Effects of Family History and Genetic Polymorphism on the Cost-Effectiveness of Chemoprevention With Finasteride for Prostate Cancer

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Purpose: Improvement in the cost-effectiveness of chemoprevention for prostate cancer could be realized through the identification of patients at higher risk. We estimated the cost-effectiveness of prostate cancer chemoprevention across risk groups defined by family history and number of risk alleles, and the cost-effectiveness of targeting chemoprevention to higher risk groups.

Materials and Methods: We developed a probabilistic Markov model to estimate costs, survival and quality adjusted survival across risk groups for patients receiving or not receiving chemoprevention with finasteride. The model uses data from national cancer registries, online sources and the medical literature.

Results: The incremental cost-effectiveness of 25 years of chemoprevention with finasteride in patients 50 years old was an estimated $89,300 per quality adjusted life-year (95% CI $58,800–$149,800), assuming finasteride decreased all grades of prostate cancer by 24.8%. Among patients with a positive family history (without genetic testing) chemoprevention provided 1 additional quality adjusted life-year at a cost of $64,200. Among patients with a negative family history at $400 per person tested, the cost-effectiveness of genetically targeted chemoprevention ranged from $98,100 per quality adjusted life-year when limiting finasteride to individuals with 14 or more risk alleles, to $103,200 per quality adjusted life-year when including those with 8 or more risk alleles.

Conclusions: Although there are small differences in the cost-effectiveness of genetically targeted chemoprevention strategies in patients with a negative family history, genetic testing could reduce total expenditures if used to target chemoprevention for higher risk groups.

Key Words: chemoprevention; cost-benefit analysis; finasteride; polymorphism, genetic; risk factors

Abbreviations and Acronyms

BPH = benign prostatic hyperplasia

CAPS = Cancer of the Prostate in Sweden

ICER = incremental cost-effectiveness ratio

PCPT = Prostate Cancer Prevention Trial

PLCO = Prostate, Lung, Colon, and Ovarian Cancer Screening Trial

QALY = quality adjusted life-year

COST-EFFECTIVENESS analyses of chemoprevention with finasteride for prostate cancer have shown that each additional year of survival would cost $1.1 million to $1.7 million.[1,2] After adjustment for differences in quality of life, the ICERs ranged from $123,000 to $200,000 per QALY.[2,3] Improvement in the cost-effectiveness of chemoprevention could be realized through identification of higher risk patients.[3] Recent studies have identified genetic variants associated with an increased risk of prostate cancer.[4–9]

Using data from the CAPS study and the PLCO in the United States,

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Xu et al published a prediction model that used 14 single nucleotide polymorphisms and family history to estimate an individual's risk of prostate cancer.[10] To evaluate the impact of targeted chemoprevention on the cost-effectiveness of finasteride we used this risk prediction model to develop a computer simulation model in Microsoft Excel® to estimate costs, survival and quality adjusted survival for risk groups defined by family history and number of risk alleles. We also evaluated the cost-effectiveness of genetic screening and targeted chemoprevention strategies, accounting for the prevalence of inherited risk alleles and family history of prostate cancer in the population.

METHODS

The Markov model in this study represents 8 distinct health states (fig. 1). We assumed all patients were free of prostate cancer at time zero. In annual cycles low grade (Gleason score 2 to 6), intermediate grade (Gleason score 7) or high grade (Gleason score 8 to 10) prostate cancer could develop in patients. Patients then underwent treatment and remained in that health state until death from other causes or biochemical recurrence of prostate cancer. Patients with biochemical recurrence could survive with recurrence, die of other causes or have progression to metastatic disease. Patients with progression to metastatic disease could survive with cancer, die of cancer or die of other causes.

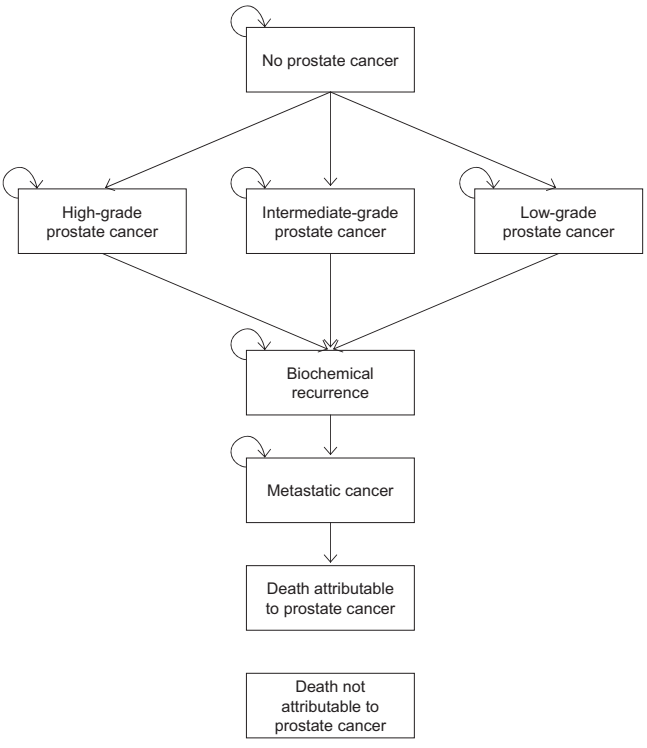

Figure 1. Markov diagram of health states and possible transitions among them. Transition to death not attributable to prostate cancer may occur from any state (arrows not shown).

We generated age specific rates of prostate cancer incidence for patients not receiving chemoprevention (DevCan version 6.4.1, National Cancer Institute) using data from the Surveillance, Epidemiology and End Results database for 2000 through 2006.[11] Distributions of cancer grades were based on for cause biopsies in the placebo group of the PCPT.[12] All cause age specific mortality rates were based on 2001 United States life tables.[13]

Base Case Assumptions

We designed the cost-effectiveness model to represent the health care system perspective. Table 1 summarizes the base case estimates including point estimates, standard errors and distributions applied in probabilistic sensitivity analyses.[14–19] We applied a 3% annual discount rate to costs and survival. Patients entered the model at age 50 years.

Patients in the chemoprevention strategy initiated daily use of finasteride for 25 years or until prostate cancer developed. We applied a constant 24.8% risk reduction with finasteride to all tumor grades and assumed the effect was maintained through 25 years.[12] We applied a 14.7% nonadherence rate based on the percentage of treatment days missed during followup in the PCPT. Although this rate decreased the cost of chemoprevention, we did not adjust the effectiveness measure because the treatment effect in the PCPT reflected this nonadherence rate. Transition probabilities for biochemical recurrence, development of metastatic cancer after biochemical recurrence and mortality attributable to prostate cancer were based on outcomes of radical prostatectomy.[16,17] Consistent with previous economic evaluations we set the prevalence of BPH at 15% in patients younger than 75 years and 22% in those 75 years old or older.[3] We assumed finasteride decreased the prevalence of BPH by 40%.[15]

Costs

Medical costs associated with prostate cancer in the year after diagnosis, the year before death and all intervening years were derived from a recent study (table 1).[18,20] In assigning costs for outpatient medications we assumed patients with BPH were treated with α-blockers and those with biochemical recurrence or metastatic disease received androgen suppression therapy. Costs of chemoprevention consisted of the cost of finasteride.

Subgroups

We estimated the impact of family history of prostate cancer and the number of inherited risk alleles from Xu et al in which the odds ratios represented the odds of prostate cancer in patients with a given family history and number of risk alleles compared with those in patients with a negative family history and 11 risk alleles.[10] In the model we converted odds ratios for each group to risk ratios based on the estimated lifetime risk of prostate cancer. Because the base case model represents the average patient, not necessarily a patient with a negative family history and 11 risk alleles, we calibrated the model to correspond to the absolute risk estimates reported by Xu et al.[10]