**LESS IS MORE**

Five-Year Downstream Outcomes Following Prostate-Specific Antigen Screening in Older Men

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**Importance:** Despite ongoing controversies surrounding prostate-specific antigen (PSA) screening, many men 65 years or older undergo screening. However, few data exist that quantify the chain of events following screening in clinical practice to better inform decisions.

**Objective:** To quantify 5-year downstream outcomes following a PSA screening result exceeding 4.0 ng/mL in older men.

**Design and Setting:** Longitudinal cohort study in the national Veterans Affairs health care system.

**Participants:** In total, 295,645 men 65 years or older who underwent PSA screening in the Veterans Affairs health care system in 2003 and were followed up for 5 years using national Veterans Affairs and Medicare data.

**Main Outcome Measures:** Among men whose index screening PSA level exceeded 4.0 ng/mL, we determined the number who underwent prostate biopsy, were diagnosed as having prostate cancer, of whom 4284 (82.1%) were treated for prostate cancer. Performance of prostate biopsy decreased with advancing age and worsening comorbidity (P < .001), whereas the percentage treated for biopsy-detected cancer exceeded 75% even among men 85 years or older, those with a Charlson-Deyo Comorbidity Index of 3 or higher, and those having low-risk cancer. Among men with biopsy-detected cancer, the risk of death from non–prostate cancer causes increased with advancing age and worsening comorbidity (P < .001). In total, 468 men (3.6%) had complications within 7 days after prostate biopsy. Complications of prostate cancer treatment included new urinary incontinence in 584 men (13.6%) and new erectile dysfunction 588 men (13.7%).

**Conclusions and Relevance:** Performance of prostate biopsy is uncommon in older men with abnormal screening PSA levels and decreases with advancing age and worsening comorbidity. However, once cancer is detected on biopsy, most men undergo immediate treatment regardless of advancing age, worsening comorbidity, or low-risk cancer. Understanding downstream outcomes in clinical practice should better inform individualized decisions among older men considering PSA screening.


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or older. Furthermore, trial results were conflicting. While the European Randomized Study of Screening for Prostate Cancer\(^2\) found that screening had reduced prostate cancer mortality by 21% at 11 years, the US Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial\(^3\) found no reduction in prostate cancer mortality. In addition, extrapolating trial results to the heterogeneous population of older men seen in clinical practice is challenging, especially because the chain of events following PSA screening in this population is unknown and likely different from that in trials.

This study makes innovative use of Veterans Affairs (VA) and Medicare claims-based data and electronic health records to determine downstream outcomes during 5 years following PSA screening in veterans 65 years or older. Specifically, we hypothesized that, in clinical practice, frequencies of abnormal PSA screening results, repeat PSA tests, prostate biopsies, prostate cancer diagnoses, prostate cancer treatment, and 5-year survival would differ according to baseline characteristics, such as age and comorbidity. These data are fundamental to informing individualized decisions about PSA screening in older men.

**METHODS**

We conducted a longitudinal cohort study of 295,645 men 65 years or older who underwent PSA screening in the VA health care system in 2003 and were followed up for 5 years to determine downstream outcomes using national VA and Medicare data. We established a cohort using the VA National Patient Care Database to identify 710,918 men 65 years or older who had at least 1 outpatient visit in both 2002 and 2003 and had an index PSA test in 2003 at 1 of 104 VA facilities (Figure 1). An index PSA test was defined as the first outpatient PSA test in the 2003 VA Decision Support System National Data Extracts Laboratory Results data set (which captured PSA results for 104 of 127 VA facilities).\(^4\) Also, we used linked claims to capture services provided to our cohort from Medicare.\(^5\) We excluded men enrolled in Medicare managed care and men for whom PSA testing was nonscreening because of a history of prostate cancer or elevated PSA level or because of specific symptoms within 3 months before the test (Figure 1). This left a final PSA screening cohort of 295,645 men.

**BASELINE CHARACTERISTICS**

Age was determined on the date of the index PSA screening. The Charlson-Deyo Comorbidity Index was calculated from VA and Medicare inpatient and outpatient claims during the 12 months before the index PSA date.\(^6\) Other factors known to influence the use and outcomes of PSA screening were obtained from VA and Medicare data and linkage to the 2000 US census (eTable: http://www.jamainternalmed.com).\(^6\)

**OUTCOMES OF SCREENING**

We linked VA National Data Systems, VA Central Cancer Registry, National Death Index, and Medicare claims to capture downstream testing and outcomes during the 5 years after the index PSA screening in 2003. All men were followed up until death or to 5 years. The eAppendix includes the data codes for defining all variables.

![Figure 1. Exclusion criteria used to define the final cohort of older men who underwent a screening prostate-specific antigen (PSA) test in 2003 at a Veterans Affairs (VA) facility. "History was defined by searching VA and Medicare inpatient and outpatient claims and the VA Central Cancer Registry between January 1, 1999, and the date of the index PSA test in 2003. Veterans Affairs and Medicare claims were used to exclude men with prostate symptoms during the 3 months before their index PSA test because this PSA result was considered a diagnostic test rather than a screening test. CPT indicates Current Procedural Terminology; ICD-9, International Classification of Diseases, Ninth Revision.](http://archive.jamanetwork.com/pdfsaccess.ashx?url=/data/journals/intemed/926981/ on 06/17/2017)

Follow-up Testing After an Abnormal PSA Result

We identified men whose index screening PSA value exceeded 4.0 ng/mL because this is the most common definition of an abnormal level for older men in the United States (to convert PSA level to micrograms per liter, multiply by 1.0).\(^7\) Among these men, we calculated the number of prostate biopsies during the next 5 years or until prostate cancer diagnosis. Men were considered to have undergone more than 1 biopsy if procedure visit dates were more than 2 weeks apart.\(^8\) Among men who underwent at least 1 biopsy, we determined the number of repeat PSA tests during the period between the index PSA screening and the first biopsy. Among men who did not undergo a biopsy, repeat PSA testing was determined between the index PSA screening date and the prostate cancer diagnosis date or the end of the 5-year study period.

**Prostate Cancer Diagnosis**

Incident prostate cancer was determined during the period between the index PSA screening and the end of the 5-year study period. The VA Central Cancer Registry collects uniformly reported information on all men who are diagnosed as having prostate cancer or receive their first course of cancer treatment at a VA facility.\(^9\) For these men, we had access to cancer stage and histologic grade. Outside of the VA, prostate cancer was identified from Medicare claims, which do not include prostate cancer characteristics.\(^10\)

![Table 1. Characteristics and outcomes of screening PSA test in 2003 at a VA medical center](http://archive.jamanetwork.com/pdfsaccess.ashx?url=/data/journals/intemed/926981/ on 06/17/2017)
Prostate Cancer Treatment and Survival

Among men diagnosed as having prostate cancer, we determined (1) receipt of treatment with curative intent (ie, radical prostatectomy or radiation therapy), (2) receipt of hormone therapy alone, or (3) no receipt of these treatments during the period between cancer diagnosis and the end of the 5-year study period.21,24 Men who underwent multiple treatments were assigned to the most aggressive treatment received (most to least aggressive therapy was radical prostatectomy, radiation therapy, and hormone therapy). Among men with prostate cancer who did not receive treatment, we determined repeat PSA testing during the period between cancer diagnosis and the end of the 5-year study period. Five-year survival was based on the VA Vital Status file, and cause of death was based on the National Death Index.

Biopsy and Treatment Complications

We determined the number of men who experienced complications (eg, sepsis, hemorrhage, urinary retention, and urinary tract infection) or death within 7 days of biopsy.26-28 We calculated the number of men treated for prostate cancer who developed new urinary incontinence or new erectile dysfunction, which was defined by claims data or by receipt of diapers, pads, incontinence supplies, or erectile dysfunction medications obtained from VA Pharmacy Benefits Management data.

STATISTICAL ANALYSIS

To determine the frequency of downstream outcomes, we observed men from the date of their index PSA screening in 2003 until death or to 5 years. Each downstream outcome is presented as the percentage of men who had the event. To determine associations between baseline characteristics and each outcome, we used χ² tests. We also present the percentages of men who had biopsy or treatment complications. To determine the combined effect of age and comorbidity on the risk for dying of non–prostate cancer causes, we categorized men with a positive biopsy result into 15 subgroups on the basis of age (5 categories) and Charlson-Deyo Comorbidity Index (3 categories) and present the percentages (95% CIs) of men who died of other causes within 5 years of screening. Differences between percentages in each age-comorbidity subgroup were determined using Cochran-Armitage trend tests. We also conducted a subgroup analysis of downstream outcomes among men diagnosed as having low-risk prostate cancer (clinical stage T1 or T2 cancer without malignant nodes or metastases, Gleason grade ≤6, and PSA level ≤10.0 ng/mL).21 We used commercially available statistical software (SAS, version 9.2; SAS Institute, Inc) for all analyses. The Committee on Human Research at the University of California, San Francisco, and the Committee for Research and Development at the San Francisco VA Medical Center approved the study.

RESULTS

PARTICIPANT CHARACTERISTICS

Our cohort included 295,645 men who had a screening PSA test in 2003 at 1 of 104 VA facilities. Their mean age was 73 years (age range, 65-107 years), 9.6% had a Charlson-Deyo Comorbidity Index of 3 or higher, and 89.6% were of white race/ethnicity (Table). Thirty-five percent had undergone PSA screening in the year before their index PSA screening in 2003. In total, 25,208 men (8.5%) had an index PSA level exceeding 4.0 ng/mL; 7399 men (2.5%) had a level exceeding 6.5 ng/mL, and 2775 men (0.9%) had a level exceeding 10.0 ng/mL. The percentage of men with an abnormal PSA result increased with age, from 5.9% for men aged 65 to 69 years to 17.3% for men 85 years or older (P < .001). Men of black race/ethnicity were 1.8 (95% CI, 1.7-1.9) times more likely to have an abnormal result than men of white race/ethnicity.

FOLLOW-UP TESTING AFTER AN ABNORMAL PSA RESULT

Of 25,208 men with an index PSA screening exceeding 4.0 ng/mL, 3077 (12.2%) had a prostate biopsy performed without repeat PSA testing, 5236 (20.8%) had 1 or more repeat PSA tests before biopsy, and 16,895 (67.0%) never had a biopsy during the 5-year study period (Figure 2). In the subgroup with a PSA level exceeding 6.5 ng/mL, 61% never had a biopsy, while in the subgroup with a PSA level exceeding 10.0 ng/mL, 58.3% never had a biopsy. Age was also a strong predictor of biopsy performance: 50.5% of men aged 65 to 69 years underwent a biopsy compared with 10.0% of men 85 years or older (P < .001) (Table). Of men who never had a biopsy, 25.9% had at least 6 repeat PSA tests, 6.8% underwent transurethral resection of the prostate, and 0.1% died of prostate cancer.

PROSTATE CANCER DIAGNOSIS

Of 8313 men who had at least 1 biopsy performed, 5220 (62.8%) were diagnosed as having prostate cancer during the study period. Among men diagnosed as having prostate cancer, 15.1% had more than 1 biopsy before diagnosis, and among men not diagnosed as having cancer, 20.8% had more than 1 biopsy before diagnosis. Age was a strong predictor of prostate cancer diagnosis, ranging from 58.2% of men aged 65 to 79 years who underwent biopsy to 71.0% of men 85 years or older who underwent biopsy (P < .001) (Table). Among the subset of 2780 men (53.3%) whose biopsy-detected prostate cancer was diagnosed within the VA system, 1161 (41.8%) had low-risk cancer.

PROSTATE CANCER TREATMENT AND SURVIVAL

Of 5220 men diagnosed as having prostate cancer on biopsy, 58.1% were treated with curative intent (ie, radical prostatectomy or radiation therapy), 23.9% were treated with hormone therapy alone, and 17.9% were not treated with any of these modalities (Figure 2). Of those treated, 95.3% started treatment within 1 year of cancer diagnosis, and among men not diagnosed as having cancer, 75.5% were treated. Five-year survival among men treated for biopsy-detected prostate cancer was 82.1% and decreased with advancing age and worsening comorbidity (Table). Figure 3 shows that the percentage of men with biopsy-detected prostate cancer who died of other causes in-
Among 8313 men who underwent prostate biopsy after an index PSA screening exceeding 4.0 ng/mL, 468 men (5.6%) had complications within 7 days after biopsy, including 131 men who were hospitalized and 9 men who died. Among 4284 men treated with radical prostatectomy, radiation therapy, or hormone therapy, 584 men (13.6%) had new incontinence, and 588 men (13.7%) had new erectile dysfunction.

BIOPSY AND TREATMENT COMPLICATIONS

This study provides frequencies in clinical practice of downstream outcomes during the 5 years following an

Table. Baseline Characteristics of 295,645 Men 65 Years or Older Who Underwent Prostate-Specific Antigen (PSA) Screening and the Downstream Outcomes That Occurred During the Following 5 Years

<table>
<thead>
<tr>
<th>Baseline Characteristic</th>
<th>All Patients</th>
<th>Downstream Outcome, No. (%)</th>
<th>Diagnosed as Having Prostate Cancer</th>
<th>Treated for Prostate Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total No. (N = 295,645)</td>
<td>Index PSA Level &gt;4.0 ng/mL (n = 25,208)</td>
<td>(n = 8313)</td>
<td>(n = 5220)</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-69</td>
<td>97,251</td>
<td>5731 (5.9)</td>
<td>2892 (50.5)</td>
<td>1682 (58.2)</td>
</tr>
<tr>
<td>70-74</td>
<td>94,422</td>
<td>7163 (7.6)</td>
<td>2869 (40.1)</td>
<td>1808 (63.0)</td>
</tr>
<tr>
<td>75-79</td>
<td>65,501</td>
<td>6789 (10.4)</td>
<td>1726 (25.4)</td>
<td>1150 (66.6)</td>
</tr>
<tr>
<td>80-84</td>
<td>39,902</td>
<td>4212 (13.6)</td>
<td>695 (16.5)</td>
<td>487 (70.1)</td>
</tr>
<tr>
<td>≥85</td>
<td>7569</td>
<td>1313 (17.3)</td>
<td>131 (10.0)</td>
<td>93 (71.0)</td>
</tr>
<tr>
<td>Charlson-Deyo Comorbidity Index</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>184,504</td>
<td>16,533 (9.0)</td>
<td>6037 (36.5)</td>
<td>3812 (63.1)</td>
</tr>
<tr>
<td>1-2</td>
<td>82,088</td>
<td>6462 (7.8)</td>
<td>1841 (28.4)</td>
<td>1146 (62.2)</td>
</tr>
<tr>
<td>≥3</td>
<td>28,533</td>
<td>2193 (7.7)</td>
<td>435 (19.8)</td>
<td>262 (60.2)</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>264,978</td>
<td>21,304 (8.0)</td>
<td>6951 (32.6)</td>
<td>4315 (62.1)</td>
</tr>
<tr>
<td>Black</td>
<td>21,706</td>
<td>2979 (13.7)</td>
<td>1101 (37.0)</td>
<td>750 (68.1)</td>
</tr>
<tr>
<td>Other</td>
<td>8,691</td>
<td>925 (10.3)</td>
<td>261 (28.2)</td>
<td>155 (59.4)</td>
</tr>
<tr>
<td>Marital statusc</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>208,827</td>
<td>16,611 (8.0)</td>
<td>5741 (34.6)</td>
<td>3574 (62.3)</td>
</tr>
<tr>
<td>Not married</td>
<td>85,019</td>
<td>8406 (9.7)</td>
<td>2512 (29.9)</td>
<td>1604 (63.9)</td>
</tr>
<tr>
<td>Census region</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Midwest</td>
<td>80,176</td>
<td>7238 (9.0)</td>
<td>2471 (34.1)</td>
<td>1550 (62.7)</td>
</tr>
<tr>
<td>Northeast</td>
<td>36,348</td>
<td>3117 (8.6)</td>
<td>963 (31.5)</td>
<td>607 (61.7)</td>
</tr>
<tr>
<td>South</td>
<td>132,890</td>
<td>10,668 (8.0)</td>
<td>3500 (32.8)</td>
<td>2172 (62.1)</td>
</tr>
<tr>
<td>West</td>
<td>46,231</td>
<td>4185 (9.1)</td>
<td>1359 (32.5)</td>
<td>891 (65.6)</td>
</tr>
<tr>
<td>Lived in ZCTA in which ≥25% of adults had a college educationc</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>81,339</td>
<td>6985 (8.6)</td>
<td>2343 (33.5)</td>
<td>1460 (61.9)</td>
</tr>
<tr>
<td>No</td>
<td>205,295</td>
<td>17,433 (8.1)</td>
<td>5707 (32.7)</td>
<td>3598 (63.0)</td>
</tr>
<tr>
<td>Median annual income of ZCTA, $d</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Highest tertile, ≥41,144</td>
<td>95,753</td>
<td>8118 (8.5)</td>
<td>2678 (33.0)</td>
<td>1662 (62.1)</td>
</tr>
<tr>
<td>Middle tertile</td>
<td>95,372</td>
<td>7805 (8.2)</td>
<td>2543 (32.6)</td>
<td>1590 (62.5)</td>
</tr>
<tr>
<td>Lowest tertile, ≤32,549</td>
<td>95,567</td>
<td>8500 (8.9)</td>
<td>2830 (33.3)</td>
<td>1787 (63.5)</td>
</tr>
<tr>
<td>Selected comorbiditiesd</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>18,698</td>
<td>1604 (8.6)</td>
<td>320 (20.0)</td>
<td>206 (64.4)</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>35,430</td>
<td>3029 (8.5)</td>
<td>752 (24.8)</td>
<td>455 (60.5)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>52,433</td>
<td>3583 (6.8)</td>
<td>984 (27.5)</td>
<td>625 (63.5)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>19,099</td>
<td>1506 (7.9)</td>
<td>356 (23.7)</td>
<td>214 (60.1)</td>
</tr>
<tr>
<td>Dementia</td>
<td>1844</td>
<td>222 (12.0)</td>
<td>18 (8.1)</td>
<td>13 (72.2)</td>
</tr>
</tbody>
</table>

Abbreviation: ZCTA, zip code tabulation area.

SI conversion factor: To convert PSA level to micrograms per liter, multiply by 1.0.

The denominator for each percentage is the number of men in the prior column. For example, among men aged 65 to 69 years, 50.5% of 5731 men with a PSA result exceeding 4 ng/mL underwent a biopsy; 58.2% of 2892 men who underwent a biopsy were diagnosed as having prostate cancer; 83.4% of 1682 men diagnosed as having prostate cancer received treatment (radical prostatectomy, radiation therapy, or hormone therapy); and 87.8% of 1403 men who were treated survived 5 years after their index screening PSA test.

These categories are not mutually exclusive. The reference group for comparisons is men without the specific comorbidity.
abnormal screening PSA result among older men, including more than 100 000 men 75 years or older. The percentage of men with an index screening PSA level exceeding 4.0 ng/mL increased with age, but only one-third of these men underwent prostate biopsy. Performance of biopsy decreased with advancing age and worsening comorbidity. Prostate cancer detection increased with age, and most men diagnosed as having cancer received immediate treatment. Therefore, while most men with a PSA level exceeding 4.0 ng/mL did not undergo biopsy, which reduced biopsy and treatment complications, those who did were often diagnosed as having prostate cancer and underwent treatment regardless of advancing age, poor health, or low-risk cancer.

Although many adjustments (eg, age-specific PSA norms and PSA velocity) have been suggested to better define an abnormal PSA result, a value exceeding 4.0 ng/mL remains the most commonly used cutoff in US practice. We found that men 85 years or older were almost 3 times more likely to have an abnormal screening result than men aged 65 to 69 years (17.3% vs 5.9%). These percentages are slightly lower than those from prior studies that did not exclude men with prostate symptoms. For example, in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, which used a PSA cutoff exceeding 4.0 ng/mL, 11% of men aged 65 to 69 years had an initial abnormal PSA result, while a cross-sectional study using the 2001-2002 National Health and Nutrition Examination Survey found that 6% of men aged 65 to 69 years and 28% of men 85 years or older had PSA values exceeding 4.0 ng/mL. Consistent with prior findings, men of black race/ethnicity were more likely to have an abnormal screening PSA result than men of white race/ethnicity.

Prostate biopsy is the standard diagnostic procedure after an abnormal screening PSA result. In the Euro-

Figure 2. Flowchart of the 5-year outcomes following a screening prostate-specific antigen (PSA) result exceeding 4.0 ng/mL (to convert PSA level to micrograms per liter, multiply by 1.0) in men 65 years or older. Boxes in bold are terminal boxes where men do not progress further down the flowchart. Men without a prostate biopsy who were diagnosed as having prostate cancer during the 5-year study period by transurethral resection of the prostate or who started hormone therapy without biopsy are included in the No prostate biopsy box.

Figure 3. Effect of age and comorbidity on the likelihood of dying of non–prostate cancer causes within 5 years of screening among men with an index screening prostate-specific antigen result exceeding 4.0 ng/mL (to convert PSA level to micrograms per liter, multiply by 1.0) and biopsy-detected prostate cancer (n = 5220). Error bars represent 95% CIs.
European Randomized Study of Screening for Prostate Cancer trial, which found that screening reduced prostate cancer mortality, 86% of men with an abnormal PSA result underwent biopsy within 1 year. In the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, which did not show a reduction in prostate cancer mortality associated with PSA screening, 40% underwent biopsy within 1 year. However, biopsy rates in both trials were much higher than what we found. In clinical practice, 33.0% of men 65 years or older underwent biopsy within 5 years of a PSA screening result exceeding 4.0 ng/mL, which is consistent with prior smaller community investigations. Even among the 0.9% of men with a PSA screening level exceeding 10.0 ng/mL, only 41.7% underwent biopsy within 5 years, suggesting that many older men in clinical practice do not pursue biopsy even when PSA levels are very high.

Among older men who undergo biopsy, many are diagnosed as having prostate cancer and receive treatment. Our cancer detection rate (62.8%) is higher than that in the initial round of the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, in which 44% of men who underwent biopsy were diagnosed as having cancer within 1 year of an abnormal PSA result. However, our population was substantially older, and we followed up men for 5 years, including those who underwent more than 1 biopsy. We also found that more than three-quarters of men diagnosed as having cancer underwent treatment within 1 year of diagnosis regardless of age or comorbidity, consistent with trials and observational data in younger men. Yet, this is the step in the downstream cascade where increasing evidence supports unlinking cancer detection from immediate treatment and pursuing active surveillance with selective, delayed treatment, especially in older men with comorbidities. Instead, most older men, including those with low-risk disease, were immediately treated. In total, 58.1% of men underwent potentially curative radical prostatectomy or radiation therapy, and 23.9% of men underwent noncurative hormone therapy alone. These findings suggest a need to better incorporate considerations of advancing age, worsening comorbidity, and aggressiveness of screen-detected cancer into treatment decisions.

Among those treated for screen-detected prostate cancer, 5-year survival was 82.1% but decreased with advancing age and worsening comorbidity as deaths from non–prostate cancer causes increased. Overall, 14.4% of men with screen-detected prostate cancer died of non–prostate cancer causes within 5 years, and this percentage increased to 71.4% among men 85 years or older with a Charlson-Deyo Comorbidity Index of 3 or higher. Because PSA screening advances cancer diagnosis 5 to 12 years before clinical diagnosis, screening in subgroups with limited life-expectancy risks diagnosing cancer that would never have caused symptoms.

Screening also places men at risk for biopsy and treatment complications, although we found in clinical practice that the screening cascade was most frequently stopped before biopsy rather than at the stage of treatment decision making. Halting the cascade early decreases any chance of screening benefit because high-risk cancers will be missed but also decreases the number of men who will have biopsy-associated and treatment-related complications. Our complication rates are lower than those reported in trials or studies of younger men, who more often pursue follow-up biopsy. Also, our estimates of urinary incontinence and erectile dysfunction likely underestimate these problems because they are undercoded in claims and many older men may not seek treatments for these problems.

Our study has several other limitations. First, laboratory data do not give reasons why a PSA test was ordered, such that some tests may have been performed for nonscreening reasons. However, a medical record review and the fact that few men had PSA levels exceeding 4.0 ng/mL suggest that our exclusion criteria selected a cohort in whom PSA tests were primarily sent for screening. Second, biopsy detection rates of cancer vary according to the number of biopsy cores obtained during a biopsy session, but we lacked these data. Twelve-core biopsy procedures were typical during this period and at present. Third, our data do not capture quality-of-life outcomes. However, understanding downstream clinical outcomes is important in their own right to help physicians and patients have more realistic expectations of screening outcomes and to allow men to individually assess the importance of these outcomes. Fourth, this study focuses on 5-year consequences following an index screening PSA test in 2003. Patterns of care might have changed subsequently, although recent data suggest that screening and treatment rates remain high. Fifth, our cohort comprises veterans, so generalizability of our findings to nonveterans is uncertain, although most also were enrolled in Medicare.

In conclusion, decisions to pursue PSA screening should include individualized discussion about when to pursue biopsy and treatment because these steps substantially affect downstream outcomes of screening in clinical practice. This study provides valuable insight into biopsy and treatment practices following PSA screening among men 65 years or older in the largest US health care system. These frequencies of downstream outcomes according to baseline characteristics, such as age and comorbidity, should better inform physicians and older men who are considering PSA screening and want to make more individualized decisions.

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