Published in final edited form as:

Ann Epidemiol. 2011 March ; 21(3): 156–163. doi:10.1016/j.annepidem.2010.10.003.

Androgen Deprivation Therapy and Cataract Incidence Among Elderly Prostate Cancer Patients in the United States

Jennifer Beebe-Dimmer, PHD, Hal Morgenstern, PHD, Karynsa Cetin, MPH, Cecilia Yee, MS, Monina Bartoces, PHD, Vahakn Shahinian, MD, Jon Fryzek, PHD, John Acquavella, PHD, and Kendra I. Schwartz, MD

Division of Population Studies and Prevention, Karmanos Cancer Institute (J.B.-D., C.Y., K.L.S.), Detroit, MI; Departments of Internal Medicine (J.B.-D., C.Y.) and Family Medicine & Public Health Sciences (M.B., K.L.S.), Wayne State University, Detroit, MI; Departments of Epidemiology and Environmental Health Sciences and Comprehensive Cancer Center (H.M.), University of Michigan School of Public Health, Ann Arbor, MI; University of Michigan Medical School (V.S.), Ann Arbor, MI; and Department of Global Epidemiology, Amgen Inc. (K.C., J.F., J.A.), Thousand Oaks, CA

Abstract

Purpose—The side-effects associated with androgen deprivation therapy (ADT) include weight gain, dyslipidemia, and insulin resistance. As cataracts have been linked to these metabolic abnormalities, an increased risk of cataract may be another adverse consequence of ADT use.

Methods—Using data from the Surveillance, Epidemiology and End Results-Medicare database, we estimated risk of cataract associated with ADT among 65,852 prostate-cancer patients. ADT treatment was defined as at least one dose of a gonadotropin-releasing hormone agonist or orchiectomy within 6 months after prostate cancer diagnosis. The outcome measure was a first claim of cataract diagnosis identified in Medicare claim files. Cox regression was used to estimate hazard ratios (HR) for the effects of ADT treatment, controlling for confounders.

Results—Gonadotropin-releasing hormone agonist use was associated with a modest increase in cataract incidence (HR 1.09, 95% confidence interval 1.06–1.12). Orchiectomy was also associated with an increased risk of cataract among men with no history of cataract prior to prostate cancer diagnosis (HR 1.26, 95% confidence interval 1.07–1.47).

Conclusions—In the first systematic investigation of the association between ADT and cataract, our results suggest an elevation in the incidence of cataract among ADT users. Further study, preferably prospective in design, is needed to provide additional evidence to support or refute these findings.

Keywords

Epidemiology; GnRH Agonist; Lens Opacities; Orchiectomy; Prostate Cancer; SEER-Medicare

Introduction

Prostate cancer is the most common invasive cancer diagnosed among men in the United States; an estimated 192,280 new cases were reported in 2009 (1). Advances in treatment for the disease coupled with the widespread adoption of prostate-specific antigen screening for early detection has resulted in marked improvement in survival among prostate cancer patients (2, 3). As a consequence of the increase in number of prostate cancer survivors in the United States, the burden of treating and monitoring patients for disease recurrence, both economically and with respect to patient quality of life, is substantial. It has been estimated that approximately one-third of all prostate cancer patients receive some form of androgen deprivation therapy (ADT) as part of their treatment (4). A number of adverse side-effects have been reported by prostate cancer patients receiving ADT, including weight gain and dyslipidemia and an increased risk of developing diabetes and cardiovascular disease, all of which are linked to the ADT-induced hypogonadal state (4).

More than 20 million Americans age 40 years and older have been diagnosed with cataracts, and this number is projected to increase approximately 50% during the next decade (5). Cost for the treatment of cataract already accounts for the majority of vision-related Medicare expenditures and is expected to expand over time with the projected increase in its prevalence (6). Reducing patient exposures to risk factors would not only reduce overall health care costs but prevent cataract-associated vision loss in the U.S. elderly population. Modifiable factors linked to cataract occurrence include smoking, obesity, chronic exposure to ultraviolet B light, multivitamin, and long-term steroid use (7–12).

In this investigation, we estimate the risk of cataract associated with ADT among prostate cancer patients, using data gathered as part of the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) registry linked with the Medicare claims database developed by the Centers for Medicare and Medicaid Services. The risk of cataract associated with ADT has never been systematically investigated, yet there are biological associations that point to the potential for a causative relationship. If a causal relation between ADT and cataract occurrence exists, it may be mediated via the onset of specific features of the insulin resistance syndrome (diabetes, abdominal obesity, hypertension and dyslipidemia), which has been identified as a consequence of ADT use (4, 13).

Methods

The SEER-Medicare dataset is a unique resource linking two population-based data sources to provide detailed information about elderly patients with cancer in the United States. Sponsored by the National Cancer Institute, the SEER program is a network of population-based cancer registries that routinely collects information on patients with a new diagnosis of invasive cancer residing within one of the registry catchment areas. SEER is currently composed of 18 statewide or regional cancer registries collecting data on patient demographics, tumor histology and pathology, first course of treatment and survival post-diagnosis. Through the linking of SEER registry data to Medicare enrollment and claims information for patients diagnosed in the SEER regions, the SEER-Medicare database provides additional information on treatment and outcomes of approximately one-quarter of patients aged 65 and older diagnosed with cancer in the United States (14).

The eligible patients for the current investigation were diagnosed at age 66 years and older with primary invasive prostate cancer (site code C61.9, International Classification of Diseases for Oncology 3rd Edition) between January 1, 1996, and December 31, 2003, captured among 1 of 16 SEER registries (Connecticut, Hawaii, Iowa, New Mexico, Utah, Atlanta, rural Georgia, Detroit, Seattle-Puget Sound, Los Angeles, San Jose-Monterey, San

San Francisco-Oakland, Greater California, Kentucky, Louisiana, or New Jersey). Patients not continuously enrolled in both Part A and Part B Medicare for the 12 months before and after being diagnosed with prostate cancer were excluded in an effort to minimize the misclassification of history of cataract as well as other comorbidities before prostate cancer diagnosis. Patients who were members of a health maintenance organization (HMO) at any point in the 12 month period before prostate cancer diagnosis as well as the 12-month period post-diagnosis were also excluded to avoid the potential for missing information because of claims not processed through Medicare. Patients receiving ADT before prostate cancer diagnosis were excluded, as well as those with cataracts occurring within the 12-month period postcancer diagnosis to eliminate cases unlikely attributable to ADT exposure. Finally, we limited our comparisons to patients receiving ADT within the first 6 months after diagnosis with those not receiving ADT at any point over follow-up, leaving a total study population of 65,852 men available for analysis (Figure 1).

Exposure to ADT was based on the documentation of at least one dose of a gonadotropin-releasing hormone (GnRH) agonist or orchiectomy within 6 months after prostate cancer diagnosis. To calculate GnRH dose, we used the methods developed by one of our co-authors (V.S.) as recommended by the National Cancer Institute (15, 16). Dose was calculated from each instance of a GnRH agonist injection noted on separate days for the 12-month period after diagnosis. Because GnRH agonists are administered as depot injections with the dosage given depending on the intended regimen (every 1, 3, 4 month[s]), the dosage recorded from the Medicare claims files was then converted to a once-a-month regimen.

Cataract diagnoses were identified through *International Classification of Diseases*, 9th revision codes and cataract surgeries using Current Procedural Terminology codes (Appendix A). Cataract history from age 65 years was documented for all patients on the basis of the presence of an aforementioned cataract diagnosis or procedure code indicating surgery for cataract in Medicare inpatient and outpatient files before the date of diagnosis of prostate cancer. The outcome measure in this investigation, incident cataract, was defined as a first claim for cataract diagnosis occurring at least 12 months post-prostate cancer diagnosis. Cataract diagnoses extracted from the Medicare physician (carrier) claims files must have been listed as the principal diagnosis and coded as an “allowable” claim. Patients were followed until December 31, 2006, for cataract claims, representing the end of complete follow-up for patients included in SEER-Medicare. Patient characteristics (listed Table 1) were examined for their relations with cataract incidence. Ecologic measures of socioeconomic position were evaluated by describing the education and income level of the census tract in which the patient resided within at the time of diagnosis (17). In addition, information on the frequency of outpatient physician visits was extracted from Medicare Part A to address the possibility of enhanced medical surveillance increasing the likelihood of cataract diagnosis, that is, detection bias (see Appendix A for codes). Multiple physician contacts within the same day were counted only once; hence, the resulting measure amounted to the number days of patient contact with any physician in the 12-month period before prostate cancer diagnosis.

Statistical Analysis

All statistical analyses were performed with Statistical Analysis Software (SAS Institute Inc. v. 9.1, Cary, NC). We calculated the proportion of patients receiving ADT as part of their treatment according to various baseline characteristics. We estimated the incidence of cataract (with 95% confidence intervals [CIs]) for all patients, as well as according to ADT treatment and cataract history before diagnosis. The Kaplan-Meier method was used to estimate unadjusted, cataract-free survival according to ADT status. Cox proportional hazards regression was used to estimate hazard ratios and 95% CIs associated with ADT

controlling for potential confounders, as well as estimates stratified by a history of cataract before prostate cancer diagnosis. The outcome was the time (in months) from 12 months after cancer diagnosis to cataract diagnosis or censoring. Prostate cancer patients with no cataract claim during follow-up were censored at (i) death, (ii) loss of, or change in, Medicare coverage, or (iii) December 31, 2006—whichever came first. Final models included age at diagnosis, race, education, Charlson comorbidity index, tumor grade, other treatments, and number of days with physician contact in the 12 months before diagnosis). We repeated the analysis restricting the outcome to cataract surgery among patients with a cataract diagnosis.

We approached our analyses by using two different methods: the first, as previously described, limited the exposed patient population to those receiving ADT within the first 6 months of diagnosis. Our second strategy considered ADT a time-dependent covariate. A 12-month moving window was selected for analysis, whereby beginning at 12 months post-prostate cancer diagnosis, patient records were reviewed for a claim of cataract and ADT exposure in the previous 12-month period. ADT exposure in the previous 12 months was evaluated for the presence of a claim for GnRH agonist or orchiectomy (ever/never), as well as ADT dose in the same 12-month period among patients with at least one claim of a GnRH agonist. Because both strategies produced nearly identical estimates of cataract risk associated with ADT use, most likely attributable to the relatively small proportion of patients initiating ADT more than 6 months after diagnosis (~5%), we elected to present the HRs generated from our original strategy.

Results

Table 1 summarizes the proportion of prostate cancer patients receiving ADT according to relevant characteristics available in the SEER-Medicare database. Of the 65,852 prostate cancer patients diagnosed at age 66 years and older included in this investigation, 49% had received some form of ADT within the first 6 months of their diagnosis, with approximately 47% of patients prescribed GnRH agonists and 2% of patients undergoing orchiectomy. The overall incidence of cataract among patients in this investigation was 111 newly diagnosed cases per 1000 person-years of observation. The crude rate of cataract was higher among patients on GnRH agonist (117 cases per 1000 person-years) than among patients not receiving any ADT (106 cases per 1000 person-years; $p < .01$; Table 2). When rates were stratified by cataract history before diagnosis, a similar trend was observed among men with no history of cataract before prostate cancer diagnosis; however, the incidence of cataract was nearly identical between those on GnRH agonists and those not on ADT among patients with a history of cataract. In contrast, almost no difference was observed in the crude incidence of cataract comparing orchiectomy patients to non-ADT users. Kaplan-Meier plots comparing ADT (GnRH agonist or orchiectomy within the first 6 months of diagnosis) to non-ADT patients also indicate increased cataract incidence among ADT users among patients with no history of cataract prior to diagnosis (Figure 2).

Use of at least one dose of a GnRH agonist in the first 6 months post-prostate cancer diagnosis was associated with a 9% increase in the incidence rate of cataract over the study period (HR 1.09; 95% CI 1.06–1.12), after adjustment for confounding variables (Table 3). The estimated effect of GnRH agonist use was slightly stronger among patients with no history of cataract (HR 1.12; 95% CI 1.08–1.16) than among patients with a cataract history (HR 1.05; 95% CI 1.01–1.09). There was no consistent monotonic trend in the association between GnRH agonist dose and cataract incidence for men with or without a cataract history. Orchiectomy was positively associated with cataract incidence among men with no previous history of cataract (HR 1.26; 95% CI 1.07–1.47), but less so among patients with a history of cataract (HR 1.07; 95% CI 0.90–1.28). Our analysis restricted to only those

patients with a cataract surgical claim produced similar hazard ratios associated with ADT use (results not shown).

Discussion

In this population-based study of elderly prostate cancer patients, we observed that androgen deprivation therapy was associated with a modest increase in cataract incidence. The hazard ratio for the estimated effect of GnRH agonists was slightly greater for patients without a history of cataract before prostate cancer diagnosis compared to patients with a history; and an association between orchiectomy and cataract was observed only among patients without a history of cataract before diagnosis and only after adjustment for confounding variables. If the observed associations reflect a causal effect of ADT on cataract incidence, the impact of these findings is worth some consideration given the prevalence of ADT use in the United States. Approximately 8% of new cataract diagnoses among ADT users would be attributable to ADT exposure. Provided the prevalence of ADT use in the total U.S. population of elderly men with prostate cancer is similar to what was observed in this investigation, approximately 5% of all newly diagnosed cataracts would be attributable to use of ADT.

The biologic mechanism whereby ADT influences development of cataract is not obvious; there is no evidence in the literature to suggest that induced hypogonadism is directly responsible for either the initiation or progression of lens opacities. However, it is worth noting that there have been several reports of clustering of hypogonadism and cataracts in patients with Bloom and Martsolf syndromes, both rare, autosomal-recessive disorders (18, 19). Another possible explanation is that weight gain and metabolic abnormalities, including insulin resistance and dyslipidemia, presumably resulting from the hypogonadic state, may induce cataracts in these patients. It has been shown that treatment with GnRH agonists results in an increase in subcutaneous fat mass, decreases in lean body mass (20, 21) and increases in total cholesterol, high-density lipoprotein cholesterol and triglyceride levels (22). GnRH agonists have also been shown to induce insulin resistance (23, 24). These phenomena occur shortly after the initiation of treatment (<3 months of therapy) and are suspected to contribute significantly to an increase in risk of diabetes and cardiovascular disease (20). However, the findings of Keating et al. (25), namely the absence of associations between orchiectomy and most measured outcomes in their study, suggest that the adverse influence of GnRH agonists on metabolic syndrome features may be a biochemical consequence of the analog rather than a hypogonadic state. A report describing a single case of cataract induced by luteinizing hormone-releasing hormone analog therapy as part of neoadjuvant treatment prescribed for localized prostate cancer was recently published (26). A 52-year-old patient without significant visual impairment was reportedly receiving monthly doses of Zoladex (goserelin acetate, 3.6 mg) coupled with external beam radiation for an unspecified period. He developed a right posterior subcapsular cataract subsequent to a change from the monthly injections to a greater-dose injection (3-month [10.8 mg]).

We acknowledge that there are several noncausal explanations for our observed findings. The increase in cataract claims among men with prostate cancer on GnRH agonists may be the result of enhanced surveillance, as these patients might have greater opportunity for cataract diagnosis as a product of more frequent contact with their physician. In an attempt to assess the impact of this bias, our analysis controlled for the number of physician visits in the 12-month period before prostate cancer diagnosis and found that accounting for prediagnosis physician surveillance reduced, but did not eliminate the association of GnRH agonist use with new cataract diagnosis. Furthermore, among our patients with no previous history of cataract diagnosis, orchiectomy was associated with the greatest risk of incident

cataract, a finding inconsistent with the hypothesis that a detection bias explains our findings.

One of the inherent limitations of observational studies examining the effect of treatment on an outcome is confounding by indication (27). ADT is widely prescribed to prostate cancer patients of varying stages of disease. Adjuvant use of ADT among patients with locally advanced disease has been shown to reduce biochemical recurrence and improve overall survival (28). It is also prescribed to patients with metastatic disease to improve bone pain and quality of life (29). Our findings indicate that ADT was used more frequently among prostate cancer patients with high-grade, advanced-stage disease. A repeat analysis including patients initiating ADT within 24 months of diagnosis found no difference in estimated effects (results not shown). Furthermore, adjustment for available baseline characteristics, including clinical tumor stage at diagnosis, between ADT users and nonusers do not explain our findings. However, because relatively little is known about the risk factors for cataract other than age, we cannot rule out the possibility that the association observed in this study might be wholly or partly due to the effects of unmeasured confounders.

Misclassification of cataract history is also a possible source of bias in this study. We recognize that we may not identify all cases of cataract because SEER-Medicare has claim data only on patients aged 65 years and older. We were able to minimize misclassification to some extent by including only those patients aged 66 years and older at time of prostate cancer diagnosis in our study cohort allowing at minimum, a 12-month review of claims data prior to diagnosis for history of cataract. Any cataract history before the age of 65 would not be captured, the net result of which would be misclassification among men with a history of cataract. Likewise, it is possible under the same circumstance that a patient classified as having a history of cataract in one eye may have in fact sustained cataracts in both eyes and could be considered no longer at risk for subsequent cataract. We cannot predict the magnitude of such bias with the available data. If one assumes that this misclassification is similar among men with respect to ADT, our analysis would underestimate any true effect of exposure.

Medicare data are limited to a small degree because of the potential for missing information on services that are either not covered by Medicare or services covered by, but not billed to, Medicare. For this reason, we excluded patients participating in an HMO in the 12 months before diagnosis and censored patients with any change or loss in Medicare coverage over the course of study. The exclusion of HMO enrollees would limit the generalizability of our findings because HMO enrollees tend to be younger and healthier than other Medicare beneficiaries (30). An assessment of the representativeness of SEER patients included in the SEER-Medicare database with the elderly U.S. population indicates that although the age and gender distribution is similar, a greater proportion of SEER-Medicare patients belong to other minority (nonblack, nonwhite) groups and reside in urban areas (30). Finally, these findings are not necessarily generalizable to patients diagnosed with prostate cancer at younger ages.

Despite these limitations, SEER-Medicare is a large, population-based, diverse, data resource that is well-suited for exploring new associations such as the ones reported here. Further study is clearly warranted to either support or refute these findings. Improving our understanding of the consequences of widely used treatments such as ADT is important, equipping physicians with important information to communicate to patients and work together to make informed choices about treatment after a cancer diagnosis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We thank the SEER-Medicare Program Office (<http://healthservices.cancer.gov/seermedicare/obtain/use.html>)

This study was funded by Amgen Inc. Thousand Oaks, CA 91320.

References

1. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Murray T, Thun M. Cancer statistics, 2008. *CA Cancer J Clin.* 2008; 58:71–96. [PubMed: 18287387]
2. Lu-Yao GL, Albertsen PC, Moore DF, Shih W, Lin Y, DiPaola R, et al. Outcomes of localized prostate cancer following conservative management. *JAMA.* 2009; 302:1202–1209. [PubMed: 19755699]
3. Etzioni R, Gulati R, Falcon S, Penson DF. Impact of PSA screening on the incidence of advanced stage prostate cancer in the United States: A surveillance modeling approach. *Med Decis Making.* 2008; 28:323–331. [PubMed: 18319508]
4. Guise TA, Oefelein MG, Eastham JA, Cookson MS, Higano CS, Smith MR. Estrogenic side effects of androgen deprivation therapy. *Rev Urol.* 2007; 9:163–180. [PubMed: 18231613]
5. Congdon N, Vingerling JR, Klein BE, West S, Friedman D, Kempen J, et al. Prevalence of cataract and pseudophakia/aphakia among adults in the United States. *Arch Ophthalmol.* 2004; 122:487–494. [PubMed: 15078665]
6. Ellwein LB, Urato CJ. Use of eye care and associated charges among the Medicare population: 1991–1998. *Arch Ophthalmol.* 2002; 120:804–811. [PubMed: 12049587]
7. Abraham AG, Condon NG, West GE. The new epidemiology of cataract. *Ophthalmol Clin North Am.* 2006; 19:415–425. [PubMed: 17067897]
8. West S. Epidemiology of cataract: Accomplishments over 25 years and future directions. *Ophthalmic Epidemiol.* 2007; 14:173–178. [PubMed: 17896293]
9. Curtis JR, Westfall AO, Allison J, Bijlsma J, Freeman A, George V, et al. Population-based assessment of adverse events associated with long-term glucocorticoid use. *Arthritis Rheum.* 2006; 55:420–426. [PubMed: 16739208]
10. Hiller R, Sperduto RD, Ederer F. Epidemiologic associations with nuclear, cortical, and posterior subcapsular cataracts. *Am J Epidemiol.* 1986; 124:916–925. [PubMed: 3776974]
11. Jacques PF, Moeller SM, Hankinson SE, Chylack L Jr, Rogers G, Tung W, et al. Weight status, abdominal adiposity, diabetes, and early age-related lens opacities. *Am J Clin Nutr.* 2003; 78:400–405. [PubMed: 12936921]
12. Weintraub JM, Willett WC, Rosner B, Colditz GA, Seddon JM, Hankinson SE. A prospective study of the relationship between body mass index and cataract extraction among US women and men. *Int J Obes Relat Metab Disord.* 2002; 26:1588–1595. [PubMed: 12461675]
13. Michaelson MD, Cotter SE, Gargollo PC, Zietman AL, Dahl DM, Smith MR. Management of complications of prostate cancer treatment. *CA Cancer J Clin.* 2008; 58:196–213. [PubMed: 18502900]
14. Potosky AL, Riley GF, Lubitz JD, Mentnech RM, Kessler LG. Potential for cancer related health services research using a linked Medicare-tumor registry database. *Med Care.* 1993; 31:732–748. [PubMed: 8336512]
15. [Accessed October 26, 2010] 2010. Available at: <http://www.healthservices.cancer.gov/seermedicare/considerations/prostate.html>
16. Shahinian VB, Kuo YF, Freeman JL, Goodwin JS. Risk of fracture after androgen deprivation for prostate cancer. *N Engl J Med.* 2005; 352:154–164. [PubMed: 15647578]

17. Bach PB, Guadagnoli E, Schrag D, Schussler N, Warren JL. Patient demographic and socioeconomic characteristics in the SEER-Medicare database applications and limitations. *Med Care*. 2002; 40:IV–25.
18. Cefle K, Ozturk S, Gozum N, Duman N, Mantar F, Guler K, Palanduz S, et al. Lens opacities in Bloom syndrome: Case report and review of the literature. *Ophthalmic Genet*. 2007; 28:175–178. [PubMed: 17896317]
19. Ehara H, Utsunomiya Y, Ieshima A, Maegaki Y, Nishimura G, Takeshita K, Ohno K. Martsolf syndrome in Japanese siblings. *Am J Med Genet A*. 2007; 143A:973–978. [PubMed: 17394201]
20. Smith MR, Finkelstein JS, McGovern FJ, Zietman A, Fallon M, Schoenfeld D, Kantoff P. Changes in body composition during androgen deprivation therapy for prostate cancer. *J Clin Endocrinol Metab*. 2002; 87:599–603. [PubMed: 11836291]
21. Smith MR. Changes in fat and lean body mass during androgen-deprivation therapy for prostate cancer. *Urology*. 2004; 63:742–745. [PubMed: 15072892]
22. Smith MR. Osteoporosis and other adverse body composition changes during androgen deprivation therapy for prostate cancer. *Cancer Metastasis Rev*. 2002; 21:159–166. [PubMed: 12465755]
23. Smith MR. Androgen deprivation therapy and risk for diabetes and cardiovascular disease in prostate cancer survivors. *Curr Urol Rep*. 2008; 9:197–202. [PubMed: 18765113]
24. Smith MR. Changes in body composition during hormonal therapy for prostate cancer. *Clin Prostate Cancer*. 2003; 2:18–21. [PubMed: 15046678]
25. Keating NL, O'Malley AJ, Smith MR. Diabetes and cardiovascular disease during androgen deprivation therapy for prostate cancer. *J Clin Oncol*. 2006; 24:4448–4456. [PubMed: 16983113]
26. Al-Enezi A, Kehinde EO, Behbehani AM, Sheikh ZA. Luteinizing hormone-releasing hormone analogue-induced cataract in a patient with prostate cancer. *Med Princ Pract*. 2007; 16:161–163. [PubMed: 17303956]
27. Salas M, Hofman A, Stricker BH. Confounding by indication: an example of variation in the use of epidemiologic terminology. *Am J Epidemiol*. 1999; 149:981–983. [PubMed: 10355372]
28. Messing E. The timing of hormone therapy for men with asymptomatic advanced prostate cancer. *Urol Oncol*. 2003; 21:245–254. [PubMed: 12954493]
29. Chodak GW, Keane T, Klotz L. Critical evaluation of hormonal therapy for carcinoma of the prostate. *Urology*. 2002; 60:201–208. [PubMed: 12137810]
30. Warren JL, Klabunde CN, Schrag D, Bach PB, Riley GF. Overview of the SEER-Medicare data: Content, research applications, and generalizability to the United States elderly population. *Med Care*. 2002; 40:IV–18.

Selected Abbreviations and Acronyms

ADT	androgen deprivation therapy
SEER	Surveillance, Epidemiology and End Results
HMO	health maintenance organization
GnRH	gonadotropin-releasing hormone
CI	confidence interval

Figure 1.
Prostate cancer patients participating in SEER-Medicare study.

Figure 2. Unadjusted cataract-free survival among ADT users and nonusers according to history of cataract before the diagnosis of prostate cancer.

Table 1
Frequency distributions of patient characteristics in SEER-Medicare study of androgen deprivation therapy and cataract risk in men with prostate cancer

Characteristic	n	%*	Proportion on ADT, %
Total	65852		48.5
Age, in years			
66–69	17721	26.9	34.9
70–74	21301	32.4	45.9
75–79	15712	23.9	56.1
80	11118	16.9	64.4
Race			
White	51961	78.9	48.1
Black	6588	10.0	45.4
Other	5842	8.9	54.0
Unknown	1461	2.5	54.8
SEER region			
San Francisco	2801	4.3	43.8
Connecticut	5249	8.0	53.9
Detroit	8661	13.2	43.1
Hawaii	1250	1.9	56.7
Iowa	5373	8.2	50.3
New Mexico	2164	3.3	37.8
Seattle	4985	7.6	39.1
Utah	3205	4.9	40.0
Atlanta	2495	3.8	33.8
San Jose	1770	2.7	58.6
Los Angeles	5948	9.0	46.7
Rural Georgia	197	0.3	36.6
Greater California	7092	10.8	46.2
Kentucky	3463	5.3	52.7
Louisiana	3479	5.3	57.0
New Jersey	7720	11.7	63.1

Characteristic	n	%*	Proportion on ADT, %
Year of diagnosis			
1996	4936	7.5	38.7
1997	5114	7.8	41.9
1998	5031	7.6	46.1
1999	5403	8.2	48.8
2000	10564	16.0	52.7
2001	11301	17.2	50.9
2002	12180	18.5	50.0
2003	11323	17.2	48.7
<12 years of education†			
< 10%	21254	32.3	44.7
10%—< 20%	22487	34.2	49.1
20%—<30%	10743	16.3	50.1
30%	11363	17.3	52.8
Income below the poverty line†			
<3%	9693	14.7	47.7
3%—<7%	20936	31.8	47.8
7%—< 14%	17582	26.7	48.4
14%	17636	26.8	49.7
Marital status			
Married	44961	68.3	47.0
Unmarried	13840	21.0	48.4
Unknown	7051	10.7	58.1
Charlson Comorbidity Index			
0	48728	74.0	46.5
1	11925	18.1	53.2
2	3409	5.2	56.4
3+	1790	2.7	57.1
Grade of prostate cancer			
Well-differentiated	3360	5.1	28.2
Moderately differentiated	43397	65.9	42.7

Characteristic	n	% [*]	Proportion on ADT, %
Poorly differentiated	16442	25.0	68.2
Unknown	2653	4.0	46.9
American Joint Committee on Cancer stage			
0	132	0.2	21.2
I	783	1.2	31.4
II	5742	8.7	47.2
III	3336	5.1	31.4
IV	3829	5.8	74.5
Unknown	52030	79.0	48.2
SEER summary stage			
Local/Regional	60932	92.5	46.7
Distant	2514	3.7	84.4
Unknown	2406	3.8	57.1
Other treatment within 6 mo of diagnosis			
Radical Prostatectomy	10506	16.0	14.8
Radiation	28223	42.9	55.1
Both	471	0.7	42.3
Neither	24853	37.7	54.9
Unknown	1799	2.7	54.8

SEER = Surveillance, Epidemiology and End Results.

^{*} Percentages may not sum 100% due to rounding.

[‡] Referring to the census tract in which the patient resided at time of diagnosis, and the proportion of residents within the tract with less than 12 years of education or household income below the poverty line.

Table 2
Number of incident* cataract cases (based upon diagnosis claims) and incidence rate (per 1000 persons per year), by ADT status† and cataract history before prostate-cancer diagnosis

ADT status‡	All patients				No cataract history				Cataract history			
	No. events/sample size	Rate	95% CI	p-value§	No. events/sample size	Rate	95% CI	p-value	No. events/sample size	Rate	95% CI	p-value
No ADT	14395/33892	106	103 to 109	ref	8310/22370	86	82 to 90	ref	6085/11522	156	149 to 163	ref
GnRH agonist	12996/30422	117	113 to 121	<.01	6430/17055	95	91 to 99	<.01	6566/13367	152	146 to 158	.38
Orchiectomy	317/999	98	79 to 117	.40	173/607	83	61 to 105	.79	144/392	124	91 to 157	.06

ADT = androgen deprivation therapy; CI = confidence interval.

* First claim of cataract occurring more than 12 months post-prostate cancer diagnosis.

† During the 6-month period after a diagnosis of prostate cancer.

‡ Derived from ² test.

Table 3
Adjusted hazard ratio* (and 95% CI) for cataract diagnosis among prostate-cancer patients, by predictor category (including ADT status) and cataract history: results of three Cox regression analyses

	All patients	No history of cataract	History of cataract
No ADT	1.00	1.00	1.00
Gonadotropin-releasing hormone agonist [†]	1.09 (1.06–1.12)	1.12 (1.08–1.16)	1.05 (1.01–1.09)
1–4 doses	1.09 (1.05–1.13)	1.12 (1.07–1.18)	1.04 (0.98–1.09)
5–8 doses	1.12 (1.08–1.17)	1.13 (1.06–1.94)	1.11 (1.04–1.17)
9 doses	1.08 (1.04–1.11)	1.11 (1.06–1.17)	1.04 (0.98–1.09)
Orchiectomy	1.18 (1.05–1.32)	1.26 (1.07–1.47)	1.07 (0.90–1.28)
No cataract history	1.00	–	–
Cataract history	1.75 (1.70–1.79)	–	–
Age			
66–69 years	1.00	1.00	1.00
70–74 years	1.10 (1.07–1.14)	1.13 (1.08–1.17)	1.00 (0.95–1.06)
75–79 years	1.07 (1.03–1.11)	1.19 (1.13–1.25)	0.92 (0.87–0.98)
80 years	0.81 (0.77–0.85)	0.95 (0.88–1.02)	0.69 (0.65–0.74)
Race			
White	1.00	1.00	1.00
Black	0.74 (0.71–0.78)	0.75 (0.70–0.79)	0.74 (0.68–0.81)
Other	0.90 (0.86–0.94)	0.93 (0.87–0.98)	0.88 (0.82–0.94)
<12 years of education			
<10%	1.00	1.00	1.00
10%–<20%	0.98 (0.95–1.01)	0.95 (0.92–0.99)	1.00 (0.96–1.04)
20%–<30%	0.89 (0.85–0.92)	0.89 (0.85–0.94)	0.87 (0.82–0.93)
30%	0.87 (0.83–0.90)	0.88 (0.84–0.94)	0.84 (0.79–0.90)
Prostate cancer grade			
Well differentiated	1.00	1.00	1.00
Moderately differentiated	0.94 (0.89–0.99)	0.94 (0.88–1.01)	0.94 (0.87–1.02)
Poorly differentiated	0.88 (0.83–0.94)	0.88 (0.81–0.95)	0.89 (0.81–0.97)
No radical prostatectomy	1.00	1.00	1.00

	All patients	No history of cataract	History of cataract
Radical prostatectomy	1.19 (1.14–1.24)	1.18 (1.12–1.24)	1.21 (1.13–1.28)
No radiation therapy	1.00	1.00	1.00
Radiation therapy	1.10 (1.07–1.13)	1.09 (1.04–1.13)	1.11 (1.07–1.16)
Comorbidity index			
0	1.00	1.00	1.00
1	0.94 (0.91–0.97)	1.01 (0.97–1.06)	0.87 (0.83–0.91)
2	0.94 (0.88–1.00)	1.02 (0.93–1.11)	0.87 (0.80–0.94)
3+	0.90 (0.82–0.98)	1.00 (0.88–1.14)	0.83 (0.73–0.93)
Physician visits 12 mo. before diagnosis			
0	1.00	1.00	1.00
1–5	1.54 (1.47–1.62)	1.63 (1.53–1.72)	1.27 (1.17–1.39)
6–9	1.69 (1.60–1.78)	1.82 (1.70–1.94)	1.37 (1.24–1.50)
10	1.79 (1.69–1.89)	2.02 (1.89–2.17)	1.40 (1.27–1.54)

ADT = androgen deprivation therapy; CI = confidence interval.

* Each hazard ratio is adjusted for the other covariates in this table (except for cataract history as indicated).

[†] At least one dose in the 6-month period after prostate cancer diagnosis.