

# Assessing Health-Related Quality of Life in Veterans With Nonmuscle-Invasive Bladder Cancer

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Are there disparities in quality of life among survivors of this disease who are treated at the VA and those who receive care at private clinics? These researchers report on what's the same and what's different.

**E**arly detection of cancer and advances in treatment have resulted in longer life for patients with cancer, making quality of life for survivors of this disease increasingly important.<sup>1</sup> VHA Directive 2003-034, *National Cancer Strategy*, points out that the nature of current treatments for cancer and their high cost as well as the often protracted nature of the disease have led to dramatic reductions in health-related quality of life (HRQOL) for cancer patients.<sup>2</sup> Similarly, an Institute of Medicine report acknowledged the challenge that cancer survivorship presents and the importance of HRQOL, recommending that health care providers ensure appropriate survivorship care.<sup>3,4</sup> Data on HRQOL, which has been studied extensively with increasing empha-

sis on cancer patients,<sup>5</sup> can be used to compare the impact of cancer on different populations and serve as a basis for the design of interventions to improve patient-centered care. Information about patients' HRQOL also can aid clinicians in helping patients cope with their condition and, in the process, help providers care for individuals' overall well-being rather than just the disease.

Patients with nonmuscle-invasive bladder cancer (NMIBC) present an ideal population for exploring these issues because of the prevalence and nature of this disease. Of 70,530 new cases of bladder cancer (BlCa) expected in U.S. adults in 2010, about three-quarters will be NMIBC.<sup>5,6</sup> In addition, patients with NMIBC often survive for many years after their diagnosis.

The literature on HRQOL in BlCa patients is limited, compared with HRQOL studies of prostate and other cancers. In addition, most BlCa HRQOL work has focused on patients who have undergone cystectomy, whereas our research targets NMIBC patients. To our knowledge, no previous study has examined differences between veterans and nonveterans with NMIBC. The investigation described here compared differences in the sociodemographics, psychological characteristics, and

HRQOL of NMIBC patients being treated at the VA with those of NMIBC patients who were seeking care at a private clinic. Our goal was to understand the particular needs of veterans living with NMIBC as the first step toward developing a patient-education and coping intervention tailored for veterans.

## BACKGROUND

The age-adjusted prevalence rate for urologic diseases overall has increased in the veteran population between 1999 and 2002.<sup>7</sup> With regard specifically to BlCa, sociodemographic characteristics of veterans—namely, being elderly, male, and white—put them at greater risk for BlCa than the general U.S. population.<sup>8</sup> The average age of diagnosis of BlCa is 65 years, and the cancer is 3 times more prevalent in men than in women and 2.4 times more prevalent in whites than in others.<sup>7,8,9-11</sup> In addition, smoking increases the risk of BlCa, and a 2007 survey showed that prevalence of smoking among veterans enrolled in the VA is higher than in the general population.<sup>12</sup> As of 2007, 30,000 veterans had BlCa on their “problem list.”<sup>1</sup>

## METHODS

We used a cross-sectional study design to assess areas of impaired

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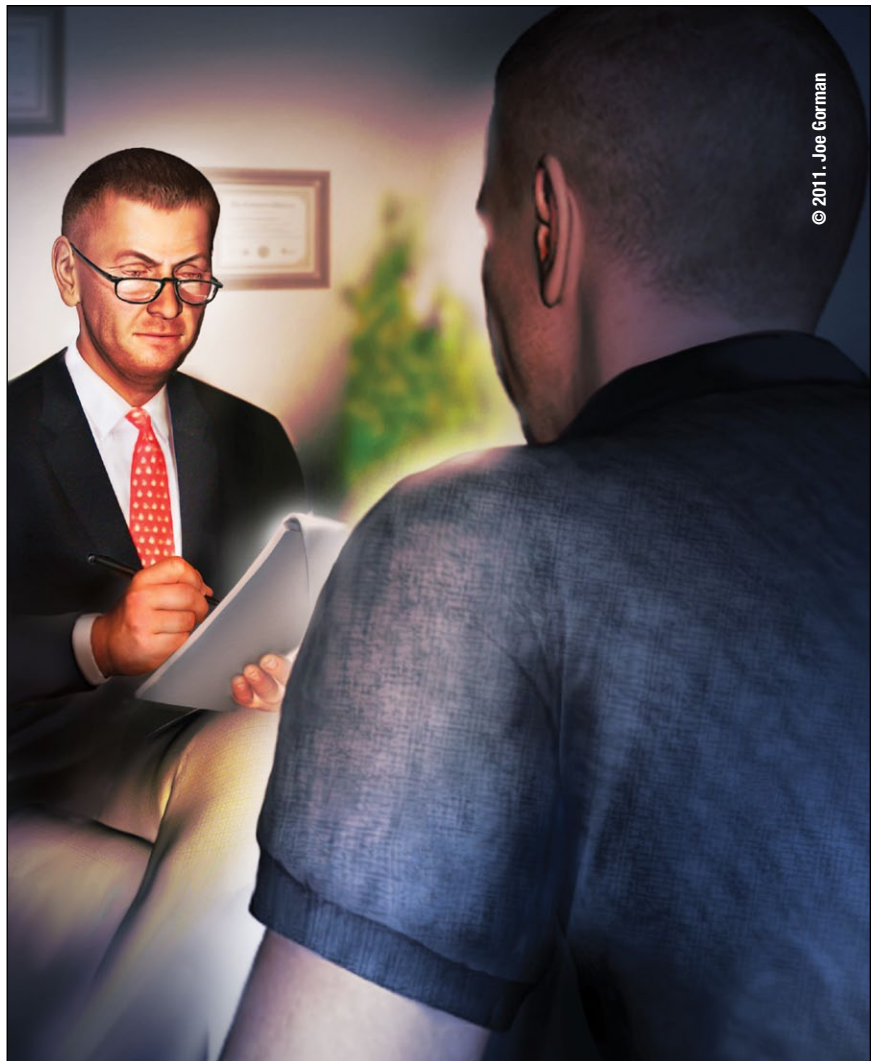
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HRQOL in NMIBC survivors and to identify differences between veterans who received care at VA facilities and patients who received care at a private clinic. Patients presenting at either type of clinic from January 2008 to February 2009 were identified for potential inclusion in the study. Study approval was obtained from the Baylor College of Medicine Institutional Review Board, and informed consent was provided by the participants.

A letter requesting participation and offering an opportunity to “opt-out” was sent to all identified individuals at both clinics, followed by a telephone call to individuals who did not opt out of participation. To be eligible, individuals needed to have a diagnosis of NMIBC in the preceding 4 years and be able to read and speak English and receive materials through the U.S. postal service. Of the initial sample of 210 possible participants, the final group consisted of 67 respondents.

We gathered data using telephone interviews and assessed HRQOL, psychological distress, fear of recurrence, and illness intrusiveness using validated scales. Interviewers asked participants about basic sociodemographic characteristics, including age at diagnosis, gender, race/ethnicity, education, and relationship status, using validated questions from previous surveys of cancer survivors. We also measured patient clinical characteristics, such as number of comorbidities, number of treatments, and time since diagnosis.

Participants’ general HRQOL was measured with a validated instrument, developed by the European Organization for Research and Treatment of Cancer (EORTC), the EORTC Quality of Life Questionnaire core module version 3 (QLQ-C30 v. 3).<sup>13</sup> This instrument, designed specifically for assessment of cancer



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patients, includes both an HRQOL subscale and a symptom subscale. The QLQ-C30 HRQOL subscale assesses how well the patient functions physically, emotionally, cognitively, and socially; the patient’s role in daily activities and the pursuit of leisure interest; and the patient’s global health status. The QLQ-C30 symptom subscale consists of 9 items, namely, fatigue, pain, dyspnea, appetite loss, nausea/vomiting, insomnia, constipation, diarrhea, and financial problems. A high score on the QLQ-C30 HRQOL subscale indicates acceptable functioning, while a high score on the

symptom subscale corresponds with severe symptoms.

We also measured disease-specific HRQOL with bladder cancer superficial-24 (BLS-24), a new measure recently developed by the EORTC and the only validated measure of disease-specific HRQOL for NMIBC patients. Questions are designed to measure the impact of NMIBC on urinary symptoms and sexual functioning; other queries assess worries about repeated cystoscopies and their convenience as well as adverse effects of intravesical treatment, such as fever and malaise.<sup>14,15</sup> A high score

**Table 1. Characteristics of NMIBC patients**

Variables (n = 67)	Veterans mean ± SD or n (%)	Private patients mean ± SD or n (%)	P value
Age, y	67.7 ± 8.5	67.3 ± 9.2	.8746
Gender, male	29 (100.0)	27 (71.1)	.0016 <sup>a</sup>
<b>Education</b>			.1133
High school diploma	7 (24.1)	8 (21.1)	
Some college	14 (48.1)	10 (26.3)	
College degree	6 (20.7)	10 (26.3)	
Graduate school	2 (6.9)	10 (26.3)	
Race, white	26 (89.7)	35 (92.1)	1.0000 <sup>a</sup>
<b>Relationship status</b>			.1527 <sup>a</sup>
Married	18 (62.1)	29 (76.3)	
Never married	1 (3.5)	1 (2.6)	
Separated/divorced	8 (27.6)	3 (7.9)	
Widowed	2 (6.9)	5 (13.2)	
Number of comorbidities	1.7 ± 1.1	1.1 ± 0.9	.0214
Number of BICa treatments	1.8 ± 0.6	1.6 ± 0.8	.3815
Time since diagnosis, y	2.3 ± 1.0	1.9 ± 1.4	.2015

<sup>a</sup>Fisher's exact test. BICa = bladder cancer; NMIBC = nonmuscle-invasive bladder cancer.

on the BLS-24 urinary urgency and frequency subscale indicates a greater number of symptoms.

Finally, we assessed psychological characteristics of respondents using 4 different scales; for each of these scales, a higher score indicates an increased level of the type of psychological distress being measured. Psychological distress was measured using the Brief Symptom Inventory-18 (BSI-18).<sup>16</sup> The scale consists of 3 subscales—depression, anxiety, and somatic symptoms—and provides symptoms and intensity of symptoms at a specific point in time. Fear of recurrence was measured with a 5-item measure used in the Cancer of the Prostate Strategic Research Endeavor study.<sup>17</sup> The Impact of Events Scale (IES) mea-

sures subjective response to stress and consists of 2 subscales: intrusive thoughts and avoidance.<sup>18</sup> Participants were instructed to indicate how often during the past 7 days they had experienced traumatic or stressful symptoms. We then calculated the mean score of each of the subscales. The Illness Intrusiveness Rating Scale (IIRS) assesses the impact of illness on functioning, with a total score for 13 items. The IIRS comprises 3 subscales, namely, relationship and personal development, intimacy, and “instrumental life.”<sup>19</sup> The relationship and personal development subscale addresses family and social relations, self-expression and improvement, religious expression, community and civic involvement, and passive recreation. The intimacy subscale score re-

lates to the patient's relationship with his/her partner and sexual activity, while the instrumental life subscale assesses health, work, financial situation, and active recreation. A high score on the IIRS scale indicates a high level of illness intrusiveness.

We used Fisher's exact test and the chi-square test to evaluate associations between the respondents by groups (veteran/private) in categorical demographic variables, such as gender, education, race, and relationship status. Differences in continuous variables were assessed using the Student's *t* test or the Wilcoxon-Mann-Whitney test, as appropriate. We used a multiple regression model to evaluate the impact of veteran status on each HRQOL domain, controlling for other covariates that were

**Table 2. NMIBC patients' responses to health-related quality of life scale**

General EORTC QLQ-C30	Veterans mean $\pm$ SD (n = 29)	Private patients mean $\pm$ SD (n = 38)	P value
<b>EORTC QLQ-C30 HRQOL subscale</b>			
Global health status/QOL	67.8 $\pm$ 23.2	84.2 $\pm$ 10.8	.0011
Physical functioning	77.0 $\pm$ 14.8	90.2 $\pm$ 12.9	.0003
Role functioning	80.5 $\pm$ 20.9	95.6 $\pm$ 11.4	.0011
Emotional functioning	84.2 $\pm$ 18.3	91.9 $\pm$ 12.3	.0569
Cognitive functioning	73.0 $\pm$ 20.6	85.1 $\pm$ 11.5	.0069
Social functioning	79.9 $\pm$ 20.1	93.9 $\pm$ 14.7	.0016
<b>EORTC QLQ-C30 symptom subscale</b>			
Fatigue	31.4 $\pm$ 27.2	11.7 $\pm$ 16.1	.0015
Nausea/vomiting	1.7 $\pm$ 6.8	0.4 $\pm$ 2.7	.4096
Pain	20.1 $\pm$ 24.6	5.7 $\pm$ 10.5	.0139
Dyspnea	31.0 $\pm$ 29.5	4.4 $\pm$ 13.8	<.0001
Insomnia	20.7 $\pm$ 28.7	10.5 $\pm$ 23.4	.0817
Appetite loss	16.1 $\pm$ 27.6	1.8 $\pm$ 7.5	.0057
Constipation	13.8 $\pm$ 4.8	6.1 $\pm$ 13.1	.2954
Diarrhea	8.1 $\pm$ 21.2	3.5 $\pm$ 10.4	.4129
Financial problems	23.0 $\pm$ 28.3	9.6 $\pm$ 21.8	.0190

EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire core module version; HRQOL = health-related quality of life; NMIBC = nonmuscle-invasive bladder cancer; QOL = quality of life.

significantly different between the 2 groups. The 2-sided statistical significance for this study was set at  $P \leq .05$ . As the study is exploratory, we did not correct for multiple testing. All analyses were performed using SAS v. 9.1.3 (SAS Institute, Inc., Cary, North Carolina).

## RESULTS

Mean age at diagnosis for all 67 respondents (29 from VA clinics, 38 from private clinics) was 65.4 ( $\pm$  8.8) years (range, 48 to 85 years) (Table 1). Most respondents were white (91.1%), male (83.6%), and married (70.2%), and the largest percentage (35.8%) reported having some college education. Respondents

overall had from 0 to 4 comorbidities, with a mean of 1.3 ( $\pm$  1.0). Mean years since diagnosis was 2.1 ( $\pm$  1.2), while mean number of treatments was 1.7 ( $\pm$  0.7).

The veterans group did not differ from the private patient group in age, education, race, relationship status, number of BlCa treatments received, or time since diagnosis ( $P > .05$ ), but significantly more women were in the private patient group ( $P = .0016$ ). The veterans group had a higher mean number of comorbidities ( $P = .0214$ ).

Compared with veteran respondents, patients from the private clinic reported a better HRQOL, with higher HRQOL scores overall

(Table 2). In fact, private patients scored higher than veterans on all the HRQOL subscales ( $P < .05$ ), except for emotional functioning, where their higher score was not statistically significant ( $P = .057$ ).

Private patients also had lower symptom scores than the veterans, with the veterans reporting more severe symptoms on 5 items of the symptom subscale, namely, fatigue, pain, dyspnea, appetite loss, and financial problems ( $P < .05$ ). The 2 groups did not differ significantly in regard to nausea/vomiting, insomnia, constipation, or diarrhea.

As to disease-specific HRQOL, the veterans group did not differ significantly from the private group

**Table 3. NMIBC patients' response to disease-specific health-related quality of life scale**

<b>EORTC BLS-24 variables</b>	<b>Veterans mean <math>\pm</math> SD (n = 29)<sup>a</sup></b>	<b>Private patients mean <math>\pm</math> SD (n = 38)<sup>b</sup></b>	<b>P value</b>
Urinary symptoms and problems	1.8 $\pm$ 0.7	1.5 $\pm$ 0.4	.1332
Future perspective on BiCa treatment	1.9 $\pm$ 0.7	1.6 $\pm$ 0.7	.1199
Did you have a fever?	1.0 $\pm$ 0.0	1.1 $\pm$ 0.3	.0809
Did you feel ill or unwell?	1.2 $\pm$ 0.5	1.1 $\pm$ 0.3	.2416
To what extent were you interested in sex?	2.5 $\pm$ 1.1	2.5 $\pm$ 1.1	.9695
To what extent were you sexually active?	3.4 $\pm$ 0.9	3.0 $\pm$ 0.8	.1219
For men only: Did you have difficulty gaining or maintaining an erection?	2.7 $\pm$ 0.9	3.0 $\pm$ 1.1	.2659
For men only: Did you have ejaculation problems? (eg, dry ejaculation)	3.2 $\pm$ 0.7	3.3 $\pm$ 1.0	.3254
Felt uncomfortable about being sexually intimate?	3.5 $\pm$ 0.7	3.6 $\pm$ 0.8	.5434
Worried may contaminate your partner during sexual contact?	3.6 $\pm$ 0.9	3.4 $\pm$ 1.2	.8396
Was sex enjoyable for you?	2.9 $\pm$ 1.2	2.3 $\pm$ 1.1	.1950

<sup>a</sup>For all questions on sexual activity, n < 15. <sup>b</sup>For all questions on sexual activity, n < 29. BiCa = bladder cancer; EORTC BLS-24 = European Organization for Research and Treatment of Cancer bladder cancer superficial-24; NMIBC = nonmuscle-invasive bladder cancer.

in urinary symptoms, future perspective about BiCa treatment, presence of fever, or feeling ill ( $P > .05$ ) (Table 3). The 2 groups also did not differ significantly with regard to sexual symptoms ( $P > .05$ ). Because patients overall were elderly and many had comorbid conditions, numerous respondents reported being sexually inactive within the past 4 weeks and the question about frequency was not designed to ascertain whether this inactivity was because of bladder cancer.

Veterans indicated significantly higher fear of recurrence than private patients, and also scored higher for psychological distress on 2 subscales, namely, somatic and anxiety ( $P < .05$ ), but not on depression, where their higher score was not statistically significant (Table 4). With regard to illness intrusiveness, vet-

erans also had significantly higher scores than private patients on intimacy and instrumental life subscales ( $P < .05$ ), but the 2 groups had statistically similar results on the impact of events scale.

Pearson correlation analysis indicated a significant ( $P < .05$ ) moderate inverse correlation between global HRQOL and psychological distress (-0.62), fear of recurrence (-0.54), illness intrusiveness (-0.55), and IES (-0.38). After we adjusted for number of comorbidities, gender, and veteran status, multiple regression analyses indicated that fear of recurrence was a significant predictor of global HRQOL (adjusted R-square = 0.41;  $P = .0026$ ), along with the number of comorbidities ( $P = .0011$ ). But once illness intrusiveness was included in the model, fear of recurrence did not predict global HRQOL ( $P = .0839$ ).

Illness intrusiveness also was a significant predictor of global HRQOL (adjusted R-square = 0.51;  $P = .0005$ ), along with having multiple comorbidities ( $P = .0007$ ). Psychological distress was a significant predictor of global HRQOL, even after inclusion of illness intrusiveness in the model (adjusted R-square = 0.56;  $P = .0032$ ).

## DISCUSSION

Results of this study describe HRQOL disparities among local veterans from a VA clinic and patients from a private clinic. Considering interventions that are designed to improve the HRQOL of individuals with NMIBC may help alleviate these disparities and enhance quality of life for these individuals. Illness intrusiveness has been suggested as a fundamental determinant of quality of life in chronic disabling conditions—a concept our

**Table 4. Psychological characteristics of NMIBC patients**

Variables (n = 67)	Veterans mean ± SD (n = 29)	Private patients mean ± SD (n = 38)	P value
Fear of recurrence	59.0 ± 19.5	42.3 ± 15.7	.0002
<b>Psychological distress</b>	8.6 ± 11.4	3.0 ± 4.4	.0183
Somatic	3.2 ± 3.6	1.3 ± 2.1	.0110
Depression	2.9 ± 5.4	1.1 ± 2.5	.0952
Anxiety	2.4 ± 3.8	0.7 ± 1.2	.0296
<b>Illness intrusiveness</b>	16.5 ± 13.5	10.2 ± 13.3	.0601
Relationship and personal development	0.6 ± 1.2	0.4 ± 0.7	.2978
Intimacy	2.5 ± 2.1	1.2 ± 1.7	.0124
Instrumental life	1.9 ± 1.5	1.2 ± 1.4	.0292
<b>Impact of events</b>	15.0 ± 14.9	10.0 ± 12.7	.1417
Intrusive thoughts	7.1 ± 8.2	5.0 ± 6.9	.2639
Avoidance	7.9 ± 7.4	5.0 ± 6.6	.0904

NMIBC = nonmuscle-invasive bladder cancer.

findings support.<sup>20</sup> Not only was illness intrusiveness associated with diminished HRQOL, but veterans experienced greater illness-induced disruptions to lifestyles, activities, and interests than private patients, suggesting that the Institute of Medicine's recommendations for increased survivorship services targeted to cancer survivors may be particularly important for veterans. These services should include programs that help patients return as much as possible to precancer functioning in all areas of HRQOL.<sup>20</sup>

HRQOL is an important outcome measure, as it aids in understanding the impact of treatment on patients' activities. Poor HRQOL may affect treatment response and limit a cancer survivor's ability to receive adequate treatment. The study results indicate that, overall, veterans had lower HRQOL, which is similar to findings by Kazis and colleagues, who com-

pared ambulatory VA patients with patients in a non-VA system of care.<sup>21</sup> In our study, veterans with NMIBC differed on several aspects of HRQOL from private patients. Veterans also had more fatigue, pain, dyspnea, appetite loss, and financial problems than the private patients, which may explain their lower HRQOL.

Psychological distress, such as anxiety and depression, also can, of course, lead to reduced quality of life.<sup>22-24</sup> A study by Soo Hyun and colleagues showed that fatigue as well as depression are negatively associated with HRQOL.<sup>25</sup> We found the veterans group had higher scores for somatic symptoms and anxiety on the distress scale as well as higher levels of fatigue than the private patient group, which may partially explain the veterans' lower HRQOL. A study investigating the short-term effect of immunotherapy found that survivors of NMIBC anticipated disease-related

disruptions of their lives, experienced fear of recurrence, and described their quality of life only as "moderate."<sup>26</sup> These and related reactions to treatment as well as clinical and psychological characteristics of patients with NMIBC likely have adverse ramifications for HRQOL. Also keep in mind that because so many NMIBC patients survive for many years after diagnosis, potential treatment-related symptoms can have important implications for their HRQOL.

Tuominen and colleagues found that comorbidities are associated with lower HRQOL.<sup>27</sup> Similarly, we found that a lower HRQOL is associated with an increased number of comorbidities, which could partly explain the lower HRQOL of the veterans group, because, on average, patients in this group had a higher number of comorbidities than those in the private patient group. It, therefore, appears that veterans and private pa-

tients have different health care needs and how they are met could affect their long-term recovery. To improve the HRQOL in veterans, we must be attentive to these differing needs.

Nonetheless, various factors influence HRQOL in different groups of patients, even in an equal-access system like the VA. In a study of veterans with localized prostate cancer, men with less education had worse HRQOL over time and a greater number of urinary and sexual symptoms than men with more education.<sup>28</sup> Gender differences also have been identified: women who received VA health care were found to have better HRQOL than male VA patients.<sup>29</sup>

Our results suggest that the psychosocial burden of cancer may be even higher than has been recognized when that cancer is BlCa because of unpredictable outcomes and the ongoing need for highly invasive monitoring procedures and possible repeated decisions about treatment that are associated with this disease.<sup>3,30,31</sup>

As the veteran population ages, we will constantly be challenged with identifying the best method to screen patients and survivors for psychosocial impairment and connect them with the appropriate referral or resource. Now is the time for providers and researchers within the VA to examine the magnitude of the need for psychosocial and other survivorship services for veterans and begin to identify the appropriate screening tools, referral pathways, and resources both within the VA and at the national and local level in the surrounding community.

Avenues for beginning that dialogue continue to develop through the VA Survivorship Advisory Group, now part of the Cancer Collaborative, and through the Association of VA Hematology/Oncology. Until guide-

lines are developed and approved for screening veteran survivors for distress, providers should strive to be sensitive to psychosocial difficulties in BlCa survivors and make referrals to supportive services as needed.

### Study limitations

Results of this study should be interpreted carefully, considering its limitations. Our sample size was relatively small, and the results may not be generalizable to the larger population. In addition, the veterans and private patients in our study may have characteristics unique to their group. For example, the literature suggests that VA ambulatory patients differ from other non-VA populations as to distribution of illness and insurance needs.<sup>21</sup> In addition, this is a cross-sectional investigation, thus the associations between variables do not indicate causal relationships. Furthermore, given the number of sexually inactive participants, additional questions should be included in studies using the disease-specific HRQOL scale (BLS-24) to determine the etiology of sexual inactivity and how BlCa may impact sexual activity. Even though our results are consistent with those found for other disease states, further confirmatory studies with a larger sample are needed.

### CONCLUSIONS

The VHA patient population has about 35,000 new cases of cancer each year, and cancer is the second leading cause of death in veterans.<sup>2</sup> As the veteran population ages, the burden of cancer on veterans and the VA health care system will continue to increase, along with concerns about enhancing HRQOL in these patients. Information on HRQOL of NMIBC patients will help in developing supportive care for these individuals and, in turn, lead to potentially

positive treatment outcomes and higher satisfaction with care. We have found that veterans with NMIBC have poorer HRQOL than patients with the same disease from a private clinic, which suggests the need for additional supportive care in veterans with NMIBC. The Institute of Medicine's report on cancer survivorship recommends psychosocial interventions to help patients manage symptoms more effectively. Educational and coping interventions should be especially beneficial for patients with NMIBC. ●

### Author disclosures

*The project described in this report was supported by development funds from the Scott Department of Urology, Baylor College of Medicine. This material is partly the result of work supported with resources and the use of facilities at the Health Services Research & Development Center of Excellence (HFP90-020), Michael E. DeBakey VA Medical Center. Dr. Latini receives support from the Mentored Research Scholar Grant 06-083-01-CPPB from the American Cancer Society. The views expressed herein reflect those of the authors and not necessarily those of Baylor College of Medicine.*

### Acknowledgment

*We wish to acknowledge the assistance of Sonora Hudson, MA, in preparing the manuscript.*

### Disclaimer

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