

# Letters

## RESEARCH LETTER

### Use of Conservative Management for Low-Risk Prostate Cancer in the Veterans Affairs Integrated Health Care System From 2005-2015

Low-risk prostate cancer has a favorable prognosis without treatment. Current guidelines recommend conservative management or deferring upfront treatment as the preferred approach,<sup>1</sup> but previous studies reported underutilization in the United States<sup>2,3</sup> compared with other countries.<sup>4</sup> Qualitative data suggest that financial incentives and medicolegal concerns are barriers to uptake by US physicians.<sup>5</sup> We examined utilization of conservative management in the US Department of Veterans Affairs (VA), an integrated health care system providing equal access for patients without financial incentives for physicians to provide high-volume care.

**Methods |** The study was approved by the VA New York Harbor institutional review board with a waiver of informed consent. Using VA's Central Data Warehouse, we examined treatment patterns for veterans diagnosed with low-risk prostate cancer (prostate-specific antigen [PSA] <10 ng/mL, Gleason ≤6, and stage cT1/T2a) from January 2005 through November 2015. Our dependent variable was receipt of curative therapy within 1 year of diagnosis (including androgen deprivation monotherapy), determined by administrative codes. Linkage to Medicare was performed to identify tests or treatment performed outside the VA for men 65 years or older. Men with PSA less than 1 ng/mL during follow-up were also classified as likely having received curative treatment outside the VA. Untreated veterans were classified as receiving conservative management, subdivided into active surveillance (≥2 PSAs and 1 biopsy within 2 years after diagnosis) or watchful waiting. The final date of follow-up was November 16, 2017.

We explored use of conservative management over time, stratified by age. The Cochran-Armitage test was used to examine trends over time, and logistic regression was used to identify the association between year of diagnosis and conservative management, adjusting for age, race, marital status, PSA, comorbidity, and region. Men without a PSA, biopsy, or treatment recorded within 2 years were excluded. Analysis was performed using SAS Enterprise Guide (SAS Institute), version 7.1, and tests were 2-sided at an  $\alpha$  of .05.

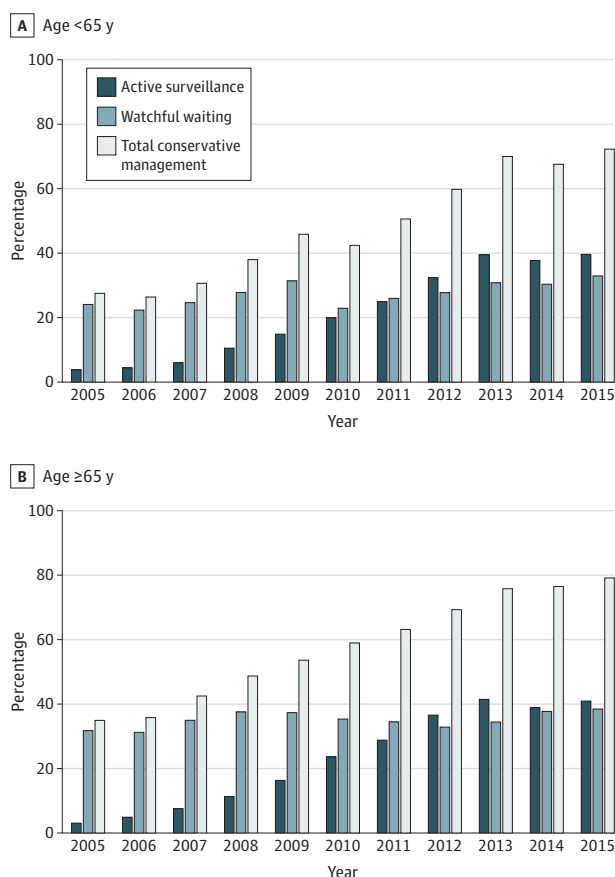
**Results |** Among 125 083 veterans with low-risk prostate cancer, mean age was 64 years (SD, 7) and mean PSA was 5.4 ng/mL (SD, 2.1). Of the 65 142 (52%) who were treated, 65% were identified through VA claims, 25% by PSA less than 1 ng/mL, and 10% through Medicare claims. Of 59 941 veterans (48%) who received conservative management, 37 717 (30%) received watchful waiting and 22 224 (18%) received active surveillance. Utilization of conservative management increased among men younger than 65 years (27% in 2005 to 72% in 2015)

and 65 years or older (35% in 2005 to 79% in 2015); both  $P$  for trend <.001 (Figure). The increase was primarily due to greater use of active surveillance (4% in 2005 to 39% in 2015 in men <65 y; 3% in 2005 to 41% in 2015 in men ≥65 y).

On multivariable analysis, more recent years were associated with greater odds of conservative management, as were increasing age, black race, unmarried status, higher PSA, increasing comorbidity, and geographic region (Table). Men older than 75 years, higher PSA, and greater comorbidity were more likely to receive watchful waiting than active surveillance.

**Discussion |** Utilization of conservative management has increased significantly among US veterans with low-risk prostate cancer, suggesting a substantial reduction in overtreatment during the past decade. These rates are higher than prior

**Figure. Proportion of US Veterans With Low-Risk Prostate Cancer Receiving Conservative Management (Active Surveillance or Watchful Waiting) From 2005-2015, by Age<sup>a</sup>**



<sup>a</sup> In the total cohort (N = 125 083), 68 463 were <65 y, of whom 43% received conservative management; 56 620 of men were ≥65 y, of whom 54% received conservative management.

**Table. Multivariable Analysis of Factors Associated With Conservative Management (Active Surveillance or Watchful Waiting) vs Active Treatment and Active Surveillance vs Watchful Waiting Among Veterans With Low-Risk Prostate Cancer<sup>a</sup>**

	Conservative Management vs Active Treatment (N = 125 083)			Active Surveillance vs Watchful Waiting (n = 59 941)		
	Conservative Management, No. (%) (n = 59 941)	Active Treatment, No. (%) (n = 65 142)	Odds Ratio (95% CI)	Active Surveillance, No. (%) (n = 22 224)	Watchful Waiting, No. (%) (n = 37 717)	Odds Ratio (95% CI)
<b>Age, y</b>						
<55	3455 (5.76)	5813 (8.92)	1 [Reference]	1163 (5.23)	2292 (6.08)	1 [Reference]
55-59	8273 (13.80)	13 074 (20.07)	1.23 (1.16-1.29)	2822 (12.70)	5451 (14.45)	1.17 (1.07-1.28)
60-64	17 413 (29.05)	20 435 (31.37)	1.37 (1.30-1.44)	7148 (32.16)	10 265 (27.22)	1.34 (1.23-1.45)
65-69	15 914 (26.55)	14 075 (21.61)	1.63 (1.54-1.71)	7099 (31.94)	8815 (23.37)	1.34 (1.23-1.45)
70-74	9101 (15.18)	7817 (12.00)	2.15 (2.04-2.28)	3048 (13.71)	6053 (16.05)	1.05 (0.96-1.15)
≥75	5785 (9.65)	3928 (6.03)	3.10 (2.91-3.30)	944 (4.25)	4841 (12.84)	0.50 (0.45-0.56)
<b>Race<sup>b</sup></b>						
White	43 131 (71.96)	46 378 (71.20)	1 [Reference]	15 870 (71.41)	27 261 (72.28)	1 [Reference]
Black	14 880 (24.82)	16 385 (25.15)	1.05 (1.02-1.09)	5663 (25.48)	9217 (24.44)	1.06 (1.02-1.11)
Other <sup>c</sup>	356 (0.59)	493 (0.76)	0.70 (0.61-0.81)	95 (0.43)	261 (0.69)	0.52 (0.41-0.67)
<b>Marital status</b>						
Married	33 147 (55.30)	37 857 (58.11)	1 [Reference]	12 386 (55.73)	20 761 (55.04)	1 [Reference]
Unmarried	26 742 (44.62)	27 167 (41.70)	1.18 (1.15-1.21)	9819 (44.18)	16 923 (44.87)	0.98 (0.94-1.01)
<b>PSA at diagnosis (per 1 ng/mL)<sup>d</sup></b>			1.03 (1.02-1.03)			0.94 (0.94-0.95)
<b>Comorbidities</b>						
0	31 212 (52.07)	36 786 (56.47)	1 [Reference]	12 058 (54.26)	19 154 (50.78)	1 [Reference]
1-2	23 757 (39.63)	23 931 (36.74)	1.10 (1.07-1.13)	8656 (38.95)	15 101 (40.04)	0.91 (0.87-0.94)
≥3	4972 (8.29)	4425 (6.79)	1.13 (1.08-1.18)	1510 (6.79)	3462 (9.18)	0.66 (0.61-0.70)
<b>Region</b>						
Northeast	8632 (14.40)	9324 (14.31)	1 [Reference]	3544 (15.95)	5088 (13.49)	1 [Reference]
Midwest	12 831 (21.41)	13 631 (20.93)	1.08 (1.03-1.12)	5251 (23.63)	7580 (20.10)	1.01 (0.95-1.07)
South	23 632 (39.43)	29 703 (45.60)	0.89 (0.86-0.93)	7956 (35.80)	15 676 (41.56)	0.66 (0.62-0.70)
West	14 278 (23.82)	11 765 (18.06)	1.41 (1.35-1.47)	5363 (24.13)	8915 (23.64)	0.90 (0.85-0.96)
<b>Year of diagnosis (per more recent y)<sup>d</sup></b>			1.25 (1.25-1.26)			1.27 (1.26-1.27)

Abbreviation: PSA, prostate-specific antigen.

<sup>a</sup> From a total of 461 425 men diagnosed with prostate cancer in the Veterans Affairs (VA) from 2005-2015, the study population was identified after excluding those with intermediate or high-risk disease, missing staging information, and those lost to follow-up (no PSA, biopsy, or treatment recorded within 2 y after diagnosis, n = 9028). All men in the study had at least 2 y of follow-up after diagnosis. The last date of follow-up was November 16, 2017.

<sup>b</sup> Data on race in this study was obtained from the VA cancer registry. A detailed chart review was used to obtain this information, considering race in the

patient's medical record, race entered by the physician treating the cancer, and patient questionnaires. Data were missing for race in 3460 (2.77%), 1574 (2.63%), and 1886 (2.90%); marital status in 170 (0.14%), 52 (0.09%), and 118 (0.18%); and region in 1287 (1.03%), 568 (0.95%), and 719 (1.10%) of the overall study population, conservative management, and active treatment groups, respectively.

<sup>c</sup> Other race includes American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, declined to answer, unknown by patient.

<sup>d</sup> PSA and year of diagnosis were included in the model as continuous variables.

US studies in different health care settings. In the Surveillance, Epidemiology, and End Results (SEER)-Medicare-linked database from 2010-2011, only 32% of suitable patients received conservative management.<sup>3</sup> In another registry of 45 US community-based urology practices, 40% of low-risk patients received conservative management from 2010-2013.<sup>2</sup> Within a Michigan quality improvement collaborative (2012-2016), the proportion of low-risk patients managed by active surveillance varied significantly across practices (range, 30.2%-72.6%).<sup>6</sup> By contrast, international rates of conservative management are considerably higher. For example, in Sweden, 74% of low-risk patients underwent active surveillance in 2014.<sup>4</sup>

Limitations of this study include possible nondetection and misclassification of treatment outside the VA that was not captured, difficulty distinguishing active surveillance vs watch-

ful waiting using administrative codes, and inability to determine participation in shared decision making. Strengths include a large, racially diverse population of US veterans, providing comprehensive nationwide data on treatment trends.

Despite some regional variation suggesting additional room for improvement in the VA, these data suggest that an integrated health care system with equitable access for patients and without volume-based incentives for physicians may overcome many barriers to guideline-recommended conservative management.

Stacy Loeb, MD, MSc  
Nataliya Byrne, BA  
Danil V. Makarov, MD, MHS  
Herbert Lopor, MD  
Dawn Walter, MPH

**Author Affiliations:** Manhattan Veterans Affairs Medical Center, New York, New York (Loeb, Makarov); Department of Urology, New York University, New York (Byrne, Lepor); Department of Population Health, New York University, New York (Walter).

**Corresponding Author:** Stacy Loeb, MD, MSc, 227 E 30th St, Ste 612, New York, NY 10016 (stacyloeb@gmail.com).

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*Concept and design:* Loeb, Makarov, Lepor, Walter.

*Acquisition, analysis, or interpretation of data:* Loeb, Byrne, Makarov, Walter.

*Drafting of the manuscript:* Loeb.

*Critical revision of the manuscript for important intellectual content:* All authors.

*Statistical analysis:* Walter.

*Obtained funding:* Loeb, Makarov.

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*Supervision:* Loeb, Lepor.

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## COMMENT & RESPONSE

### Wait Time for Hip Fracture Surgery and Mortality

**To the Editor** Dr Pincus and colleagues<sup>1</sup> found that increased wait time for hip fracture surgery was associated with greater risk for 30-day mortality. We would like to point out 3 concerns.

First, as Pincus and colleagues mentioned, confounding by indication may exaggerate the association of early surgery

with mortality, with medically complex patients being predisposed to both complications and awaiting optimization, such as declining anticoagulant effect prior to surgery. Although the authors performed propensity score-matching analyses to adjust confounding factors and several sensitivity analyses to confirm the robustness of the results, propensity score analysis cannot reduce bias due to unmeasured confounding factors and confounding by indication cannot be mitigated by sensitivity analyses.

Pincus and colleagues could use an instrumental variable to estimate the average treatment effectiveness. For example, the day of hospital admission might be used as an instrumental variable, as was the day of the week of admission used by McGuire et al.<sup>2</sup> Sheikh et al<sup>3</sup> reported that the day of the week of admission was associated with waiting time but not with outcome in hip fracture surgery. Theoretically, the day of the week of admission appears to meet the criteria for an instrumental variable in studying surgical delays in patients with hip fractures.

Second, the type of anesthesia was not included in the analysis. Two reports that compared spinal with general anesthesia showed that spinal anesthesia had a lower occurrence of deep vein thrombosis and overall complications postoperatively<sup>4</sup> and a higher 30-day mortality.<sup>5</sup> Type of anesthesia is generally a key factor associated with wait time for hip fracture and should be included as a confounding factor.

Third, we are concerned that the patients included in this analysis were elderly. We would be interested to know whether advanced age was associated with death related to wait time.

Eriko Okada, MD, PhD

Koichi Inukai, MD

Hiromichi Aoyama, MD

**Author Affiliations:** Department of Medical Education Research and Development, Tokyo Medical and Dental University, Tokyo, Japan (Okada); Department of Surgery, Kariya Toyota General Hospital, Aichi, Japan (Inukai); Department of Orthopedic Surgery, JA Toride General Hospital, Ibaraki, Japan (Aoyama).

**Corresponding Author:** Eriko Okada, MD, PhD, Department of Medical Education Research and Development, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo 113-8519, Japan (eriko.gast@tmd.ac.jp).

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