Cost-Effectiveness of Androgen Suppression Therapies in Advanced Prostate Cancer

Ahmed M. Bayoumi, Adalsteinn D. Brown, Alan M. Garber

Background: The costs and side effects of several antiandrogen therapies for advanced prostate cancer differ substantially. We estimated the cost-effectiveness of antiandrogen therapies for advanced prostate cancer. Methods: We performed a cost-effectiveness analysis using a Markov model based on a formal meta-analysis and literature review. The base case was assumed to be a 65-year-old man with a clinically evident, local recurrence of prostate cancer. The model used a societal perspective and a time horizon of 20 years. Six androgen suppression strategies were evaluated: diethylstilbestrol (DES), orchiectomy, a nonsteroidal antiandrogen (NSAA), a luteinizing hormone-releasing hormone (LHRH) agonist, and combinations of an NSAA with an LHRH agonist or orchiectomy. Outcome measures were survival, quality-adjusted life years (QALYs), lifetime costs, and incremental cost-effectiveness ratios. Results: DES, the least expensive therapy, had a discounted lifetime cost of $3600 and the lowest quality-adjusted survival, 4.6 QALYs. At a cost of $7000, orchiectomy was associated with 5.1 QALYs, resulting in an incremental cost-effectiveness ratio of $7500/QALY relative to DES. All other strategies—LHRH agonists, NSAA, and both combined androgen blockade strategies—had higher costs and lower quality-adjusted survival than orchiectomy. These results were sensitive to the quality of life associated with orchiectomy and the efficacy of combined androgen blockade and they changed little when prostate-specific antigen results were used to guide therapy. Under a wide range of other assumptions, the cost-effectiveness of orchiectomy relative to DES was consistently less than $20 000/QALY. Androgen suppression therapies were most cost-effective if initiated after patients became symptomatic from prostate metastases. Conclusions: For men who accept it, orchiectomy is likely to be the most cost-effective androgen suppression strategy. Combined androgen blockade is the least economically attractive option, yielding small health benefits at high relative costs. [J Natl Cancer Inst 2000;92:1731–9]
3) symptomatic distant metastases, and 4) death (Fig. 1). In our base case, we assumed that biochemical monitoring (with prostate-specific antigen) was not used to guide treatment decisions. Local recurrence (meaning recurrent prostate cancer confined to the organ or capsule, invading the seminal vesicles, or involving pelvic lymph nodes) required a treatment approach based on clinical, rather than biochemical, markers. Such an approach is consistent with the best evidence available to date and is the approach used in almost all clinical trials; therefore, we modeled this approach in our base case and addressed the use of biochemical markers in a sensitivity analysis (11,12).

At the end of each 1-month cycle, patients could experience progression of their disease (including death from prostate cancer), die of unrelated causes, or remain in the same health state. Health states were further defined according to the androgen suppression therapy used (first-line, second-line, or none), side effects from treatment (present or absent), and benefits from medication withdrawal where appropriate. At any time, patients could also experience local bladder outlet obstruction, leading to a transient decrease in quality of life and extra costs (13). The occurrence of local obstruction did not alter the risk of future events, such as recurrent obstruction. At the conclusion of the model’s 20-year time horizon, nearly all patients will have died, and none will be cured of their prostate cancer.

Transitions between health states depended on the biologic behavior of the cancer and the response to treatment. We calculated the probability of moving from one health state to the next from natural history data and randomized controlled trials (4,14–21). We estimated transition rates—the proportion of individuals moving from one state to the next in a given period—based on the mean time spent in each state. We next calculated monthly transition probabilities, assuming constant rates, using the formula (22) probability $= 1 - \exp(-\text{annual rate}/12)$.

We refined our estimates to account for both treatment effects and the substantial competing risk of death from other causes (23). With these model assumptions, men with hormone-sensitive disease would have an average cancer-free survival of about 4.5 years, following the first diagnosis of a distant metastasis, in close agreement with a recent observational study (24,25). The meta-analysis provided a point estimate of the efficacy of each therapy (relative to orchietomy) and a 95% confidence interval. While the point estimates varied between strategies, all 95% confidence intervals overlapped. Thus, our base case assumption was that all strategies were of equal efficacy. In a sensitivity analysis, we examined how using the point estimates of efficacy might change the results.

The models incorporated two additional advantages when an NSAA was used as part of a CAB regimen. First, we assumed that patients intolerant of one NSAA would start another. Second, we assumed that some patients would benefit from NSAA withdrawal with a transiently decreased risk of disease progression. The net effect of these assumptions was to bias the model in favor of CAB strategies.

### Side Effects

We distinguished between fatal side effects, severe side effects that required discontinuation of treatment, and bothersome but tolerable minor side effects. Fatal side effects, including hepatic failure from an NSAA and excess cardiac death from DES, could occur at any time during treatment (19,20,26). Severe side effects, such as copious diarrhea, occurred only in the first month of treatment and were assigned a one-time incremental cost and decrease in quality of life (13,27). Minor side effects, such as hot flashes, were assigned a continuous incremental cost and loss of quality of life for the duration of medication use. We assumed that minor side effects occur with equal frequency in all strategies. Rates for severe and minor side effects were pooled estimates of toxic effects reported in trials included in the meta-analysis (12).

### Quality of Life

We assigned a quality-of-life weight to each health state, reflecting the symptoms associated with advanced prostate cancer and its treatment (25,28–32).

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**Fig. 1.** Markov cycle diagram of prostate cancer natural history model. Simplified model is shown. Patients are treated with one of six possible androgen suppression strategies. Circles represent Markov states in the model. Arrows represent transitions between states. Patients can also experience local bladder outlet obstruction, as well as side effects from androgen suppression therapy. DES = diethylstilbestrol; NSAA = nonsteroidal antiandrogen; LHRH = luteinizing hormone-releasing hormone.
We based these estimates on a review of the literature assessing prostate cancer-related quality of life from the perspectives of patients and physicians (27,33,34). We assumed that men did not experience a substantial decrease in quality of life until hormone-resistant symptomatic distant metastases developed.

Perhaps our most controversial base case assumption is that orchiectomy and medical androgen suppression therapies had similar effects on quality of life. We also assumed that costs not in the model, such as the costs of treating other health conditions, were equivalent with each androgen suppression strategy. This assumption is reasonable, since no therapies were developed.

We investigated the effect of modifying several base case assumptions in sensitivity analyses. First, we relaxed the assumption that all treatments were equally effective. Instead, we based our alternative efficacy assumptions on the previous estimate of the cost of transurethral prostatectomy for local obstruction (43).

**Sensitivity Analysis**

We based our alternative efficacy assumptions on the previous estimate of the cost of transurethral prostatectomy for local obstruction (43).

**Costs**

Our model included the costs of androgen suppression strategies, other prostate cancer treatments, and side effects. We assumed that costs not in the model, such as the costs of treating other health conditions, were equivalent with each androgen suppression strategy. This assumption is reasonable, since no therapies conferred large survival advantages; thus, we anticipate the rates of other diseases among the various strategies to be similar. All costs were updated to 1998 U.S. dollars with the use of the Gross Domestic Product deflator (40). We based medication costs on the manufacturer’s wholesale drug price (41). We assumed that an NSAA was included in the first 2 weeks of LHRH agonist therapy to avoid worsening the androgen-dependent symptoms of prostate cancer. The cost of orchiectomy was derived from an estimate based on Medicare physician and outpatient facility charges (33). Other costs were based on comprehensive cost-studies (27,42,43). We assumed that minor side effects were associated with the cost of one additional office visit per year (43). We assumed that severe side effects were associated with a cost greater than the annual cost associated with minor side effects but less than that of treating the first recurrence of prostate cancer. We estimated the cost of treating bladder outlet obstruction from a previous estimate of the cost of transurethral prostatectomy for local obstruction (43).
The use of PSA testing after definitive radiation therapy may allow for the
diagnosis of recurrent prostate cancer by biochemical markers before it is clinically
apparent (14,44). Because some clinicians initiate therapy at the first rise
in PSA levels after definitive treatment, patients may use androgen suppression
for longer periods than assumed in the base case (11,45). To investigate how
such clinical strategies might change our cost-effectiveness estimates, we rede-
efined the health states and adjusted transition rates in the model to describe
disease progression from the first rise in PSA levels after definitive treatment to
the development of asymptomatic and then symptomatic distant metastases
(14,46). Incorporating PSA monitoring increased the time spent after initiation of
androgen suppression therapy to death by about 2.3 years over the base case and
resulted in an average time of 8 years from PSA-level rise to first diagnosed
distant metastasis, estimates consistent with the literature (14,47).

Calculating Cost-Effectiveness Ratios

The incremental cost-effectiveness of one strategy (A) relative to another (B)
was calculated as

\[
\text{cost of strategy } A - \text{cost of strategy } B \\
\text{health effects of strategy } A - \text{health effects of strategy } B
\]

Health effects were expressed as life years or quality-adjusted life years (QALY)
saved. The analysis was conducted with DATA software version 3.0.16 (Tree-
Age, Williamstown, MA).

RESULTS

We first estimated the health effects associated with androgen suppression strategies. Although each therapy was associated
with an equal reduction in risk of disease progression among patients receiving treatment, overall survival differed because of
differential rates of side effects, both nonfatal (but severe enough to require discontinuation of therapy) and fatal. DES
treatment resulted in an average survival of 6.9 years for a 65-
year-old man with advanced prostate cancer. NSAA treatment
increased survival to 7.4 years, while orchiectomy increased
survival to 7.6 years. Treatment with an LHRH agonist or either
CAB strategy resulted in an average survival of 7.5 years. The
effects on discounted quality-adjusted survival were similar:
DES resulted in a survival of 4.6 QALYs; orchiectomy and
LHRH agonists each resulted in a survival of 5.1 QALYs, and
NSAA and both CAB strategies yielded survivals of 5.0 QALYs (Table 3).

In contrast to the similar effects on quality-of-life and survival
estimates, the lifetime costs of the strategies differed mark-
edly. The discounted lifetime costs associated with treatment
were $3600 (DES), $7000 (orchiectomy), $16100 (NSAA), and
$27000 (LHRH agonists). The costs associated with orchiec-
tomy were least prone to discounting effects, since they were incurred early. The lifetime cost of CAB with NSAA plus orchi-
tomy was $20700; with NSAA plus LHRH agonist, the lifetime cost was $40300.

These cost and effectiveness estimates implied that the incre-
mental cost-effectiveness of orchiectomy relative to DES was
$6100 per life year gained. When quality-of-life effects were
incorporated, the incremental cost-effectiveness of orchiectomy
relative to DES was $7500 per QALY gained. All other strate-
gies—LHRH agonists, NSAA, and both CAB regimens—had
higher costs and lower quality-adjusted survival than orchiec-
tomy at the base case estimates of quality of life.

Results of Sensitivity Analysis

We repeated the analysis assuming that the therapies differed in
efficacy and basing our new efficacy values on the point
estimates from the meta-analysis (12). Under these assumptions,
the lowest quality-adjusted discounted survival was 4.6 QALYs

<table>
<thead>
<tr>
<th>Variable</th>
<th>Base case (range)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality-of-life weights</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local recurrent disease</td>
<td>0.92 (0.8–1)</td>
<td>(13,31,32,34); see text</td>
</tr>
<tr>
<td>Distant asymptomatic disease</td>
<td>0.9 (0.8–1)</td>
<td></td>
</tr>
<tr>
<td>Distant symptomatic disease, hormone responsive</td>
<td>0.8 (0.4–0.9)</td>
<td></td>
</tr>
<tr>
<td>Distant symptomatic disease, hormone resistant</td>
<td>0.4 (0.1–0.7)</td>
<td></td>
</tr>
<tr>
<td>Adjustment for living with minor side effect†</td>
<td>0.85 (0.5–1)</td>
<td></td>
</tr>
<tr>
<td>Medication cost (annual)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DES, 1 mg daily</td>
<td>$36 ($20–$120)</td>
<td>(41)</td>
</tr>
<tr>
<td>NSAA: nilutamide, 150 mg daily†</td>
<td>$2842 ($800–$3000)</td>
<td></td>
</tr>
<tr>
<td>Second NSAA: bicalutamide, 50 mg daily</td>
<td>$3890 ($2000–$6000)</td>
<td></td>
</tr>
<tr>
<td>LHRH agonist: goserelin, 10.8 mg every 3 mo</td>
<td>$4995 ($2000–$7000)</td>
<td></td>
</tr>
<tr>
<td>Second-line therapy: ketoconazole, 1200 mg daily</td>
<td>$7043 ($10–$1000)</td>
<td></td>
</tr>
<tr>
<td>Cost of orchiectomy</td>
<td>$3360 ($1500–$7000)</td>
<td>(33)</td>
</tr>
<tr>
<td>Cost of disease states (annual)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local recurrence</td>
<td>$320 ($200–$800)</td>
<td>(27,33,42); see text</td>
</tr>
<tr>
<td>Distant, asymptomatic</td>
<td>$320 ($200–$800)</td>
<td></td>
</tr>
<tr>
<td>Distant symptomatic</td>
<td>$410 ($200–$800)</td>
<td></td>
</tr>
<tr>
<td>Additional cost of living with a side effect</td>
<td>$30 ($0–$100)</td>
<td></td>
</tr>
<tr>
<td>Cost of preterminal care</td>
<td>$17000 ($5000–$35 000)</td>
<td></td>
</tr>
<tr>
<td>Outcomes incurred during transitions between states, per episode</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Annual probability of a local bladder outlet obstruction</td>
<td>2.20% (0%–4.4%)</td>
<td>(13,31,32,34)</td>
</tr>
<tr>
<td>Cost of a severe side effect</td>
<td>$150 ($50–$200)</td>
<td></td>
</tr>
<tr>
<td>Cost of local bladder outlet obstruction</td>
<td>$4830 ($3000–$6000)</td>
<td></td>
</tr>
<tr>
<td>Quality-of-life loss with local bladder outlet obstruction, quality-adjusted mo</td>
<td>0.1 (0–0.2)</td>
<td></td>
</tr>
</tbody>
</table>
| Dis-
with NSAA, and the highest was 5.1 QALYs with the combination of NSAA plus LHRH agonist. The lowest lifetime cost was $3600 with DES, and the highest was $41 400 with the combination of NSAA plus LHRH agonist. The incremental cost-effectiveness of orchiectomy relative to DES was $8100/QALY (Fig. 3). Monotherapy with NSAA, NSAA plus orchiectomy, and LHRH agonists had higher costs, lower survival, and lower quality-adjusted survival than orchiectomy. The cost-effectiveness of CAB with NSAA plus LHRH compared with orchiectomy was $1 110 000/QALY. CAB with NSAA plus orchiectomy had higher costs and lower quality-adjusted survival.

We evaluated various estimates of the efficacy of CAB relative to orchiectomy, using a range for sensitivity analysis based on the 95% confidence intervals from the meta-analysis (Fig. 4). Compared with orchiectomy, the cost-effectiveness of CAB with NSAA plus LHRH agonists in this range was always greater than $100 000/QALY. In contrast, the cost-effectiveness of CAB with NSAA plus orchiectomy in this range was as low as $43 400/QALY.

We examined the assumption that quality of life with orchiectomy was similar to that of other strategies (quality weight of 0.92). If the quality-of-life weight assigned to the state of living with an orchiectomy and no distant metastases were 0.88 or greater, the incremental cost-effectiveness of other strategies compared with orchiectomy would exceed $100 000/QALY. If the quality-of-life weight assigned to orchiectomy were less than 0.83, the incremental cost-effectiveness of LHRH agonists relative to orchiectomy would be less than $50 000/QALY.

If strategies involving orchiectomy are not viable options, the incremental cost-effectiveness of NSAA relative to DES becomes relevant; it was $43 200/QALY. The incremental cost-effectiveness of LHRH agonists relative to NSAA was $73 900/QALY. The combination of LHRH agonist plus NSAA resulted in higher costs and less quality-adjusted survival than LHRH agonists alone.

The model was insensitive to other input assumptions. For example, the cost-effectiveness ratio of orchiectomy relative to DES did not vary greatly when we changed the following parameters over the prespecified ranges: the quality-of-life weight for minor side effects ($6500–$15 200/QALY); the cost of orchiectomy was similar to that of other strategies (quality weight of 0.92). If the quality-of-life weight assigned to the state of living with an orchiectomy and no distant metastases were 0.88 or greater, the incremental cost-effectiveness of other strategies compared with orchiectomy would exceed $100 000/QALY. If the quality-of-life weight assigned to orchiectomy were less than 0.83, the incremental cost-effectiveness of LHRH agonists relative to orchiectomy would be less than $50 000/QALY.

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chiectomy ($3400–$15 400/QALY), the discount rate ($6000–$11 700/QALY), and the age of the patient ($5800–$11 000/QALY when the age was 50 or 75 years, respectively).

Timing also affects cost-effectiveness. For patients presenting with regional metastases at diagnosis, the greatest benefits and least cost were obtained by performing orchiectomy when patients developed symptomatic distant metastases. Quality-adjusted survival was 7.0 discounted QALYs if orchiectomy was delayed until symptomatic distant metastases developed and quality of life was low. Slightly less benefit (6.8 discounted QALYs) resulted when orchiectomy was performed as soon as asymptomatic distant metastases were detected, and the least benefit (6.2 QALYs) when orchiectomy was performed when stage C prostate cancer was initially diagnosed. Costs were lower when orchiectomy was performed late rather than early—$5200 with symptomatic distant disease, $5600 with asymptomatic distant disease, and $7400 at diagnosis with stage C prostate cancer—because fewer patients underwent the procedure. These results were only mildly sensitive to changes in the discount rate.

After the states and transition rates were modified to simulate

Table 3. Cost-effectiveness estimates*

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Cost, $†</th>
<th>Effectiveness, life years</th>
<th>Incremental cost-effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>DES</td>
<td>4100</td>
<td>6.86</td>
<td>referent</td>
</tr>
<tr>
<td>Orchiectomy</td>
<td>7500</td>
<td>7.58</td>
<td>$4900/life year</td>
</tr>
<tr>
<td>NSAA</td>
<td>18 400</td>
<td>7.39</td>
<td>Dominated‡</td>
</tr>
<tr>
<td>NSAA + orchiectomy</td>
<td>23 200</td>
<td>7.54</td>
<td>Dominated</td>
</tr>
<tr>
<td>LHRH agonist</td>
<td>30 900</td>
<td>7.54</td>
<td>Dominated</td>
</tr>
<tr>
<td>NSAA + LHRH agonist</td>
<td>46 200</td>
<td>7.52</td>
<td>Dominated</td>
</tr>
</tbody>
</table>

Costs and life years with discounting

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Cost, $</th>
<th>Effectiveness, life years</th>
<th>Incremental cost-effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>DES</td>
<td>$3600</td>
<td>5.96</td>
<td>referent</td>
</tr>
<tr>
<td>Orchiectomy</td>
<td>7000</td>
<td>6.52</td>
<td>$6100/life year</td>
</tr>
<tr>
<td>NSAA</td>
<td>16 100</td>
<td>6.38</td>
<td>Dominated</td>
</tr>
<tr>
<td>NSAA + orchiectomy</td>
<td>20 700</td>
<td>6.49</td>
<td>Dominated</td>
</tr>
<tr>
<td>LHRH agonist</td>
<td>27 000</td>
<td>6.50</td>
<td>Dominated</td>
</tr>
<tr>
<td>NSAA + LHRH agonist</td>
<td>40 300</td>
<td>6.48</td>
<td>Dominated</td>
</tr>
</tbody>
</table>

Costs and quality-adjusted life years with discounting

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Cost, $</th>
<th>Effectiveness, QALYs</th>
<th>Incremental cost-effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>DES</td>
<td>3600</td>
<td>4.64</td>
<td>referent</td>
</tr>
<tr>
<td>Orchiectomy</td>
<td>7000</td>
<td>5.10</td>
<td>$7500/QALY</td>
</tr>
<tr>
<td>NSAA</td>
<td>16 100</td>
<td>4.98</td>
<td>Dominated</td>
</tr>
<tr>
<td>NSAA + orchiectomy</td>
<td>20 700</td>
<td>5.05</td>
<td>Dominated</td>
</tr>
<tr>
<td>LHRH agonist</td>
<td>27 000</td>
<td>5.08</td>
<td>Dominated</td>
</tr>
<tr>
<td>NSAA + LHRH agonist</td>
<td>40 300</td>
<td>5.03</td>
<td>Dominated</td>
</tr>
</tbody>
</table>

*DES = diethylstilbestrol; LHRH = luteinizing hormone-releasing hormone; NSAA = nonsteroidal antiandrogen; QALY = quality-adjusted life years.
†All costs are rounded to the nearest $100.
‡Dominated strategies are less effective than cheaper alternatives.

Fig. 3. Health benefits and costs associated with androgen suppression strategies using alternative efficacy assumptions. Efficacy assumptions are based on point estimates from the meta-analysis. Lines connecting points representing two treatments indicate the incremental cost-effectiveness of the therapies. DES = diethylstilbestrol; NSAA = nonsteroidal antiandrogen; LHRH = luteinizing hormone-releasing hormone; QALY = quality-adjusted life years.
The acceptability of orchietomy undoubtedly varies greatly from patient to patient. For many, it will be a highly cost-effective treatment option. For others, the very concept of orchietomy may be objectionable. Epidemiologic studies (49) indicate that for every two Medicare beneficiaries treated with orchietomy, five are treated with LHRH agonists. However, it is unclear whether treatment decisions are guided by patient preference or if orchietomy diminishes quality of life more than medical therapies for most men. How patients value the quality-of-life effects of different androgen suppression strategies and how they use these values in making treatment decisions are topics for future research.

Combined androgen blockade is popular but expensive and, according to the results of a meta-analysis, differences between its efficacy and that of orchietomy are not statistically significant (12). For the incremental cost-effectiveness of combined androgen blockade with an NSAA compared with orchietomy to be less than $100 000/QALY, this combination must decrease the rate of disease progression by at least 20%. Less expensive combined androgen blockade can be achieved with orchietomy plus an NSAA. This combination must reduce the rate of disease progression by 10% to reach an incremental cost-effectiveness ratio of less than $100 000/QALY relative to orchietomy alone. For perspective, the lower bound of the 95% confidence interval of the rate of progression relative to orchietomy was 22% for each CAB strategy.

The greatest quality-of-life gains and least cost may be obtained by initiating therapy in later stages of disease. Consistent with our results, a small study (50) found that the quality of life of asymptomatic patients with prostate cancer who did not receive hormonal therapy was similar to or better than that of patients who received hormonal therapy. Furthermore, we modeled the effects of late therapy as delaying the time until severe illness occurs, although androgen suppression therapies likely also improve the health of patients with symptomatic metastases. Thus, our estimate of the benefit of delaying therapy may still be too low. Our study further indicates that initiating a palliative treatment based on a biochemical rather than on a clinical marker of disease progression has little clinical support and is unlikely to be cost-effective.

Our results are consistent with a previous analysis that examined the incremental cost-effectiveness of CAB with orchietomy plus flutamide compared with orchietomy alone (32,33). The principal difference with the earlier study is that our assumptions about the efficacy of CAB, based on a rigorous meta-analysis, were less optimistic. In addition, our analysis incorporates more clinical events, including local bladder outlet obstruction, the influence of biochemical monitoring, and issues related to the optimal timing of androgen suppression therapy. Our results do not apply to other clinical uses of androgen suppression, such as adjuvant chemotherapy of early prostate cancer. Furthermore, we did not evaluate therapies that are not approved for use in the United States, such as cyproterone acetate.

Our analysis calls into question the cost-effectiveness of widespread use of expensive androgen suppression strategies for men with advanced prostate cancer and the initiation of such therapy solely because of biochemical evidence of disease progression. Since Medicare spent more than $477 million on...
LHRH agonists in 1994, the potential for cost savings are considerable (51), yet our analyses also indicate the difficulties associated with determining the most efficient option while incorporating individual preferences. For example, orchietomy is most economically attractive for many patients, but medical therapies are likely to be the most cost-effective choice for others. Quality of life is a paramount concern when evaluating therapies for advanced prostate cancer; careful assessment of how individuals value orchietomy will help clinicians, patients, and policy makers determine which of the available surgical and medical therapies yields the best value for the money.

REFERENCES


NOTES

Editor’s note: The authors of this article are responsible for its contents, including any clinical or treatment recommendations. No statement in this article should be construed as an official position of the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

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