Outcomes of Localized Prostate Cancer Following Conservative Management

Grace L. Lu-Yao; Peter C. Albertsen; Dirk F. Moore; et al.


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In Reply:
Outcomes of Localized Prostate Cancer Following Conservative Management

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Among men, prostate cancer is the most common non-skin cancer and the second most common cause of cancer death in the United States.1 When diagnosed, prostate cancer is contained within the prostate in approximately 85% of cases,2 and standard treatment options usually include surgery, radiation, or conservative management (active surveillance or deferral of treatment until necessitated by disease signs or symptoms).

For men younger than 65 years with clinically localized prostate cancer, results of a large, randomized clinical trial have demonstrated that surgery improves survival compared with conservative management.3 The majority of men diagnosed with localized prostate cancer, however, are older than 65 years.4 Although not specifically designed to address age effects, this same clinical trial5 was unable to demonstrate a survival benefit for surgery among older men.5,6 Coupled with data showing that the lifetime risk of being diagnosed with prostate cancer is about 17%, while the corresponding risk of dying of this disease is only about 3%,6 the evidence suggests that conservative management may be an important treatment consideration for the sizable majority of men diagnosed with localized prostate cancer.

Despite its potential as a reasonable treatment choice, however, conservative management has been used in only about 10% of patients,7 perhaps because of a limited understanding of and contemporary data on the anticipated course and outcomes of this approach.

Context Most newly diagnosed prostate cancers are clinically localized, and major treatment options include surgery, radiation, or conservative management. Although conservative management can be a reasonable choice, there is little contemporary prostate-specific antigen (PSA)–era data on outcomes with this approach.

Objective To evaluate the outcomes of clinically localized prostate cancer managed without initial attempted curative therapy in the PSA era.

Design, Setting, and Participants A population-based cohort study of men aged 65 years or older when they were diagnosed (1992-2002) with stage T1 or T2 prostate cancer and whose cases were managed without surgery or radiation for 6 months after diagnosis. Living in areas covered by the Surveillance, Epidemiology, and End Results (SEER) program, the men were followed up for a median of 8.3 years (through December 31, 2007). Competing risk analyses were performed to assess outcomes.

Main Outcome Measures Ten-year overall survival, cancer-specific survival, and major cancer related interventions.

Results Among men who were a median age of 78 years at cancer diagnosis, 10-year prostate cancer-specific mortality was 8.3% (95% confidence interval [CI], 4.2%-12.8%) for men with well-differentiated tumors; 9.1% (95% CI, 8.3%-10.1%) for those with moderately differentiated tumors, and 25.6% (95% CI, 23.7%-28.3%) for those with poorly differentiated tumors. The corresponding 10-year risks of dying of competing causes were 59.8% (95% CI, 53.2%-67.8%), 57.2% (95% CI, 52.6%-63.9%), and 56.5% (95% CI, 53.6%-58.8%), respectively. Ten-year disease-specific mortality for men aged 66 to 74 years diagnosed with moderately differentiated disease was 60% to 74% lower than earlier studies: 6% (95% CI, 4%-8%) in the contemporary PSA era (1992-2002) compared with results of previous studies (15%-23%) in earlier eras (1949-1992). Improved survival was also observed in poorly differentiated disease. The use of chemotherapy (1.6%) or major interventions for spinal cord compression (0.9%) was uncommon.

Conclusions Results following conservative management of clinically localized prostate cancer diagnosed from 1992 through 2002 are better than outcomes among patients diagnosed in the 1970s and 1980s. This may be due, in part, to additional lead time, overdiagnosis related to PSA testing, grade migration, or advances in medical care.

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METHODS

Data Sources

Data were obtained from Medicare insurance program files linked to the population-based Surveillance, Epidemiology, and End Results (SEER) cancer registries, which are 98% complete for case ascertainment.12 The SEER regions encompassed approximately 14% of the US population before 2000 and 25% thereafter.12 The Medicare database covers approximately 97% of US persons aged 65 years or older. Linkage to the SEER database is complete for approximately 93% of the patients.12 This study was approved by the University of Medicine and Dentistry of New Jersey institutional review board, as well as by the SEER program, and the Center for Medicare & Medicaid Services. Informed consent was waived by the University of Medicine and Dentistry of New Jersey institutional review board because the data did not contain personal identifiers.

Cancer stage and grade for each case were abstracted from SEER data files. Well differentiated cancers were characterized by a Gleason score of 2 to 4; moderately differentiated, 5 to 7, and poorly differentiated, 8 to 10. Information about treatment was obtained from both SEER and Medicare files. A Charlson comorbidity score was derived from Medicare claims during the year prior to prostate cancer diagnosis using a validated algorithm.13 Race was self-determined by the patients. Outcomes in the pre-PSA era were obtained from published literature except for the study by Albertsen et al,10 for which age-specific data were obtained directly from the authors. In this study, the pre-PSA era refers to the period before 1988. The contemporary PSA era refers to outcomes among patients diagnosed in 1992 or thereafter.

Study Participants

The study cohort consisted of men older than 65 years who were SEER residents and diagnosed with AJCC (American Joint Committee on Cancer) stage T1 or T2 cancer from 1992 through 2002 (N=89 877). This ensured that every patient had at least 12 months of Medicare claims data to assess their comorbidity status prior to cancer diagnosis (1991 was the first year Medicare claims data were available for all cancer cases). Men who died within 180 days of diagnosis (n=1761), or who received attempted curative therapy such as prostatectomy or radiation within 180 days of diagnosis were excluded (n=31 485). Patients who had other cancers diagnosed either before or after prostate cancer were excluded (n=3965) to ensure that all cancer therapies were for prostate cancer. Men who did not have both Medicare Part A and Part B as their primary health insurance coverage during the study period were excluded (n=34 777) because their cancer treatment history might be incomplete. Men with missing data (n=2995), an unknown cancer grade (n=255), or who received androgen deprivation therapy prior to diagnosis (n=123) were also excluded. In this study, we classified T1c cancer as detected by PSA screening results and the rest as a nonscreen detected cancer. Results (both mortality and secondary cancer therapies) remained similar when patients receiving attempted curative therapy more than 180 days after diagnosis were excluded.

Outcomes Assessment

Overall survival was available through December 31, 2007, and prostate cancer–specific survival, through December 31, 2005. Underlying causes of death were obtained from the SEER database. Previous studies have shown high agreement (87%-92%) between cause of death in the SEER database and that determined through medical record review.14,15 Follow-up cancer therapies were identified from SEER and Medicare claims data through the end of 2005. External beam radiation that consisted of less than 20 visits within a 6-week period was considered palliative, whereas brachytherapy or external beam radiation delivered over 20 visits within 6 weeks was considered attempted curative therapy. Chemotherapy use was identified through previously published algorithms (κ=0.73 compared with medical record review).16 A validated algorithm was used to identify androgen deprivation therapy.17,18 We developed and validated a new algorithm to identify palliative surgery or radiation for spinal cord compression, impending cord compression, or painful metastasis based on chart review.

Statistical Analyses

The primary study end points were time to death from prostate cancer and time to death from other causes, stratified by patient age, cancer grade, and stage at diagnosis. Our study had more than 95% power to detect a change of 10 percentage points in the prostate cancer death rate estimates compared with previously reported rates. For the analysis of competing risks, we tabulated the numbers of men with each of the 3 outcomes of interest (alive, dead from prostate cancer, and dead from other causes) for each of the age-grade-stage combinations. Results for men with T1 and T2 well-differentiated cancers were combined because of limited sample sizes. Confidence intervals (CIs) for the current study were based on 95% per-

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centiles of 1000 bootstrap replications of the competing risks model for death from either prostate cancer or other causes.19 Confidence intervals for Albertsen et al were estimated using a Weibull survival model that matched the 5- and 10-year prostate cancer death rates reported in that article. The rest of the CIs were extracted from published literature. Our study, with much larger sample sizes than the study by Albertsen et al,20 had more than 95% power to detect a change of 10 percent-

age points in the prostate cancer death rate estimates over rates for moderately differentiated disease reported by Albertsen et al and more than 80% power for poorly differentiated disease, based on simulations with 1000 replications. Confidences intervals were based on percentiles of 1000 bootstrap replications of the competing risks model for the 3 outcomes.19

Estimates of competing risks and P values were computed using cumulative incidence functions.20 For the analysis of competing risks for secondary cancer therapy, we computed the competing risks of each outcome independently, with death treated as a competing risk, because 1 individual could have had more than 1 secondary treatment. To provide more stable estimates of the survival curves, we used a nearest neighbor hazard smoother with an Epanechnikov kernel21 as implemented in the R statistical system (R Foundation for Statistical Computing, Vienna, Austria). All P values were 2 sided. P < .05 were considered statistically significant.

RESULTS

Baseline characteristics of the study population are summarized in TABLE 1. Seventy-six percent of the men had Gleason scores of 5 to 7 (n = 10,988) and 4493 men (31%) had screen detected cancer (T1c). Palpable disease (T2) at diagnosis was present in 42% of the cases, and most men (≥70%) did not have significant comorbid conditions. The median age at diagnosis was 78 years and median follow-up was 8.3 years. At the end of the study period, most men were either alive or had died of other causes (TABLE 2). During the first 10 years, among the 222 patients diagnosed with well-differentiated prostate cancer, 15 died of prostate cancer and 133 died of other causes. Among the 10,988 patients diagnosed with moderately differentiated prostate cancer, 642 died of prostate cancer and 5005 died of other causes. Among the 3306 patients diagnosed with poorly differentiated prostate cancer, 684 died of prostate cancer and 1652 died of other causes. Ten-year prostate cancer-specific mortality was 8.3% (95% CI, 4.2%-12.8%) for men with well-differentiated, 9.1% (95% CI, 8.3%-10.1%) moderately differentiated, and 25.6% (95% CI, 23.7%-28.3%) poorly differentiated tumors. The corresponding 10-year risks of dying of causes other than prostate cancer were 59.8% (95% CI, 53.2%-67.8%), 57.2% (95% CI, 52.6%-63.9%), and 56.5% (95% CI, 53.6%-58.8%) for each respective group. The Figure illustrates the competing risk of death according to age at diagnosis, cancer stage, and grade. Results for well-differentiated tumors were not shown because sample sizes were too small for reliable estimates. When the analyses were restricted to men without androgen deprivation therapy within 6 months of cancer diagnosis, the results were comparable or even more favorable than those shown in the Figure.

Survival results in our contemporary PSA era study cohort were more favorable than results previously reported. For example, in the current study, 10-year prostate cancer-specific mortality was 6% (95% CI, 4.4%-8%) in the contemporary PSA era (1992-2002) compared with results of previous studies (15%-23%) in earlier eras (1949-1992) for men aged 65 to 74 years diagnosed with moderately differentiated disease (TABLE 3). Improvement in survival among men with older age or poorly differentiated disease was also observed.

TABLE 4 summarizes 10-year cumulative risks of various secondary cancer therapies based on the analyses of competing risks. Overall, androgen deprivation therapy use was high: about 60% to 83% within 10 years. Forty-one percent of our cohort received androgen deprivation therapy within 6 months of cancer diagnosis; among the remaining cohort members, 28.4% with moderately and 45.4% with poorly differentiated cancer received androgen deprivation therapy within 10 years. Relatively few patients received chemotherapy (n = 237, 1.6%), or underwent spinal surgery or radiation for metastatic disease (n = 134, 0.9%). Ten-year cumulative risks of palliative therapy (palliative radiation, chemotherapy, or spinal surgery or radiation) were 4.1% and 6.9% among older men, respectively. The long-term impact of these therapies on survival has not been well-studied.
patients (≥75 years) with nonscreen-detected moderately and poorly differentiated cancer, respectively. Younger age was associated with higher use of palliative therapy (P < .001). Outcomes were similar when analyses were restricted to relatively healthy men (comorbidity score, 0).

**COMMENT**

The appropriate treatment of men with clinically localized prostate cancer diagnosed in the PSA era has been a subject of great controversy. For the majority of men older than 65 years who are diagnosed with localized disease, randomized clinical trial data have not been able to demonstrate a survival benefit for surgery or for any other approach compared with conservative management. Despite these data raising the possibility that conservative management may be a reasonable treatment choice, little data exist that describe outcomes following conservative management in the contemporary PSA era.

To address this lack of data, we examined 14,516 men with localized T1 or T2 prostate cancer without initial attempted curative therapy and found that 10-year prostate cancer–specific mortality declined by more than 60% compared with previous studies (Table 3). We also found that for the majority of men managed without initial attempted curative therapy (ie, those >65 years with moderately differentiated cancer), only a limited proportion (4%-11%) used palliative ra-

**Table 2. Sample Sizes by Age and Vital Status as of December 31, 2005, Among 14,516 Patients With Clinically Localized Prostate Cancer**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>66-69 (n = 1450)</th>
<th>70-74 (n = 3005)</th>
<th>75-79 (n = 4376)</th>
<th>≥80 (n = 5685)</th>
<th>All Ages (N=14,516)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gleave 2-4, stages I and II</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall sample size</td>
<td>27 (100)</td>
<td>53 (100)</td>
<td>63 (100)</td>
<td>79 (100)</td>
<td>222 (100)</td>
</tr>
<tr>
<td>Died of prostate cancer</td>
<td>NA</td>
<td>NA</td>
<td>8 (13)</td>
<td>8 (10)</td>
<td>17 (8)</td>
</tr>
<tr>
<td>Died of other cause</td>
<td>NA</td>
<td>NA</td>
<td>37 (59)</td>
<td>62 (78)</td>
<td>141 (64)</td>
</tr>
<tr>
<td>Alive</td>
<td>16 (59)</td>
<td>21 (40)</td>
<td>18 (29)</td>
<td>9 (11)</td>
<td>64 (29)</td>
</tr>
<tr>
<td>Moderately Differentiated Cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall sample size</td>
<td>345 (100)</td>
<td>713 (100)</td>
<td>946 (100)</td>
<td>1231 (100)</td>
<td>3235 (100)</td>
</tr>
<tr>
<td>Died of prostate cancer</td>
<td>NA</td>
<td>21 (3)</td>
<td>40 (4)</td>
<td>79 (6)</td>
<td>143 (4)</td>
</tr>
<tr>
<td>Died of other cause</td>
<td>NA</td>
<td>252 (35)</td>
<td>411 (43)</td>
<td>738 (60)</td>
<td>1485 (46)</td>
</tr>
<tr>
<td>Alive</td>
<td>258 (75)</td>
<td>440 (62)</td>
<td>495 (52)</td>
<td>414 (34)</td>
<td>1607 (50)</td>
</tr>
<tr>
<td>Poorly Differentiated Cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall sample size</td>
<td>415 (100)</td>
<td>818 (100)</td>
<td>1127 (100)</td>
<td>1199 (100)</td>
<td>3559 (100)</td>
</tr>
<tr>
<td>Died of prostate cancer</td>
<td>9 (2)</td>
<td>26 (3)</td>
<td>64 (6)</td>
<td>75 (6)</td>
<td>174 (5)</td>
</tr>
<tr>
<td>Died of other cause</td>
<td>66 (16)</td>
<td>190 (23)</td>
<td>311 (28)</td>
<td>501 (42)</td>
<td>1068 (30)</td>
</tr>
<tr>
<td>Alive</td>
<td>340 (82)</td>
<td>602 (74)</td>
<td>752 (67)</td>
<td>623 (52)</td>
<td>2317 (65)</td>
</tr>
</tbody>
</table>

Abbreviation: NA, not available because Surveillance Epidemiology, and End Results (SEER)−Medicare privacy rules prohibit disclosure of numbers of less than 5 in any specific cell; therefore, numbers in those rows do not sum.

SEER clinical extension information was used to determine cancer stage (T1, T2).
Radiation therapy, chemotherapy, or treatments for spinal cord compression over the ensuing 10 years following diagnosis. In contrast, use of androgen deprivation therapy was quite common.

The substantial improvement in survival that we observed in our study compared with previous reports might be explained, in part, by additional lead time, overdiagnosis related to PSA testing, or grade migration, among other factors. Prostate-specific antigen testing identifies disease 6 to 13 years before it presents clinically. Contemporary patients identified through such testing would be expected to live at least 6 to 13 years longer because of this lead time. In addition, previously documented systematic upgrading of modern tumors compared with earlier eras makes more recently graded tumors appear to have a more benign course, resulting in longer survivals. Finally, it is also possible that advancements in medical care might have led to improved outcomes. The net overall effect is that outcomes following conservative management are now significantly better than those reported in previous eras; therefore, physicians and their patients may need to reconsider this management option, particularly in light of randomized trial data from the pre-PSA era suggesting little if any benefit to more aggressive intervention.

Our documentation of a major improvement in conservative management outcomes is important, not only because it provides updated information for physicians and patients but also because the results may color the interpretation of maturing randomized clinical trials. For example, in the widely cited Scandinavian randomized study of prostatectomy vs conservative management, disease-specific survival in the conservative management group (~85% at 10-year) was found to be very similar to that documented in several observational cohort studies of conservative management from the same pre-PSA or early PSA era (~87%,~88%,~86%,~83%~83%). The use of radical prostatectomy resulted in an approximate 5.3% absolute percentage point increase to about 90% in cancer-specific survival in this study.

The results of our study, however, demonstrated that 10-year cancer-specific survival with conservative management has now increased from about 83% to 87% in the pre-PSA or early PSA era to about 94% in the PSA era, which is now beyond the approximate 90%
10-year cancer-specific survival rate for a similar population of men treated with prostatectomy in the pre-PSA or early PSA era Scandinavian trial (ie, those aged 66-74 years with moderately-differentiated cancer; Table 3). The room available for additional improvement when 10-year cancer-specific survival is already close to 94% with conservative management may be limited, and the absolute benefit of surgery in the Scandinavian trial may be difficult to reproduce in similar studies like the US Prostate Cancer Intervention vs Observation Trial (PIVOT), in which most men were diagnosed through PSA screening. Nevertheless, the only true way to determine whether this will be the case is to await the results of contemporary randomized studies like PIVOT, and it is not our intent to suggest that benefit for the majority of men with localized prostate cancer (ie, those ≥65 years old) can be excluded based on our results and those of the Scandinavian study.3 On the other hand, for men with poorly differentiated dis-

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Table 3. Ten-Year Competing Risk of Dying of Prostate Cancer According to Cancer Grade and Age Group for Men Aged 65 to 74 Years Without Initial Attempted Curative Therapy

<table>
<thead>
<tr>
<th>Cancer Grade, % (95% Confidence Interval)</th>
<th>Year of Cancer Diagnosis</th>
<th>Moderately Differentiated, Gleason 5-7, Age at Diagnosis, y</th>
<th>Poorly Differentiated, Gleason 8-10, Age at Diagnosis, y</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>65-69</td>
<td>70-74</td>
</tr>
<tr>
<td></td>
<td></td>
<td>65-69</td>
<td>70-74</td>
</tr>
<tr>
<td>Current study, stage T1a</td>
<td>1992-2002</td>
<td>2 (1-4)</td>
<td>5 (3-7)</td>
</tr>
<tr>
<td>Current study, stage T1 or T2a</td>
<td>1992-2002</td>
<td>6 (4-8)</td>
<td>6 (5-8)</td>
</tr>
<tr>
<td>Albertsen et al.a, 2005</td>
<td>1971-1984</td>
<td>21 (10-32)</td>
<td>23 (13-34)</td>
</tr>
<tr>
<td>Johansson et al.a, 2004</td>
<td>1977-1984</td>
<td>15 (4-26)</td>
<td>15 (4-26)</td>
</tr>
<tr>
<td>Lu-Yao et al.a, 1997</td>
<td>1983-1992</td>
<td>23 (20-26)</td>
<td>23 (20-26)</td>
</tr>
<tr>
<td>Chodak et al.a, 1994</td>
<td>1949-1989</td>
<td>16 (11-20)</td>
<td>16 (11-20)</td>
</tr>
<tr>
<td>Adolfsson et al.a, 1992</td>
<td>1978-1982</td>
<td>16 (9-23)</td>
<td>16 (9-23)</td>
</tr>
</tbody>
</table>

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Table 4. Ten-Year Cumulative Risk of Selected Secondary Cancer Treatments After Diagnosis in Patients With Localized Prostate Cancer Without Initial Attempted Curative Therapy

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Modestly Differentiated, Gleason 5-7 (95% Confidence Interval)d</th>
<th>Poorly Differentiated, Gleason 8-10, % (95% Confidence Interval)d</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Screen Detected T1c (n = 1233)</td>
<td>Nonscreen Detected</td>
</tr>
<tr>
<td></td>
<td>10-y Risk (95% CI)</td>
<td>10-y Risk (95% CI)</td>
</tr>
<tr>
<td></td>
<td>No. of Events</td>
<td>No. of Events</td>
</tr>
<tr>
<td>Attempted curative therapyb</td>
<td>257</td>
<td>23.7 (21.2-26.9)</td>
</tr>
<tr>
<td>Androgen deprivation therapy</td>
<td>590</td>
<td>60.3 (56.7-64.4)</td>
</tr>
<tr>
<td>Palliative radiation, chemotherapy, or spinal surgery or radiationc</td>
<td>109</td>
<td>10.9 (9.2-13.3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Screen-Detected, T1c (n = 2377)</td>
<td>Nonscreen Detected</td>
</tr>
<tr>
<td></td>
<td>10-y Risk (95% CI)d</td>
<td>10-y Risk (95% CI)d</td>
</tr>
<tr>
<td></td>
<td>No. of Events</td>
<td>No. of Events</td>
</tr>
<tr>
<td>Attempted curative therapyb</td>
<td>24</td>
<td>14.1 (9.5-20.1)</td>
</tr>
<tr>
<td>Androgen deprivation therapy</td>
<td>157</td>
<td>81.8 (75.1-97.4)</td>
</tr>
<tr>
<td>Palliative radiation, chemotherapy, or spinal surgery or radiationc</td>
<td>35</td>
<td>30.1 (16.1-51.1)</td>
</tr>
</tbody>
</table>

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ease managed conservatively, the 10-year cancer-specific survival was substantially lower (~58%-74%) than what was reported in the Scandinavian trial and, therefore, the potential for benefit with attempted curative therapy may be greater for these men.

Our study had some limitations. The men in our study, like the majority of patients with prostate cancer, were 65 years or older and our results might not apply to younger patients. In addition, we were limited to data available in the SEER registries. For example, PSA values at diagnosis were not collected during the study period and Gleason 5, 6, and 7 tumors were grouped together as moderately differentiated disease. Consequently, the results for moderately differentiated disease as a whole may overestimate survival for Gleason 7 tumors and underestimate survival for Gleason 5 tumors. In addition, there may be unmeasured patient or disease characteristics beyond age, tumor stage, and tumor grade unique to patients selecting conservative management that effect results so that they may not apply to patients with more aggressive disease characteristics not captured in the database. Another limitation is the length of follow-up. Because of the protracted nature of the disease, longer follow-up data are needed for men with a life expectancy of greater than 10 years.

Finally, as in other observational and randomized trials and studies, the secondary end points were supportive, exploratory, and less robust than the primary end points. For example, although the Medicare database is generally able to capture the initiation of secondary therapy accurately (surgery, radiation, androgen deprivation therapy, and chemotherapy, etc), the actual accuracy may vary somewhat from procedure to procedure and, therefore, comparisons between rates of secondary therapies may be less exact.12,16,37 In addition, the Medicare database does not consistently capture the use of oral agents, such as the antiandrogens, that may be used for androgen deprivation therapy. In the case of antiandrogens, however, data from the CAPSURE (Center of the Prostate Strategic Urologic Research Endeavor) database have shown that the use of antiandrogens as sole treatment for localized prostate cancer is uncommon (~2%) and, therefore, it is unlikely that the use of hormonal therapy would be significantly underestimated. Irrespective of the strengths and limitations of each secondary end point, however, it is important to recognize that the purpose of these additional analyses was to provide additional insight and context for the interpretation of the primary end points of cancer-specific and overall survival and not necessarily for these end points to stand alone as definitive conclusions.

In addition to the study’s limitations, there were also some important strengths. The study was population-based, and all-inclusive in the regions studied, rather than limited to specific institutions or networks. Consequently, the results are more likely to apply more broadly. Furthermore, the study was much larger than previous studies and, therefore, provided more stable estimates on which to base future clinical decisions. In particular, conservative management is often an especially relevant treatment choice for men aged 75 years or older. However, data on this older population are rare and this group is often excluded or underrepresented in randomized trials. Our study, with more than 10,061 men aged 75 years or older, provided crucial information to fill this important knowledge gap.

In summary, our findings suggest that outcomes following conservative management of contemporary PSA era patients with localized prostate cancer are substantially more favorable than in studies from earlier eras, and patients with well- or moderately differentiated disease managed conservatively are generally even more likely to die of causes other than prostate cancer.10,12,24,31 Considering favorable 10-year outcomes following conservative management, men with a life expectancy of less than 10 years may wish to consider an active surveillance or watchful waiting protocol as an alternative to immediate attempted curative therapy.10,24,30,34,39

Author Contributions: Dr Lu-Yao had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Lu-Yao, Albertsen, DiPaola, Barry, Zietman, Yao.

Acquisition of data: Lu-Yao, Walker-Corkery.

Analysis and interpretation of data: Lu-Yao, Albertsen, Moore, Shih, Lin, Barry, Zietman, O’Leary, Yao.

Drafting of the manuscript: Lu-Yao, Albertsen, Lin, Yao.

Critical revision of the manuscript for important intellectual content: Lu-Yao, Albertsen, Moore, Shih, DiPaola, Barry, Zietman, O’Leary, Walker-Corkery, Yao.

Statistical analysis: Lu-Yao, Moore, Shih, Lin.

Obtained funding: Lu-Yao.

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