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Cost-Effectiveness of Fracture Prevention in Men Who Receive Androgen Deprivation Therapy for Localized Prostate Cancer

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Abstract

Background—Androgen deprivation therapy (ADT) increases the risk for fractures in patients with prostate cancer.

Objective—To assess the cost-effectiveness of measuring bone mineral density (BMD) before initiating ADT followed by alendronate therapy in men with localized prostate cancer.

Design—Markov state-transition model simulating the progression of prostate cancer and the incidence of hip fracture.

Data Sources—Published literature.

Target Population—A hypothetical cohort of men aged 70 years with locally advanced or high-risk localized prostate cancer starting a 2-year course of ADT after radiation therapy.

Time Horizon—Lifetime.

Perspective—Societal.

Intervention—No BMD test or alendronate therapy, a BMD test followed by selective alendronate therapy for patients with osteoporosis, or universal alendronate therapy without a BMD test.

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Outcome Measures—Incremental cost-effectiveness ratio (ICER), measured by cost per quality-adjusted life-year (QALY) gained.

Results of Base-Case Analysis—The ICERs for the strategy of a BMD test and selective alendronate therapy for patients with osteoporosis and universal alendronate therapy without a BMD test were $66 800 per QALY gained and $178 700 per QALY gained, respectively.

Results of Sensitivity Analyses—The ICER for universal alendronate therapy without a BMD test decreased to $100 000 per QALY gained, assuming older age, a history of fractures, lower mean BMD before ADT, or a lower cost of alendronate.

Limitations—No evidence shows that alendronate reduces actual fracture rates in patients with prostate cancer who receive ADT. The model predicted fracture rates by using data on the surrogate BMD end point.

Conclusion—In patients starting adjuvant ADT for locally advanced or high-risk localized prostate cancer, a BMD test followed by selective alendronate for those with osteoporosis is a cost-effective use of resources. Routine use of alendronate without a BMD test is justifiable in patients at higher risk for hip fractures.

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Androgen deprivation therapy (ADT) comprises orchiectomy or gonadotropin-releasing hormone agonists with or without an antiandrogen. Once used primarily to treat metastatic prostate cancer, ADT is now used as adjuvant therapy for locally advanced or high-risk localized prostate cancer and as treatment of biochemical failure after primary therapy (1–3). Because most men with prostate cancer receive the diagnosis at an older age and because androgen deficiency is associated with low bone mineral density (BMD), men with prostate cancer who receive treatment with ADT are at particularly increased risk for osteoporosis and related fractures (4–9).

A physician survey and several descriptive studies done at single centers suggest that most patients with prostate cancer who receive ADT do not receive screening or treatment for bone loss (10–13). In the absence of consensus guidelines about fracture prevention in these patients, many experts have recommended a case-finding approach: measuring BMD by dual-energy x-ray absorptiometry before ADT and administering antiresorptive agents to patients who are at high risk for fractures (14–17). Others have advocated routine use of antiresorptive agents regardless of baseline BMD (18, 19). These recommendations go beyond available evidence because only oral alendronate and risedronate have been shown to reduce fracture rates in healthy men with osteoporosis (20, 21) and because none of the several antiresorptive agents shown to prevent bone loss from ADT has been shown to prevent fractures and none has been approved by the U.S. Food and Drug Administration for this indication (22–31). Furthermore, the cost-effectiveness of various screening and treatment strategies has not been determined.

We sought to estimate the cost-effectiveness of no BMD test or alendronate therapy, a BMD test followed by selective alendronate therapy for patients with osteoporosis, and universal alendronate therapy without a BMD test for men starting adjuvant ADT for locally advanced or high-risk localized prostate cancer.

Methods

We developed a Markov state-transition model simulating the progression of prostate cancer and the incidence of hip fractures. We assumed a societal perspective, a lifetime horizon, and a discount rate of 3% per year for both health benefits and costs (32). The analysis was done by using TreeAge Pro Suite 2008 software (TreeAge Software, Williamstown, Massachusetts).

Population

The model simulated a hypothetical cohort of men aged 70 years with locally advanced or high-risk localized prostate cancer (T2c to T4N0) starting a 2-year course of ADT after radiation therapy (33). We did not target patients who received ADT as monotherapy for low- or intermediate-risk localized prostate cancer (1, 2, 34). We assumed that no patients in the base-case cohort had a history of fragility fractures (for example, hip, vertebral, or wrist fractures). In sensitivity analyses, we varied assumptions about patient age and history of fractures.

Strategies

We compared 3 strategies: no BMD test and no alendronate therapy; a one-time BMD test before initiating ADT, followed by selective alendronate therapy for patients with osteoporosis; and universal alendronate therapy without a BMD test (Figure, *top*). In the test strategy, all patients had femoral neck BMD measurement by dual-energy x-ray absorptiometry before starting ADT. Bone mineral density was quantified by a T-score—the number of SDs above or below the mean for non-Hispanic white men aged 20 to 29 years (35). A T-score of −2.5 or less indicated osteoporosis. We assumed that alendronate therapy was continued for 5 years (36).

Model

The progression of prostate cancer was modeled through a sequence of health states: localized disease, rising prostate-specific antigen, noncastrate metastasis, castrate metastasis, and death from prostate cancer (Figure, *bottom*) (37). We assumed that if ADT had been discontinued after 2 years, it was resumed if patients developed noncastrate metastasis and was continued until death. Patients could die of other causes or experience hip fracture at any time and from any health state. We restricted analysis to hip fractures because the relationship between femoral neck BMD and fracture rates seems the most robust (38, 39). We assumed that the progression of prostate cancer was not altered by alendronate or hip fractures. We also assumed that recommended doses of supplemental calcium and vitamin D were administered in all patients and intravenous zoledronic acid was administered as a cancer-directed therapy in patients who developed castrate metastasis. All patients made annual transitions between the health states until they died or reached 100 years of age. Table 1 summarizes the model variables.

Progression of Prostate Cancer—Base-case estimates of disease progression were from the 10-year follow-up analysis of Radiation Therapy Oncology Group protocol 92-02

(33), a natural history study of patients with rising prostate-specific antigen after ADT, and a previous cost-effectiveness model for localized prostate cancer (40, 41).

BMD and Incidence of Hip Fracture—We simulated changes in BMD over time and predicted the incidence of hip fractures as a function of age and BMD (59, 60). As patients aged, the model calculated an updated BMD on the basis of baseline BMD at the onset of ADT and the number of years since model entry. We assumed that no difference was found in baseline BMD between patients with prostate cancer who did not receive ADT and the white male population from the Third National Health and Nutrition Examination Survey (35). The estimated prevalence of osteoporosis in the base-case cohort was 11%. The rate of BMD loss in the absence of ADT was assumed to follow the rate reported in the Framingham Osteoporosis Study (42). The rate of BMD loss during ADT was calculated by fitting a linear regression to cross-sectional data of total hip BMD over a broad spectrum of therapy durations up to 10 years (43). We assumed that the rate of BMD loss was constant during the course of ADT and returned to the baseline rate of BMD loss in the year after completion of ADT. We converted the updated BMD to an equivalent Z score and then calculated the incidence of hip fractures specific for age and BMD ($i_{age,\ BMD}$) by using the following relationship (38):

$$i_{age,BMD} = i_{age} \times a^{-Z}$$

in which "i_{age}" denotes the hip fracture incidence in men with mean BMD for that age (Z score of 0), "a" is the relative risk per each decrease in Z score, and "Z" is the Z score. We obtained i_{age} from fracture data for white men from the 2001 Nationwide Inpatient Sample database (44). A history of fractures confers an increased risk for subsequent fractures (7, 45). We assumed that the prevalence of osteoporosis was 1.91 times higher in patients with a previous fracture than in those without fracture (53).

Treatment Effect—The effect of treatment on fracture incidence was modeled under the assumption that patients had no BMD loss throughout the course of alendronate therapy (22, 23, 59, 60). In the base case, we assumed 100% adherence to alendronate therapy and tested lower adherence in a sensitivity analysis (46). We assumed that alendronate did not affect BMD in patients who stopped taking alendronate and that zoledronic acid reduced the risk for hip fracture by 24% in patients with castrate metastasis (61).

Side Effects—We assumed that 0.8% of patients had serious upper gastrointestinal side effects (such as perforation, ulcer, or bleeding) in the first year of alendronate therapy (47). We assumed that each episode required a hospitalization, 2 additional physician visits, and treatment with a proton-pump inhibitor for 1 year. Alendronate therapy was stopped and never restarted after these events.

Death—Background mortality rates were based on 2004 U.S. life tables published by the National Center for Health Statistics (48). Excess mortality from a hip fracture was modeled only in the same year that the hip fracture occurred (49, 50).

Quality of Life—We assigned a utility to each health state that reflected the preference for, or desirability of, that state. Health state utilities were taken from studies that used standardized methods (the time-tradeoff or standard gamble technique) to elicit preferences. Because no utility has been reported for the rising prostate-specific antigen state, we assigned a slightly lower utility than that for localized disease. The utility multiplier of hip fractures was obtained from the Swedish prospective study of fracture patients (52). The utility for serious upper gastrointestinal side effects of alendronate was a value for complicated peptic ulcer that required hospitalization (55). All health state utilities were varied in sensitivity analyses.

Costs—The costs of dual-energy x-ray absorptiometry, a physician visit, and a hospitalization for serious upper gastrointestinal side effects of alendronate (diagnosis-related group code 183) were based on average Medicare reimbursement for these services (56). We used retail prices of alendronate and a proton-pump inhibitor (omeprazole) reported by the New York State Board of Pharmacy (57). Patients who did not adhere to alendronate therapy accrued the medication cost for only 6 months (46). Fracture costs were taken from a population-based cost analysis in Olmsted County, Minnesota (53, 54, 58). We assumed that the cost of treating prostate cancer was independent of BMD and fracture status. All costs were inflated to 2008 dollars by using the Consumer Price Index for Medical Care for All Urban Consumers (62).

Outcomes

We measured health benefits in quality-adjusted life-years (QALYs) gained. Incremental cost-effectiveness analysis was done by first ranking the strategies in order of increasing cost. Then, after eliminating strategies that were more or equally costly and less effective than a competing strategy (that is, ruled out by simple dominance), we calculated the incremental cost-effectiveness ratio (ICER) of each strategy as the additional cost of that strategy divided by its additional benefit compared with the next most costly strategy. If a strategy was less effective and had a higher ICER than another strategy, it was ruled out by extended dominance. We eliminated strategies exhibiting extended dominance from the rank-ordered list, and we recalculated ICERs of the remaining strategies. After these standard methods, each nondominated strategy was compared with the next most costly strategy. The incremental cost-effectiveness of the least costly, viable (nondominated) strategy was not calculated (32) because there was no comparator.

Model Validation

Ten-year overall survival was 51%, and disease-free survival was 15% in the simulated cohort, which approximated estimates of 54% (95% CI, 50% to 58%) and 23% (CI, 19% to 26%) found in Radiation Therapy Oncology Group protocol 92-02 (33). The estimated mean overall survival was 11.0 years. The cumulative lifetime probability of hip fracture, assuming no BMD test or alendronate therapy, was 12.6% (1.15% per patient-year), slightly lower than claim-based data (1.26% to 1.36% per patient-year) (8, 9).

Role of the Funding Source

We received no funding for this study.

Results

Base-Case Analysis

Table 2 shows the cumulative lifetime probability of hip fracture and mortality due to hip fractures, cost, undiscounted life-years, QALYs, and ICER for each strategy. Among all strategies, the no test–no alendronate strategy became the reference strategy because it was the least costly, viable (nondominated) option. Compared with the no test–no alendronate strategy, the strategy of a BMD test and selective alendronate therapy for patients with osteoporosis was more costly and more effective and had an ICER of $66 800 per QALY gained. Compared with the strategy of a BMD test and selective alendronate therapy for patients with osteoporosis, universal alendronate therapy without a BMD test was even more costly and more effective but had an ICER of $178 700 per QALY gained.

Sensitivity Analyses

The ICER for each strategy improved with older age at the onset of ADT and was substantially better for patients with a previous fracture (Table 3). If society would be willing to pay $100 000 per QALY gained, universal alendronate therapy without a BMD test would be preferred for patients 75 years or older without a previous fracture, as well as patients 65 years or older with a previous fracture. Universal alendronate therapy without a BMD test would become more effective and less costly than the strategy of a BMD test and selective alendronate therapy for patients aged 80 years with a previous fracture.

Our results were sensitive to assumptions about the cost of alendronate. If society would be willing to pay $100 000 per QALY gained, universal alendronate therapy without a BMD test would be preferred if the cost of alendronate decreased to $430 per year. If society would be willing to pay $50 000 per QALY gained, universal alendronate therapy without a BMD test would be preferred if the cost of alendronate decreased to $320 per year.

Our results were also sensitive to assumptions about the mean BMD in the base-case population and the effectiveness of alendronate in preventing bone loss (Table 4). If society would be willing to pay $100 000 per QALY gained, universal alendronate therapy without a BMD test would be preferred if the mean BMD was lower than 0.6970 g/cm^2 (that is, prevalence of osteoporosis was higher than 21%), assuming no bone loss during alendronate therapy. If society would be willing to pay $50 000 per QALY gained, universal alendronate therapy without a BMD test would be preferred if the mean BMD was lower than 0.6490 g/cm^2 (that is, the prevalence of osteoporosis was higher than 33%), assuming no bone loss during alendronate therapy. The ICER for each strategy remained greater than $100 000 per QALY gained assuming a 50% reduction in bone loss from alendronate therapy.

The ICER for each strategy did not substantially change across a wide range of assumptions evaluated in all other sensitivity analyses (Appendix Table, available at www.annals.org).

Discussion

The American College of Physicians recently concluded that osteoporosis screening would not be cost-effective in U.S. men younger than 80 years and recommended screening only

for “men who are at increased risk for osteoporosis” and candidates for drug therapy, with ADT identified as an important risk factor for low BMD–mediated fractures (64). The results of our analysis support that recommendation. In men aged 70 years with locally advanced or high-risk localized prostate cancer, a BMD test before adjuvant ADT followed by selective alendronate therapy for those who received a diagnosis of osteoporosis was reasonably cost-effective. Although universal alendronate therapy without a BMD test yielded the greatest average health benefit, its estimated ICER was higher than generally accepted cost-effectiveness thresholds in the United States (32, 63). Our analysis suggested that universal alendronate therapy without a BMD test had a potential to become reasonably cost-effective if the target population was older, had a history of fractures, or had lower mean BMD before ADT or if the cost of alendronate was lower than our base-case estimates.

The National Osteoporosis Foundation recommends shifting the treatment approach from one based on BMD to one based on absolute fracture risk calculated by the World Health Organization Fracture Risk Assessment Tool (FRAX) (65, 66). The FRAX is designed to help physicians decide when to initiate antiresorptive therapy by providing a person’s 10-year absolute fracture probability based on clinical risk factors with or without femoral neck BMD. The concept of treating patients regardless of BMD status is intuitively appealing, although it depends on an unproven assumption that antiresorptive therapy reduces the incidence of fractures across all levels of BMD (67, 68). Even though the FRAX is derived and validated for population-based cohorts across the world, the algorithm does not take into account accelerated bone loss during the course of ADT or excess mortality due to prostate cancer and has yet to be validated for patients with prostate cancer who receive ADT. Therefore, we used the presence of osteoporosis, as defined by T-score of BMD, as a treatment threshold.

The most frequently cited barriers for osteoporosis screening include uncertainty about effectiveness, costs, and potential side effects of treatment (69). Relative to the strategy of no BMD test and no alendronate therapy, the estimated health benefits of more active strategies were modest: an added 4.1 days of quality-adjusted life for universal alendronate therapy without a BMD test and even fewer for the strategy of a BMD test and selective alendronate therapy. Compared with the recently published cost-effectiveness analyses for U.S. men, our base-case assumptions related to the effectiveness of alendronate are conservative (53, 54). By excluding the effect of non-hip fractures, we may have underestimated the total health benefit of alendronate therapy. Also, the retail price of alendronate has decreased substantially since the loss of patent protection in February 2008, and our sensitivity analysis suggested that universal alendronate therapy without testing is increasingly more cost-effective with a progressive reduction in cost of alendronate. We chose alendronate as a therapeutic intervention because other, particularly intravenous, bisphosphonates are associated with substantially higher direct costs (70). Although the long-term safety of oral alendronate has not been formally evaluated in patients with prostate cancer, a pooled analysis of clinical trials showed no difference in upper gastrointestinal events between alendronate and placebo (71). Our conclusions were robust to a reasonable range of assumptions about the incidence, cost, and quality-of-life effects of upper gastrointestinal adverse events of alendronate. Recently, osteonecrosis of the jaw has been recognized as an

important complication of bisphosphonate therapy, with a large effect on quality of life (72). The reported incidence is low (from 1 in 10 000 to 1 in 100 000 patient-treatment-years) in patients who receive oral bisphosphonates for osteoporosis (73, 74), and we therefore did not model it explicitly.

The main limitation of our analysis is that BMD is a surrogate measure of risk for hip fractures and fracture risk reduction by alendronate. Whether the beneficial effect of alendronate on BMD correlates with a decreased fracture incidence has yet to be determined in patients with prostate cancer who receive ADT. Evidence of a statistically significant reduction of nonvertebral fractures in men is currently insufficient, but clinical trials of newer agents have been emerging. For example, a clinical trial of denosumab, a human monoclonal antibody against receptor activator of nuclear factor-κB ligand, showed a statistically significant reduction of new vertebral fractures and a trend toward a reduction of nonvertebral fractures in patients who receive ADT for prostate cancer (31).

As ADT is used with increasing frequency in men with localized prostate cancer, maintenance of their bone health is a growing public health challenge. Our results suggest that in patients with locally advanced or high-risk localized prostate cancer starting a 2-year course of ADT after radiation therapy, the strategy of a BMD test and alendronate therapy in those with osteoporosis for 5 years is a cost-effective use of resources. Routine use of alendronate is not justifiable unless patients are older, have a history of fractures, or have lower mean BMD before ADT. These results are encouraging and suggest that prevention of bone loss with alendronate is cost-effective when treatment is targeted to patients at high risk for fractures. Our results also suggest that Medicare coverage of a BMD test could be expanded to this patient population (75). Future research should assess whether the effect of alendronate on BMD correlates with a reduction in fracture rates in this patient population.

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Appendix

Appendix Table

ICERs for Each Strategy in Additional 1-Way Sensitivity Analyses*

Variable	ICER, *$/QALY*	
	Test and Selective Alendronate Therapy	**No Test and Universal Alendronate Therapy**
Base case	66 800	178 700
ADT for 5 y	47 800	160 000
Progression of prostate cancer (per year)		
Localized disease to rising PSA		
11%	45 200	135 500

Variable	ICER, $/QALY	
	Test and Selective Alendronate Therapy	No Test and Universal Alendronate Therapy
17%	87 300	220 300
Rising PSA to noncastrate metastasis		
14%	48 800	143 400
22%	82 000	208 500
Noncastrate metastasis to castrate metastasis		
24%	67 200	179 200
52%	66 400	178 000
Castrate metastasis to prostate cancer death		
43%	66 900	178 800
58%	66 600	178 500
Rate of BMD loss (per year)		
No ADT		
0.0026 g/cm^2	77 100	198 100
0.0044 g/cm^2	57 300	160 800
During ADT		
0.0141 g/cm^2	112 000	256 300
0.0235 g/cm^2	37 200	127 700
Incidence of hip fractures per patient-year in patients with mean BMD †		
50% lower (0.098%)	202 300	429 200
50% higher (0.293%)	19 600	94 600
Relative risk for hip fractures per *Z* score †		
2.39	107 900	211 700
3.23	35 400	151 600
Relative risk for hip fractures due to a previous fracture †		
1.37	72 500	183 300
2.65	60 600	173 800
Adherence rate to alendronate therapy		
75%	87 300	194 700
50%	128 200	226 800
Incidence of upper gastrointestinal adverse events		

Variable	ICER, $/QALY	
	Test and Selective Alendronate Therapy	No Test and Universal Alendronate Therapy
0%	64 900	173 300
2%	69 800	187 300
Background mortality per year †		
25% lower (2.04%)	48 300	141 700
25% higher (3.40%)	86 100	217 200
Relative risk for death within the first year after a hip fracture		
1.00	68 200	190 100
2.00	64 400	163 500
Health state utility of prostate cancer		
Localized disease		
0.630	75 400	200 400
1.000	61 500	165 100
Rising PSA		
0.600	76 400	205 700
1.000	59 300	158 000
Noncastrate metastasis		
0.330	67 500	180 500
0.550	66 200	176 900
Castrate metastasis		
0.098	66 800	178 800
0.163	66 800	178 600
Utility multiplier		
Hip fracture (first year)		
0.594	53 800	144 600
0.990	88 200	233 900
Hip fracture (subsequent years)		
0.610	40 000	105 200
1.000	174 200	501 800
Upper gastrointestinal side effects of alendronate		
0.735	71 600	216 600

Variable	ICER, *$/QALY*	
	Test and Selective Alendronate Therapy	No Test and Universal Alendronate Therapy
1.000	66 500	176 200
Cost		
BMD test		
$98	54 400	182 600
$164	79 200	174 800
Hip fracture (first year)		
$24 900	80 300	191 500
$41 500	53 300	165 900
Hip fracture (subsequent years)		
$6450	74 100	186 200
$10 750	55 100	166 600
Upper gastrointestinal side effects of alendronate		
$2250	66 600	178 000
$3750	67 100	179 300
Discount rate		
0%	45 800	134 200
6%	87 700	222 300

ADT = androgen deprivation therapy; BMD = bone mineral density; ICER = incremental cost-effectiveness ratio; PSA = prostate-specific antigen; QALY = quality-adjusted life-year.

* ICER was measured by cost per QALY gained. The no test–no alendronate strategy was the reference strategy because it was the least costly, viable (nondominated) option. The strategy was considered cost-effective if its ICER was less than $100 000 per QALY gained (32, 63). None of the strategies was excluded by simple or extended dominance.

† Variables were age-specific. Values shown were for persons aged 70 years.

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Context

Androgen deprivation therapy increases fracture risk in men with prostate cancer.

Contribution

This analysis suggests that in a population of men with prostate cancer who receive androgen deprivation therapy, dual-energy x-ray absorptiometry screening followed by treatment of those with osteoporosis is more cost-effective than no screening and no treatment, and more cost-effective than treating all men.

Caution

No data show that bisphosphonates decrease fractures in men with prostate cancer. The estimates apply only to men older than 70 years.

Implication

In men with prostate cancer who receive androgen deprivation therapy, dual-energy x-ray absorptiometry screening followed by treatment of selective alendronate for those with osteoporosis might be a cost-effective way to prevent fractures.

—The Editors

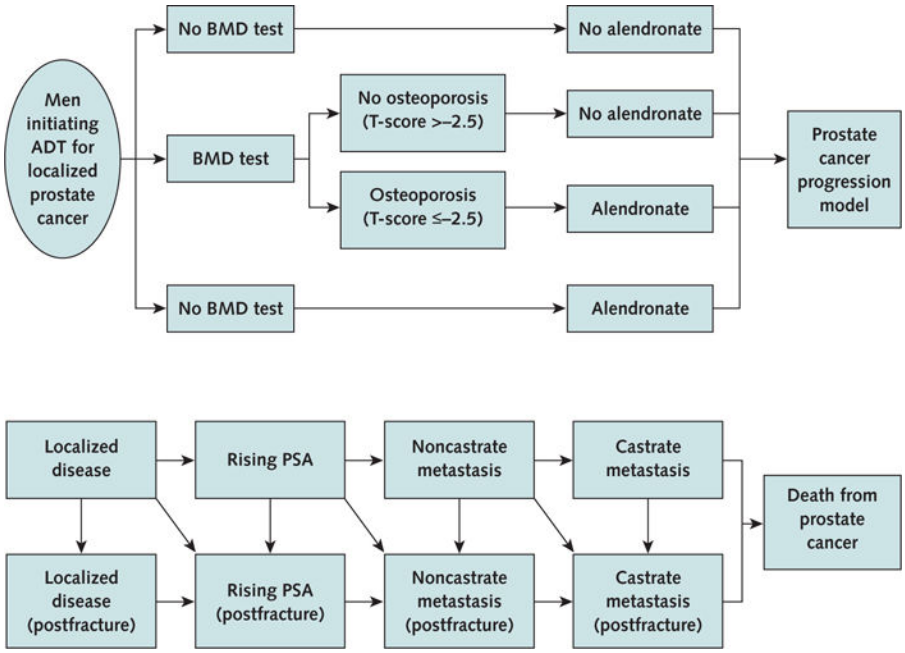

Figure. Clinical strategies and progression model for prostate cancer

ADT = androgen deprivation therapy; BMD = bone mineral density; PSA = prostate-specific antigen. **Top**. Algorithm showing a decision made at the onset of ADT for localized prostate cancer. Patients assigned to the alendronate group received alendronate for 5 years after proceeding to the prostate cancer progression model. **Bottom**. Prostate cancer progression model. Patients enter the model with localized disease. Each year, patients are at risk for the progression of prostate cancer, the occurrence of a hip fracture, or both. Throughout the patients' lifetime, all patients are at risk for death from causes unrelated to prostate cancer (not shown by the state or arrows). Squares represent the health states in the model. Arrows represent transitions between health states.

Table 1

Model Variables

Variable	Value	Range	Data Source
Age at onset of ADT, *y*	70	60–80	33
Progression of prostate cancer (per year), *%*	14	11–17*	33
Localized disease to rising PSA			
Rising PSA to noncastrate metastasis	18	14–22*	40
Noncastrate metastasis to castrate metastasis	36	24–52	41
Castrate metastasis to prostate cancer death	50	43–58	41
Mean BMD before ADT, *g/cm²*	0.7540	0.5915–0.8069	35
Rate of BMD loss (per year), *g/cm²*			
No ADT	0.0035	0.0026–0.0044	42
During ADT	0.0188	0.0141–0.0235	43
Incidence of hip fractures per patient-year in patients with mean BMD, by age, *%*			44
60–64 y	0.055	0.028–0.083	–
65–69 y	0.094	0.047–0.141	–
70–74 y	0.195	0.098–0.293	–
75–79 y	0.402	0.201–0.603	–
80–84 y	0.922	0.461–1.383	–
85–100 y	2.357	1.179–3.536	–
Relative risk for hip fractures per *Z* score, by age			39
60–64 y	3.07	2.42–3.89*	–
65–69 y	2.89	2.39–3.50*	–
70–74 y	2.78	2.39–3.23*	–
75–79 y	2.58	2.30–2.90*	–
80–84 y	2.28	2.09–2.50*	–
85–100 y	1.93	1.76–2.10*	–
Relative risk for hip fractures due to a previous fracture, by age			45
60–64 y	3.16	1.88–5.32*	–
65–69 y	2.28	1.52–3.41*	–

Variable	Value	Range	Data Source
70–74 y	1.90	1.37–2.65 *	–
75–79 y	1.64	1.24–2.17 *	–
80–84 y	1.41	1.12–1.78 *	–
85–100 y	1.32	1.04–1.68 *	–
Bone loss prevented by alendronate, *%*	100	50–100	Assumed
Adherence rate to alendronate therapy, *%*	100	50–100	46
Incidence of upper gastrointestinal side effects of alendronate, *%*	0.8	0–2	47
Background mortality per year, *%*†	2.72	2.04–3.40	48
Relative risk for death within the first year after a hip fracture	1.375	1–2	49, 50
Health state utility of prostate cancer			
Localized disease	0.840	0.630–1.000	51
Rising PSA	0.800	0.600–1.000	Assumed
Noncastrate metastasis	0.440	0.330–0.550	51
Castrate metastasis	0.130	0.098–0.163	51
Utility multiplier			
Hip fracture			
First year	0.792	0.594–0.990	52–54
Subsequent years	0.813	0.610–1.000	52–54
Upper gastrointestinal side effects of alendronate	0.980	0.735–1.000	55
Cost, *$*			
BMD test	131	98–164	56
Alendronate (per year)	600	300–900	57
Hip fracture, first year	33 200	24 900–41 500	52, 54, 58
Hip fracture, subsequent years (per year)	8100	6450–10 750	52, 54, 58
Upper gastrointestinal side effects of alendronate	3000	2250–3750	56, 57
Discount rate, *%*	3	0–6	32

ADT = androgen deprivation therapy; BMD = bone mineral density; PSA = prostate-specific antigen.

* 95% CI.

† Variable was age-specific. Values shown are for persons aged 70 years.

Table 2

Base-Case Analysis*

Strategy	Cumulative Lifetime Probability, %		Cost, $	Life-Years†	QALYs	Incremental Cost, $	Incremental QALYs	ICER, $/QALY‡
	Hip Fracture	Death Due to Hip Fracture						
No test and no alendronate therapy	12.6	0.43	75 474	10.9965	6.5930	Reference§	Reference§	Reference§
Test and selective alendronate therapy	12.0	0.40	75 652	10.9971	6.5957	178	0.0027	66 800
No test and universal alendronate therapy	9.9	0.33	77 153	10.9991	6.6041	1501	0.0084	178 700

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life-year.

* The strategy was considered cost-effective if its ICER was less than $100 000 per QALY gained (32, 63).

† Undiscounted results.

‡ ICER was measured by cost per QALY gained.

§ The no test–no alendronate strategy was the reference strategy because it was the least costly, viable (nondominated) option.

Table 3

ICERs for Each Strategy, by Age and Previous Fracture Status*

Age, *y*	ICER, by Previous Fracture, *$/QALY*			
	No Previous Fracture†		Previous Fracture	
	Test and Selective Alendronate Therapy	No Test and Universal Alendronate Therapy	Test and Selective Alendronate Therapy	No Test and Universal Alendronate Therapy
60	156 900	470 300	19 600	119 000
65	95 500	283 000	8500	72 300
70†	66 800	178 700	6300	44 500
75	46 900	103 000	5700	17 300
80	37 200	61 500	Dominated‡	2300

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life-year.

*ICER was measured by cost per QALY gained. The no test–no alendronate strategy was the reference strategy because it was the least costly, viable (nondominated) option. The strategy was considered cost-effective if its ICER was less than $100 000 per QALY gained (32, 63).

†Base-case assumptions.

‡Universal alendronate therapy without a bone mineral density test dominated this strategy by simple dominance because it was less effective and more costly.

Table 4

ICERs for Each Strategy, by Mean BMD Before ADT and Effectiveness of Alendronate *

Mean BMD, *g/cm²*	Prevalence of Osteoporosis, %†	ICER, by Bone Loss Prevented by Alendronate, *$/QALY*					
		100%‡		75%		50%	
		Test and Selective Alendronate Therapy	No Test and Universal Alendronate Therapy	Test and Selective Alendronate Therapy	No Test and Universal Alendronate Therapy	Test and Selective Alendronate Therapy	No Test and Universal Alendronate Therapy
0.8069	5	123 300	271 700	185 900	391 500	312 100	615 600
0.7540‡	11	66 800	178 700	112 700	257 400	205 400	417 200
0.7017	20	44 000	104 800	83 200	161 500	162 200	276 400
0.6601	30	35 200	60 500	71 700	104 200	145 600	192 600
0.6246	40	Dominated§	30 500	Dominated§	65 600	Dominated§	136 400
0.5915	50	Dominated§	17 500	Dominated§	48 900	Dominated§	112 300

BMD = bone mineral density; ICER = incremental cost-effectiveness ratio; QALY quality-adjusted life-year.

* ICER was measured by cost per QALY gained. The no test–no alendronate strategy was the reference strategy because it was the least costly, viable (nondominated) option. The strategy was considered cost-effective if its ICER was less than $100 000 per QALY gained (32, 63).

† Assumed a normal distribution of BMD and 0.5915 g/cm^2 as a BMD cut-off value for the diagnosis of osteoporosis.

‡ Base-case assumptions.

§ Universal alendronate therapy without a BMD test dominated this strategy by simple dominance because it was less effective and more costly.