Atrophy, and Advanced Age-related Macular Degeneration

Readers in the CAPT Reading Center evaluated the follow-up images for the presence of CNV, end point GA, and serous detachment of the RPE. Fluorescein angiograms were used to identify CNV, defined as expansion or persistence of hyperfluorescence in the late phase of the fluorescein angiogram. We defined GA as present when the color photographs showed an area of atrophy $\geq$250 μm and 2 of the following 3 features: visible choroidal vessels, sharp edges, and more or less circular shape. End point GA was defined as a total of $>$1 Macular Photocoagulation Study disc area of atrophy when all areas of GA were combined. Serous detachment of the RPE was defined as a smooth dome-shaped elevation of the RPE with uniform fluorescein dye pooling and well-defined borders. Advanced AMD was defined as CNV, end point GA, or serous detachment of the RPE.

Statistical Analyses

The patient's statin use during CAPT was based on the date of enrollment in CAPT, the calendar year statin use began, and the calendar year statin use ended. The CAPT patients were scheduled for follow-up at 6 months after enrollment, 12 months, and then annually. Event times for the AMD outcomes (advanced AMD, CNV, or GA) were assigned to the closest scheduled visit. Statin use was assumed to have started, or ended, on July 1 of the reported calendar year. The association of statin use with CNV, GA, and advanced AMD was analyzed using the Cox proportional hazards model with statin use defined as a time-dependent covariate. Time 0 was defined as the time of enrollment into CAPT. Both patient-specific and eye-specific analyses were performed. For patient-specific analyses, the time to an event (detection of either CNV, GA, or advanced AMD) was the time to the event in the first affected eye. Eye-specific analyses, which may be more powerful in detecting effects, used a robust variance estimator to accommodate the correlation between 2 eyes of the same patient.[22] Because an effect of statins on AMD may not begin immediately with the initiation of use, analyses were also performed on a patient subgroup restricted to only those patients who had no change in statin use from their time of enrollment into CAPT to their last visit; that is, patients who either started or stopped taking statins after enrollment into CAPT were excluded from the analysis.

The risk ratios for the association between statin use and events were assessed using univariate and multivariate Cox proportional hazards models. The risk factors previously identified for each event were included in the multivariate models.[23] For CNV, the

Table 1. Baseline Characteristics of Patients with Completed Interviews

Characteristics	n (%)
Patient characteristics (n = 744)	
Age (yrs)	
50–59	74 (10.0)
60–69	240 (32.3)
70–79	374 (50.3)
>79	56 (7.5)
Mean (standard deviation)	70 (7.4)
Gender	
Female	472 (63.4)
Male	272 (36.6)
Race	
White	740 (99.5)
Non-white	4 (0.5)
Cigarette smoking	
Never	343 (46.1)
Quit	362 (48.7)
Current	39 (5.2)
Hypertension	
Normal	264 (35.5)
Suspect	136 (18.3)
Definite	340 (45.7)
Unknown	4 (0.5)
Eye characteristics (n = 1477)	
Percent of global area covered by drusen (>63 μ)	
<10	958 (64.9)
10–24	412 (27.9)
≥25	87 (6.0)
Cannot grade/determine/missing	20 (1.4)
Focal hyperpigmentation	
None/questionable	430 (29.1)
<250 μ	818 (55.4)
≥250 μ	206 (14.0)
Cannot grade/determine/missing	23 (1.6)
Depigmentation of the retinal pigment epithelium	
None	1387 (93.9)
Any	73 (4.9)
Cannot grade/determine/missing	17 (1.2)

factors were age, cigarette smoking status, hypertension, and level of focal hyperpigmentation. For GA, the factors were age, percent of retinal area covered by drusen, level of focal hyperpigmentation, and RPE depigmentation. For patient-specific analyses, the baseline ocular characteristics of the worse eye were used. Risk factors for either CNV or GA were included in the multivariate model for detection of advanced AMD.

All these analyses included treated and untreated eyes. Analyses of untreated eyes only were also performed and compared with those from the combined group of treated and untreated eyes. Statistical computations were performed with SAS 9.1 (SAS, Inc., Cary, NC).

Results

Among 764 CAPT patients with a clinic visit after May 2005, 744 (97.4%) completed the interview. Baseline demographic and ocular characteristics of the 744 patients who completed the interview are presented in Table 1 and are similar to those of the entire CAPT patient population.[19]

A total of 296 (39.8%) of the 744 patients interviewed reported ever using statins, with the majority, 187 (63.2%) of the 296, beginning use after enrollment in CAPT. Few patients (29 [9.8%]) stopped using statins once they started them. Most (448 [60.2%]) never used statins either before CAPT enrollment or during their CAPT follow-up. Among the 1477 eyes of 744 patients, advanced AMD developed in 332 (22.5%) eyes of 242 (32.5%) patients, CNV in 222 (15.0%) eyes of 176 (23.7%) patients, and GA in 114 (7.7%) eyes of 80 (10.8%) patients.

Table 2 provides the estimated risk ratios for AMD outcomes associated with statin use without and with adjustment of other risk factors of AMD. For development of advanced AMD, the estimated risk ratios ranged from 1.0 to 1.2 for all analysis models with 95% CIs spanning 1.0 in all cases. Within CAPT patients, statin use was associated with slightly elevated risk for CNV. The estimated risk ratios associated with statin use for CNV ranged from 1.2 to 1.4 for all analysis models with 95% CIs spanning 1.0 in all cases. Statin use was associated with lower risk for GA. The estimated risk ratios ranged from 0.5 to 0.8 in the various models and with 95% CIs spanning 1.0 in all cases. Overall, adjusted and unadjusted estimates of the risk ratios were similar, as were estimates from analyses conducted using both eyes of the patient and those using only the first affected eye for the patient. Analyses including only the subgroup of patients who either never used statins or who used statins continuously during their follow-up yielded risk ratio estimates that were slightly lower than in the corresponding models including all patients. Similar results were obtained when only untreated eyes were considered in each of the models in Table 2 (data not shown).

Table 2. Risk Ratios Associated with Statin Use from the Time-Dependent Cox Proportional Hazards Model

Outcome	Unit of Analysis	Patients Included	No. at Risk	Events	Unadjusted RR (95% CI)	Adjusted RR (95% CI)
Advanced age-related macular degeneration	Eye	All	1477	332	1.12 (0.85–1.47)	1.15 (0.87–1.52)
		Subgroup	1097	231	0.99 (0.66–1.50)	1.06 (0.69–1.63)
	Patient	All	744	242	1.14 (0.86–1.53)	1.19 (0.89–1.60)
		Subgroup	553	170	1.03 (0.68–1.56)	1.14 (0.75–1.74)
Choroidal neovascularization	Eye	All	1477	222	1.36 (1.00–1.84)	1.35 (0.99–1.83)
		Subgroup	1097	151	1.29 (0.81–2.03)	1.30 (0.82–2.04)
	Patient	All	744	176	1.33 (0.96–1.84)	1.32 (0.95–1.84)
		Subgroup	553	122	1.25 (0.79–1.98)	1.30 (0.82–2.06)
Geographic atrophy	Eye	All	1468	114	0.71 (0.41–1.23)	0.80 (0.46–1.39)
		Subgroup	1089	85	0.58 (0.24–1.41)	0.66 (0.26–1.65)
	Patient	All	743	80	0.70 (0.41–1.19)	0.75 (0.43–1.30)
		Subgroup	552	61	0.54 (0.23–1.27)	0.69 (0.29–1.66)

CI = confidence interval; RR = risk ratio.

Discussion

The established link between AMD and the Y402H genetic variant of complement factor H, the finding of elevated C-reactive protein levels among patients with all stages of AMD, and the ability of statins to reduce C-reactive protein levels create a strong biological basis for statins to lower the risk of AMD.[24–29] Based on reports of a strong protective effect of statin use on AMD by Hall and some of the previous investigations,[1,3,5,7,8,11] a few researchers have called for the initiation of clinical trials of statins as a protective treatment for AMD.[5,30,31] However, when all observational epidemiologic studies to date are considered, the evidence has been inconsistent on the association of statins and AMD. In addition, the feasibility of a clinical trial of statins among a group of older individuals is jeopardized by the high proportion, approaching 50%, of such people who already use statins for control of cholesterol and other cardiovascular indications.[32,33]

The data from CAPT contain the largest number of patients with advanced AMD to date in any study of the association with statins. Participants in CAPT provided starting and stopping years for their statin use so that the timing of statin use could be established as preceding the development of advanced AMD, and the presence of advanced AMD was determined from review of color fundus photography and annual fluorescein angiography. The data from CAPT do not support a large effect of statins in decreasing the risk of developing advanced AMD among patients with bilateral drusen. Overall, the estimated risk ratio was slightly above 1.0 and the lower bound of the 95% CI (0.87) includes only modest treatment effects. Statistical models that include the status of each eye of a patient theoretically have more precision; that is, lower *P* values and narrower CIs, than models that consider only the development of advanced AMD in the first eye affected. However, they did not yield statistically significant results for statin use among the CAPT patients. Similarly, there were no statistically significant effects of statins detected for the development of CNV only or for the development of GA.

The starting and stopping dates of statin use reported by patients based on their own recall may not have been accurate. Report of never using statins and for sustained use of statins during participation in CAPT is less sensitive to errors in recalling dates. There was little impact on the risk estimates when only this second group of patients was included in the analysis. Also, information on some established risk factors, for example, risk alleles for genes associated with complement activation, was not available for all CAPT participants. However, we have no reason to believe that statin use is associated with these genetic risk factors.

If statins have a protective effect, it is unlikely that the effect would be immediate with the initiation of use. The expected length of a possible lag period for statins to have an effect on inflammation or on another step in the causal pathway is unknown. The analyses limited to the subgroup of patients who either were taking statins at entry into CAPT and maintained their use or did not ever take statins were performed to explore whether longer term users were at decreased risk. Risk ratios for developing AMD, CNV, and GA did not change appreciably when only this subgroup was analyzed. However, only 12% of CAPT patients were using statins when they enrolled in CAPT.

Because of the effects of statins on both inflammation and vascular endothelial function, a more pronounced effect might be expected for protection from CNV than for GA. However, the CAPT data yielded risk ratios for statins that were lower for GA (risk ratio, 0.8) than for CNV (risk ratio, 1.30). Risk ratios $\geq$1.0 for CNV and $<$1.0 for GA were also reported from the 2 other studies that have examined the risk of CNV and GA separately.[4,14] Confidence intervals for all the estimates are wide; however, it does not seem that the results for GA are masking a strong protective effective for CNV. In the Beaver Dam Eye Study, the risk ratio for prevalence of CNV was 1.50 (95% CI, 0.20–11.34) and of GA was 0.76 (95% CI, 0.10–5.78); the risk ratio for incident CNV was 1.25 (95% CI, 0.16–9.54) and was 0.25 for incident GA (95% CI, 0.05–1.22).[4] In the Women's Health Initiative Sight Exam, the risk ratio for prevalent CNV was 0.99 (95% CI, 0.45–2.18) and was 0.73 (95% CI, 0.16–3.34) for GA.[14]

All of the observational studies of the effect of statins on AMD, including CAPT, suffer from the fact that statins are prescribed for primary and secondary prevention of coronary heart disease, myocardial infarction, stroke, and peripheral artery disease. Because AMD shares some of the same risk factors as these diseases, there is the possibility that a protective effect of statins for AMD is masked by the fact that only patients at high risk for AMD are prescribed statins. Only a randomized clinical trial can definitively address the impact of statin use on AMD; however, the high proportion of the older people already on statins would make recruitment and treatment compliance difficult. In addition, if the use of statins in older people continues to increase, the relevance of the question will diminish.

References

1. Hall NF, Gale CR, Syddall H, et al. Risk of macular degeneration in users of statins: cross sectional study. BMJ 2001;323:375–6.
2. Guymer RH, Chiu AW, Lim L, Baird PN. HMG CoA reductase inhibitors (statins): do they have a role in age-related macular degeneration? Surv Ophthalmol 2005;50:194–206.
3. Delcourt C, Michel F, Colvez A, et al, POLA Study Group. Associations of cardiovascular disease and its risk factors with age-related macular degeneration: the POLA study. Ophthalmic Epidemiol 2001;8:237–49.
4. Klein R, Klein BE, Tomany SC, et al. Relation of statin use to the 5-year incidence and progression of age-related maculopathy. Arch Ophthalmol 2003;121:1151–5.
5. McCarty CA, Mukesh BN, Guymer RH, et al. Cholesterol-lowering medications reduce the risk of age-related maculopathy progression [letter]. Med J Aust 2001;175:340.
6. McCarty CA, Mukesh BN, Fu CL, et al. Risk factors for age-related maculopathy: the Visual Impairment Project. Arch Ophthalmol 2001;119:1455–62.
7. McGwin G Jr, Owsley C, Curcio CA, Crain RJ. The association between statin use and age related maculopathy. Br J Ophthalmol 2003;87:1121–5.
8. McGwin G Jr, Xie A, Owsley C. The use of cholesterol-lowering medications and age-related macular degeneration. Ophthalmology 2005;112:488–94.

9. McGwin G Jr, Modjarrad K, Hall TA, et al. 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors and the presence of age-related macular degeneration in the Cardiovascular Health Study. Arch Ophthalmol 2006;124:33–7.
10. Smeeth L, Cook C, Chakravarty U, et al. A case control study of age related macular degeneration and use of statins. Br J Ophthalmol 2005;89:1171–5.
11. Wilson HL, Schwartz DM, Bhatt HR, et al. Statin and aspirin therapy are associated with decreased rates of choroidal neovascularization among patients with age-related macular degeneration. Am J Ophthalmol 2004;137:615–24.
12. van Leeuwen R, Tomany SC, Wang JJ, et al. Is medication use associated with the incidence of early age-related maculopathy? Pooled findings from 3 continents. Ophthalmology 2004; 111:1169–75.
13. Chuo JY, Wiens M, Etminan M, Maberley DA. Use of lipid-lowering agents for the prevention of age-related macular degeneration: a meta-analysis of observational studies. Ophthalmic Epidemiol 2007;14:367–74.
14. Klein R, Deng Y, Klein BE, et al. Cardiovascular disease, its risk factors and treatment, and age-related macular degeneration: Women's Health Initiative Sight Exam ancillary study. Am J Ophthalmol 2007;143:473–83.
15. Klein R, Knudtson MD, Klein BE. Statin use and the five-year incidence and progression of age-related macular degeneration. Am J Ophthalmol 2007;144:1–6.
16. Tan JS, Mitchell P, Rochtchina E, Wang JJ. Statins and the long term risk of incident age-related macular degeneration: the Blue Mountains Eye Study. Am J Ophthalmol 2007;143:685–7.
17. Complications of Age-Related Macular Degeneration Prevention Trial Research Group. Laser treatment in patients with bilateral large drusen: the Complications of Age-related Macular Degeneration Prevention Trial (CAPT). Ophthalmology 2006;113:1974–86.
18. Complications of Age-Related Macular Degeneration Prevention Trial Study Group. The Complications of Age-related Macular Degeneration Prevention Trial (CAPT): rationale, design and methodology. Clin Trials 2004;1:91–107.
19. Complications of Age-Related Macular Degeneration Prevention Trial Research Group. Baseline characteristics, the 25-Item National Eye Institute Visual Functioning Questionnaire, and their associations in the Complications of Age-Related Macular Degeneration Prevention Trial (CAPT). Ophthalmology 2004;111:1307–16.
20. Klein R, Davis MD, Magli YL, et al. The Wisconsin Age-Related Maculopathy Grading System. Ophthalmology 1991; 98:1128–34.
21. Bird AC, Bressler NM, Bressler SB, et al, International ARM Epidemiological Study Group. An international classification and grading system for age-related maculopathy and age-related macular degeneration. Surv Ophthalmol 1995;39:367–74.
22. Wei LJ, Lin DY, Weissfeld L. Regression analysis of multivariate incomplete failure time data by modeling marginal distributions. J Am Stat Assoc 1989;84:1065–73.
23. Complications of Age-Related Macular Degeneration Prevention Trial (CAPT) Research Group. Risk factors for choroidal neovascularization and geographic atrophy in the Complications of Age-Related Macular Degeneration Prevention Trial. Ophthalmology 2008;115:1474–9.
24. Hageman GS, Luthert PJ, Victor Chong NH, et al. An integrated hypothesis that considers drusen as biomarkers of immune-mediated processes at the RPE-Bruch's membrane interface in aging and age-related macular degeneration. Prog Retin Eye Res 2001;20:705–32.
25. Despriet DD, Klaver CC, Witteman JC, et al. Complement factor H polymorphism, complement activators, and risk of age-related macular degeneration. JAMA 2006;296:301–9.
26. Seddon JM, Gensler G, Milton RC, et al. Association between C-reactive protein and age-related macular degeneration. JAMA 2004;291:704–10.
27. Seddon JM, George S, Rosner B, Rifai N. Progression of age-related macular degeneration: prospective assessment of C-reactive protein, interleukin 6, and other cardiovascular biomarkers. Arch Ophthalmol 2005;123:774–82.
28. Ridker PM, Rifai N, Pfeffer MA, et al, Cholesterol and Recurrent Events (CARE) Investigators. Long-term effects of pravastatin on plasma concentration of C-reactive protein. Circulation 1999;100:230–5.
29. Ridker PM, Rifai N, Lowenthal SP. Rapid reduction in C-reactive protein with cerivastatin among 785 patients with primary hypercholesterolemia. Circulation 2001;103:1191–3.
30. McGwin G Jr, Owsley C. Statins and age-related macular degeneration [letter]. Am J Ophthalmol 2004;138:688; author reply 688–9.
31. Wong TY, Rogers SL. Statins and age-related macular degeneration: time for a randomized controlled trial? Am J Ophthalmol 2007;144:117–9.
32. Miller GE, Stagnitti MN. Statin use in the civilian noninstitutionalized Medicare population in 2002. Statistical Brief #96. September 2005. Available at: http://www.meps.ahrq.gov/mepsweb/data_files/publications/st96/stat96.pdf. Accessed May 20, 2009.
33. Stagnitti MN. Trends in statins utilization and expenditures for the U.S. civilian noninstitutionalized population, 2000 and 2005. Statistical Brief #205. May 2008. Available at: http://www.meps.ahrq.gov/mepsweb/data_files/publications/st205/stat205.pdf. Accessed May 20, 2009.

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