Published in final edited form as:
Cancer. 2011 December 1; 117(23): 5392–5401. doi:10.1002/cncr.26198.

COMPLIANCE WITH GUIDELINES FOR PATIENTS WITH BLADDER CANCER: VARIATION IN THE DELIVERY OF CARE

Karim Chamie, MD, MSHS[1,2], **Christopher S. Saigal, MD, MPH**[1,2,3], **Julie Lai, MS**[3], **Jan M. Hanley, MS**[3], **Claude M. Setodji, PhD**[4], **Badrinath R. Konety, MD, MBA**[5], **Mark S. Litwin, MD, MPH**[1,2,3,6], and **Urologic Diseases in America Project**

[1]Department of Urology, Health Services Research Group, David Geffen School of Medicine at UCLA, Los Angeles, California

[2]Jonsson Comprehensive Cancer Center, David Geffen School of Medicine at UCLA, Los Angeles, California

[3]RAND Corporation, Santa Monica, California

[4]RAND Corporation, Pittsburgh, Pennsylvania

[5]Department of Urology, University of Minnesota, Minneapolis, Minneapolis, Minnesota

[6]Department of Health Services, University of California Los Angeles School of Public Health, Los Angeles, California

Abstract

Background—Clinical practice guidelines for the management of patients with bladder cancer encompass strategies that minimize morbidity and improve survival. We sought to characterize practice patterns in patients with high-grade non-muscle-invasive bladder cancer in relation to established guidelines.

Methods—We used Surveillance, Epidemiology and End Results (SEER)-Medicare-linked data to identify subjects diagnosed with high-grade non-muscle-invasive bladder cancer in 1992–2002 who survived at least two years without undergoing definitive treatment (*n*=4,545). We used multilevel modeling to estimate the association and partitioned variation of patient sociodemographic, tumor, and provider characteristics with compliance measures.

Results—Of 4,545 subjects analyzed, only one received all the recommended measures. Approximately 42% of physicians have not performed on a single patient nested within their practice in a two-year period, at least one cystoscopy, cytology and a single instillation of immunotherapy. After 1997, only utilization of radiographic imaging (OR 1.19; 95% CI 1.03–1.37) and instillation of immunotherapy (OR 1.67; 95% CI 1.39–2.01) significantly increased. Surgeon-attributable variation for individual guideline measures (cystoscopy 25%; cytology 59%;

Corresponding Author: Karim Chamie, UCLA Department of Urology, Health Services Research Group, 924 Westwood Blvd., Suite 1000, Los Angeles, California 90024, Office: (310) 794-2526, Fax: (310) 794-2538, kchamie@mednet.ucla.edu.

Author Contributions: Dr. Chamie 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.

Financial Disclosures: No financial disclosures to report.

Disclaimer: This study used the linked SEER-Medicare database. The interpretation and reporting of these data are the sole responsibility of the authors.

Additional Contributions: We acknowledge the efforts of the Applied Research Program, National Cancer Institute; the Office of Research, Development, and Information, Centers for Medicare & Medicaid Services; Information Management Services Inc; and the SEER program tumor registries in the creation of the SEER-Medicare database.

radiographic imaging 10%; intravesical chemotherapy 45%; and intravesical immunotherapy 26%) contributes to this low-compliance rate.

Conclusion—There is marked underuse of guideline-recommended care in this potentially curable cohort. Unexplained provider-level factors significantly contribute to this low-compliance rate. Future studies that identify barriers and modulators of provider-level adoption of guidelines are critical to improving care for patients with bladder cancer.

Keywords (MeSH Terms)

Urinary Bladder Neoplasms; Guideline Adherence; Quality of Care

INTRODUCTION

While bladder cancer is not routinely referred to as a chronic condition, it shares many properties with other medical ailments. It is common—fifth most frequent malignancy with an estimated 70,980 new cases in 2009 and accounts for 7% of all incident cancer cases;[1] requires close surveillance due to the high recurrence and progression rates (50–70%) with the attendant morbidity;[2] and costly—with a prevalence of 535,000 Americans and the invasive nature of follow-up and treatment strategies, it remains the most expensive malignancy to treat on a per-patient basis ($96,000–$187,000).[3] To address these concerns, best-practice guidelines, like those set forth by the National Comprehensive Cancer Network (NCCN) in 1998, the American Urological Association (AUA) in 1999 and the European Association of Urology (EAU) in 2002 were established in an attempt to the minimize morbidity and mortality associated with recurrence and progression of non-muscle-invasive bladder cancer.

Despite infusion of surveillance and treatment strategies into many areas of education, specialty certification and reimbursement models, practice patterns do not appear to reflect ubiquitous adoption of these guidelines. In an analysis of a single quality-of-care measure (endoscopic surveillance), Schrag *et al*., using a relaxed definition for endoscopic surveillance (once every six months instead of every three months), discovered that only 40% patients underwent the recommended number procedures.[4] Using MEDTAT claims data, Messing and colleagues discovered that out of 14,677 subjects with non-muscle-invasive bladder cancer who underwent resection of their bladder tumor, only 49 (0.3%) received perioperative instillation of chemotherapy.[5] Moreover, established clinical practice guidelines incorporate a comprehensive surveillance and treatment schedule and not just a single quality-of-care measure. [6, 7] Due to the invasive nature of the surveillance and treatment strategies, non-adherence with clinical-practice guidelines may be attributed to patient factors such as advanced age or the pre-existing comorbid conditions. In the context of low compliance, we sought to characterize practice patterns on a population-level using claims data.

PATIENTS AND METHODS

Data Source

We used the Surveillance, Epidemiology and End Results (SEER)-Medicare-linked database of the National Cancer Institute (NCI), which contains clinical, demographic, and medical claims data on individuals aged 65 years and older, to identify bladder cancer patients who were diagnosed in 1992–2002. SEER data are summarized in the Patient Entitlement and Diagnosis Summary File (PEDSF) and contain demographics (age, gender, race/ethnicity, marital status, county-level socioeconomic information), tumor characteristics (histology, grade, TNM and American Joint Committee on Cancer summary stage) and follow-up

information (vital status, cause of death, and time to death from date of diagnosis) The PEDSF was linked with 100% of the Medicare claims from the inpatient, outpatient, and national claims history files and was restricted to subjects who had Medicare Fee-for-Service coverage and for whom Medicare Parts A and B claims data were available for 12 months prior and 24 months after diagnosis of bladder cancer.[8]

Study Population

The cohort consisted of patients at least 66 years of age with an incident diagnosis of high-grade (poor or undifferentiated tumor) urothelial (histology codes 8120 or 8130) non-muscle-invasive (Ta, Tis or T1) bladder cancer (*International Classification of Diseases, Ninth Revision* (*ICD-9*) codes 188.0–188.9 and 233.7) diagnosed between January 1, 1992 and December 31, 2002, for whom claims data were available through December 31, 2004. While beneficiaries are eligible for Medicare coverage at 65 years of age, we limited our cohort to those 66 years of age or older to allow at least one year of eligibility in Medicare before the date of bladder cancer diagnosis to ascertain comorbidity data. We restricted our analysis to those who survived at least two years and did not undergo definitive treatment (radical cystectomy, radiation therapy or systemic chemotherapy) during that timeframe. Receipt of definitive treatment was derived from PEDSF as well as *ICD-9* and *Healthcare Common Procedure Coding System* (*HCPCS*) codes from the Medicare claims record.

Quality-of-Care Measures

While there are slight variations between clinical practice guidelines from the NCCN, AUA, and EAU we amalgamated the three published guidelines to generate compliance measures *a priori*. The general consensus from these guidelines is that since patients with high-grade, non-muscle-invasive bladder cancer have high recurrence and progression rates, they should undergo frequent surveillance (to detect recurrence and progression) and be treated with intravesical agents (to minimize recurrence and progression). Frequent lower urinary tract surveillance is specified as cystoscopy and urine cytology every three months for the first two years after diagnosis. Upper tract imaging surveillance should be performed at the time of diagnosis and at least every two years thereafter. Treatment strategies include instillation of perioperative mitomycin C (i.e., an intravesical chemotherapeutic) after any transurethral urethral resection of the bladder tumor (TURBT) and an induction course of immunotherapy, Bacillus Calmette-Guérin (BCG), postoperatively. Translated into claims data, we anticipated that patients with high-grade, non-muscle-invasive bladder cancer should undergo at least eight cystoscopies, eight cytologies, two upper tract imaging studies, one instillation of perioperative mitomycin C, and six instillations of BCG (or another agent) after the diagnostic TURBT. We relaxed the definition to count as compliant the use of BCG anytime during the first two years as long as the first instillation occurred within 90 days of diagnosis (to distinguish providers who instilled BCG based on the initial diagnosis, the "preventers", from those who utilized it in response to recurrences, the "reactors"). We also relaxed the definition of perioperative mitomycin C to include a claim for instillation within three days of TURBT. While recent guidelines highlight compelling evidence for the utility of repeat TURBT in T1 disease, more frequent upper-tract imaging and maintenance BCG (an induction course, plus three weekly instillations at 3, 6, 9, 12, 18, 24, 30 and 36 months after diagnosis), we used an *a fortiori* argument with less stringent requirements and an exhaustive set of *ICD-9* and *HCPCS* codes from the Medicare claims record, to posit that if non-compliance with our measures were found to be high, then the non-compliance rate with more stringent criteria would be far greater.

Study Variables

From the PEDSF, we determined patient age (66–69, 70–74, 75–79, ≥80), gender, race/ethnicity (White, Black, Hispanic, Other), marital status (married, other), tumor grade (poor

or undifferentiated tumor), T-stage (Ta, Tis, T1), and year of diagnosis (categorical: 1992–1997, 1998–2002). We imputed subject socioeconomic status by utilizing 2000 US Census data in the PEDSF to derive quartiles of ZIP code-level median household income (< $35,000, $35,000–$45,000, $45,000–$55,000 and >$55,000) and percent of residents 25 years of age or older with at least four years of college education (categorical: <15%, 15%–25%, 25%–35% and >35%).[9] We used the Klabunde *et al*. modification of the Charlson Comorbidity index to quantify severity of preexisting comorbidities (0, 1, 2, ≥3).[10, 11] For each patient, we noted the provider and institution where the initial bladder cancer was diagnosed utilizing the Unique Physician Identifier Number (UPIN) and the corresponding institution (Medicare provider number). The Medicare provider number was linked with the American Medical Association Masterfile to derive institution type—medical school affiliation as well as NCI designation as a Comprehensive Cancer Center. We discovered that only four patients (0.1%) were diagnosed at an NCI designated cancer center without medical school affiliation, and were subsequently included with those diagnosed at an NCI designated cancer center with medical school affiliation. Institution type was therefore stratified into (1) academic cancer center (NCI designated cancer center with medical school affiliation); (2) academic non-cancer center (not NCI designated as a cancer center but with medical school affiliation); and (3) non-academic non-cancer center (not NCI designated as a cancer center and no medical school affiliation); and (4) unknown. Cumulative volumes for surgeon (using UPIN) and hospital (using Medicare provider number) were calculated after adjusting for inclusion of new providers and the four new SEER registries in 2000. Caseload for endoscopic resections was stratified into low, medium and high for each surgeon (low <4, medium 4–11, high ≥12) and hospital (low <11, medium 11–25, high >25). We generated a region variable (West, Midwest, South, Northeast) from the SEER registry.

Statistical Analysis

We report differences in means and proportions compliant with the quality-of-care measures using two sample t-test and Chi-square, respectively. This was performed on a patient and provider level. The provider-level compliance rate was defined as adherence with the measure(s) of interest on at least one patient nested within that provider's practice. This method of quantifying compliance was used to counter the argument that due to the invasive and frequent nature of the surveillance and treatment strategies, patients with bladder cancer are non-compliant. Hence, a physician only needs to deliver care that is consistent with a corresponding measure just once to be categorized as compliant.

Since receipt of services may be clustered on the treating physician, we generated multilevel logistic regression models for each primary outcome (receipt of individual measures) to account for both fixed and random effects associated with compliance with the quality-of-care measures. For our multilevel models, we defined the following individual outcome measures: 1) ≥8 cystoscopy, 2) ≥8 cytology, 3) ≥2 imaging studies, 4) perioperative instillation of mitomycin C and 5) ≥6 instillations of BCG postoperatively. Each model included patient age, gender, race, marital status, Charlson comorbidity score, education, household income, region, year of diagnosis, tumor grade and stage, institution type, hospital and surgeon volume as fixed terms, while each unique surgeon identifier (UPIN) was appended to the random effects part of the multilevel model.

Partitioning of variance was conducted utilizing the following equation: $\frac{\sigma_F^2}{\sigma_F^2+\tau_0^2+\sigma_R^2}$ Where is σ_F^2 defined as the variance of the fixed term (covariate or group of covariates) derived from latent-variable approach; τ_0^2 is defined as the intercept (level-2) variance; and σ_R^2 is defined

as the level-one residual variance ($\pi^2/3$ in our logistic model). Groups of patient- and provider-level variables were included as fixed effects for each outcome measure. We stratified these groups as the following: 1) sociodemographic (patient age, race/ethnicity, gender, education, and income), 2) severity of illness (tumor grade and stage and Charlson comorbidity score), 3) provider characteristics (hospital and surgeon volume, institution type and region) and 4) year of diagnosis. Surgeon-attributable residual intraclass correlation coefficient (ICC)—representing unexplained provider-level variance—was estimated from the full model of each outcome measure. Unexplained surgeon factors were derived from the intraclass correlation coefficient of the unconditional or *null* model of each outcome measure. To test the robustness of these findings, the proportions of attributable variance were recomputed only for providers caring for >3 patients. Sensitivity analysis using year of diagnosis was performed for the multilevel model. While the estimates and the odds ratios changed slightly, there was no change in which variables were significant. Additionally, we used year of diagnosis as a continuous variable when partitioning variance, to augment explained variance. We conducted all analyses with STATA software (version 11.1; College Station, Texas). All statistical tests were two-tailed, and the probability of a type I error was set at <0.05. The institutional review board at the University of California, Los Angeles, approved the study protocol.

RESULTS

We identified 4,545 subjects who were nested within 1,536 providers' practices and 667 institutions nationally. The plurality were octogenarian, male, white, married, without any comorbid conditions, and were diagnosed with a poorly differentiated T1 tumor. The majority were diagnosed in the West, by a medium-volume surgeon (a provider who diagnosed 4–11 bladder cancer patients in an 11 year period of time), in a non-academic, non-cancer center and after 1997. The distribution of the cohort is depicted in Table 1.

Univariate analysis (Table 2) demonstrates that with the exception of receipt of an induction course of BCG (20.5% to 28.9%%, p <0.001), the proportion subjects in receipt of compliant care did not significantly increase after publication of clinical practice guidelines. This finding was further echoed on provider-level compliance. With the exception of an induction course of BCG (33.1% to 44.3%, p<0.001), there was no statistically significant increase in provider compliance. In fact, the number of providers who have utilized ≥8 cytology decreased (11.0% to 8.3%, p=0.04).

With regard to comprehensive care, out of the 4,545 subjects who survived and did not undergo definitive treatment during the initial two years after diagnosis, only one case was compliant with all the quality-of-care measures. In table 3, relaxing the definition so as to not necessarily require upper tract imaging or perioperative mitomycin C, yet to mandate ≥8 cystoscopies, ≥8 cytologies and an induction course of BCG, yielded 19 cases (0.4%). In fact, nearly two-thirds of the cohort did not have receipt of at least ≥1 cystoscopy, ≥1 cytology and a single instillation of intravesical BCG (62.5%). We then repeated the analysis by determining the number of providers who were compliant with a corresponding quality-of-care measure on at least one patient. We find that 99% of providers did not provide ≥8 cystoscopy, ≥8 cytology and ≥6 BCG within a two-year period of time after diagnosis to a single patient. And 42% of providers did not provide at least ≥1 cystoscopy, ≥1 cytology and a single instillation of intravesical BCG for a single patient in a two-year period.

Table 4 presents a multivariate mixed-effects logistic regression model assessing receipt for each outcome measure (cystoscopy, cytology, imaging, mitomycin C and BCG instillation). For cystoscopy, female gender and academic affiliation were independent predictors of

higher odds of compliance. For cytology, octogenarians had lower odds, while education (>35% of adults with a 4-year college education), region (Midwest), academic affiliation and stage (Tis) were all associated with higher odds of compliance. For imaging studies, octogenarians and increasing surgeon volume (medium and high) were associated with lower odds of compliance, while significant comorbid conditions (Charlson score 1 or 2), region (Midwest and South) and stage (T1) were associated with a higher odds of compliance. For perioperative mitomycin C instillation, region (Northeast) was associated with lower odds, while race (Asian and other) and increasing surgeon volume (medium and high) were associated with a higher compliance rate. For BCG, advancing age (≥75) and Black race were associated with lower odds, while marital status, region (South and Northeast), diagnosis after 1997, undifferentiated grade and stage (T1) were independently associated with a higher odds of compliance.

With the exception of radiographic imaging (residual ICC 10% in the full model), unexplained surgeon-attributable variance significantly contributed to the low compliance rate (Table 5). Unexplained surgeon-attributable factors were greatest for cytology (residual ICC 59%) and perioperative mitomycin C (residual ICC 45%). Less than 8% of the variance for cystoscopy, cytology, radiographic imaging, perioperative mitomycin C, and BCG instillation, were explained by measured patient-level characteristics.

DISCUSSION

There is a marked underutilization of care in patients with high-grade, non-muscle-invasive bladder cancer—a single case of comprehensive compliance out of 4,545 eligible patients. We had to significantly ease our definition of compliance to at least one cystoscopy, one cytology and a single instillation of intravesical BCG, to achieve a 37% compliance rate on the patient level and 58% compliance (for at least one patient in a two-year period) on the provider level. Moreover, a significant proportion of variation in low compliance rate is attributable to the provider. Unexplained provider-level variation contributed significantly to the low compliance rate for cystoscopy (25%), cytology (59%), perioperative intravesical chemotherapy (45%) and postoperative instillation of BCG (26%). As a comparison, the proportion of unexplained provider-level variation that contributed to underuse of radical cystectomy for muscle-invasive bladder cancer was 31%, while underutilization of renal-preserving surgery (partial nephrectomy) for kidney cancer was 17%. [12, 13] While some may contend that radical cystectomy and partial nephrectomy are difficult procedures that warrant additional specialty surgical training or hospital resources, one cannot make that same argument for cystoscopy, cytology, perioperative intravesical chemotherapy or postoperative instillation of BCG. Not only have these quality measures been integrated into the reimbursement models, but also these are office-based procedures—the site of most urologic care. Additionally, our unexplained provider-attributable variation is significantly greater than the Hollenbeck *et al*. study whereby they discovered that 9% of unexplained treatment intensity variance was accounted for by unmeasured provider factors. [14] The differences in explained variation is attributed to differences in the outcome measures—we used receipt of individual services and they used cost. Thus, while receipt of cancer-based services may be attributed to unexplained provider-level variation, costs may not differ substantially.

So, why is the inadequacy of compliance with guideline-recommended care so prevalent? Can one attribute this insufficiency to the dearth of evidence-based medicine? While there has been a paucity of studies assessing surveillance strategies, [15] there is significant evidence for the benefits of BCG,[7, 16–18] mitomycin C, [6, 19, 20] as well as other intravesical chemotherapeutics, [21–26] in minimizing the recurrence or progression rate in patients with non-muscle-invasive bladder cancer. Alternatively, since the guidelines were published only

in 1998, the insufficient care seen may have been attributed to preference-sensitive variation in the absence of clinical evidence. However, we encounter sensationalism over innovations, such as robotic technology or intensity-modulated radiation therapy despite an evidence vacuum.[27, 28]. Also, the benefits of BCG were well known prior to 1992. Also, by limiting our cohort to those with high-grade disease, we expected preference-sensitive variation to err on the side of overutilization, not gross underutilization.

Our findings are commensurate with others depicting the underutilization of effective care in patients with bladder cancer. [4, 5, 29] While our findings may appear at odds with those of Hollenbeck *et al*., who have queried a similar cohort and discovered increased utilization of services over time,[30] we too report an increase in utilization of services such as intravesical therapy and radiographic imaging. Additionally, increased utilization of BCG and radiographic imaging does not necessarily translate into improved compliance if care is not comprehensive, as evidenced by a decreasing rate of urine cytology with time.

While our sample size is robust, our study is not with its limitations. As with any observational study, omitted-variable bias may impact adherence rates with clinical guidelines. Patient preferences for surveillance and treatment strategies may have confounded our findings of significant underutilization. The discomfort and its subsequent impact on quality of life from endoscopic evaluation every three months as well as the adverse effects of intravesical therapy (primarily lower urinary tract symptoms) may have contributed to noncompliance. While we were able to exclude individuals who likely progressed and underwent cystectomy, radiotherapy, or systemic chemotherapy, we do not know who stopped as a result of side effects. It is not uncommon that BCG therapy is associated local and systemic side effects so severe that cessation of intravesical immunotherapy occurs (up to 30% of patients). [31] In our cohort, only 16% of subjects received 1–5 instillations; hence, the vast majority (84%) either received 6 more instillations or never received a single dose. Moreover, relaxing the definition from ≥6 instillations to ≥1 instillation(s) had modest impact on compliance (Table 3; lines 1→2 yielding 4 additional patients and lines 4→5 yielding additional 202 patients (4.5%)). This is slight when compared with the transition from ≥1 cystoscopy and ≥1 BCG instillation to just ≥1 cystoscopy (lines 8→9 yielding 1936 subjects (42.6%)). That notwithstanding, the underutilization rate may be in part attributed to patients terminating therapy early (16% in our cohort received 1–5 instillations) or not initiating therapy altogether for fear of treatment toxicities. Another limitation is that our findings may not be generalizable to those who are younger than 65 years of age or have alternative forms of insurance coverage. However, 75% of all bladder cancer patients are 65 years of age or older, and the vast majority of the elderly have Medicare benefits.[32, 33] Last, while there is level-1 evidence demonstrating recurrence- and progression-free survival advantage in patients who received intravesical therapy, the surveillance schedule of cystoscopy and cytology every three months and imaging every other year have not thoroughly tested.

Despite these limitations, our findings serve to alert patients and providers to the wide gap between guideline-recommended care and routine practice. While providers may not always be responsible for patient non-compliance, we must remember that the Institute of Medicine report outlining the six dimensions of high quality care—safe, timely, effective, efficient, patient-centered and equitable—focuses on both technical and interpersonal excellence. Akin to the argument advocating for differential compensation for surgeons who perform technically challenging procedures, so too should physicians be incentivized for establishing a working relationship with their bladder cancer patients and facilitating compliance with clinically effective surveillance and treatment strategies.

How do we bridge the chasm between clinical practice guidelines and routine care? One approach relies on restructuring payment policies through performance-based incentive programs to explicitly promote improvements in quality of care. *Pay-for-performance* incentives and accountable care organizations have been integrated into more than half of commercial health plans in the US and into public health plans.[34] By linking incentives with physician adherence to clinically effective measures, facilitating positive patient outcomes and avoiding complications, we hope to improve quality of care while containing cost.

The age-old adage that, "A chain is only as strong as its weakest link," is fitting with our findings. While bladder cancer care may not be the weakest link in our health care system, it sheds light on the fact that clinically effective measures are not readily practiced by mere publication of best-practice guidelines. In the absence of a broad quality-improvement initiative, the diffusion of clinically effective care will be slow, and many more unnecessary recurrences, procedures and deaths will be realized. This is an especially critical point since progress in preventing bladder cancer-related mortality lags behind other diseases. [35]

Acknowledgments

Role of the Sponsor: The sponsor was not involved with the design and conduct of the study; collection, management, analysis, and interpretation of the data; or preparation, review, or approval of the manuscript.

FUNDING SOURCE: This work was supported by the American Cancer Society (117496-PF-09-147-01-CPHPS (Principal Investigator: KC)); Ruth L. Kirschstein National Research Service Award Extramural (1 F32 CA144461-01 (Principal Investigator: KC)); Jonsson Comprehensive Cancer Center Seed Grant (Principal Investigator: MSL)); and National Institute of Diabetes and Digestive and Kidney Diseases (N01-DK-7-0003 (Principal investigator: M.S.L.))

References

1. Jemal A, Siegel R, Xu J, Ward E. Cancer statistics, 2010. CA Cancer J Clin. 2010; 60(5):277–300. [PubMed: 20610543]
2. Dobruch J, Herr H. Should all patients receive single chemotherapeutic agent instillation after bladder tumour resection? BJU Int. 2009; 104(2):170–4. [PubMed: 19493266]
3. Botteman MF, Pashos CL, Redaelli A, Laskin B, Hauser R. The health economics of bladder cancer: a comprehensive review of the published literature. Pharmacoeconomics. 2003; 21(18):1315–30. [PubMed: 14750899]
4. Schrag D, Hsieh LJ, Rabbani F, Bach PB, Herr H, Begg CB. Adherence to surveillance among patients with superficial bladder cancer. J Natl Cancer Inst. 2003; 95(8):588–97. [PubMed: 12697851]
5. Madeb R, Golijanin D, Noyes K, et al. Treatment of nonmuscle invading bladder cancer: do physicians in the United States practice evidence based medicine? The use and economic implications of intravesical chemotherapy after transurethral resection of bladder tumors. Cancer. 2009; 115(12):2660–70. [PubMed: 19455607]
6. Tolley DA, Parmar MK, Grigor KM, et al. The effect of intravesical mitomycin C on recurrence of newly diagnosed superficial bladder cancer: a further report with 7 years of follow up. J Urol. 1996; 155(4):1233–8. [PubMed: 8632538]
7. Lamm DL, Blumenstein BA, Crawford ED, et al. A randomized trial of intravesical doxorubicin and immunotherapy with bacille Calmette-Guerin for transitional-cell carcinoma of the bladder. N Engl J Med. 1991; 325(17):1205–9. [PubMed: 1922207]
8. Warren JL, Klabunde CN, Schrag D, Bach PB, Riley GF. Overview of the SEER-Medicare data: content, research applications, and generalizability to the United States elderly population. Med Care. 2002; 40(8 Suppl):IV-3–18.
9. Bach PB, Guadagnoli E, Schrag D, Schussler N, Warren JL. Patient demographic and socioeconomic characteristics in the SEER-Medicare database applications and limitations. Med Care. 2002; 40(8 Suppl):V-19–25.

10. Klabunde CN, Potosky AL, Legler JM, Warren JL. Development of a comorbidity index using physician claims data. J Clin Epidemiol. 2000; 53(12):1258–67. [PubMed: 11146273]
11. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987; 40(5):373–83. [PubMed: 3558716]
12. Gore JL, Litwin MS, Lai J, et al. Use of radical cystectomy for patients with invasive bladder cancer. J Natl Cancer Inst. 2010; 102(11):802–11. [PubMed: 20400716]
13. Miller DC, Saigal CS, Banerjee M, Hanley J, Litwin MS. Diffusion of surgical innovation among patients with kidney cancer. Cancer. 2008; 112(8):1708–17. [PubMed: 18330868]
14. Hollingsworth JM, Zhang Y, Krein SL, Ye Z, Hollenbeck BK. Understanding the variation in treatment intensity among patients with early stage bladder cancer. Cancer. 2010; 116(15):3587–94. [PubMed: 20564128]
15. Olsen LH, Genster HG. Prolonging follow-up intervals for non-invasive bladder tumors: a randomized controlled trial. Scand J Urol Nephrol Suppl. 1995; 172:33–6. [PubMed: 8578253]
16. Lamm, DL. BCG immunotherapy in bladder cancer. In: Rouse, SN., editor. Urology Annual. Los Angeles: Appleton and Lange; 1987. p. 67
17. Camacho, F.; Pinsky, CM.; Kerr, D.; Whitmore, WF., et al. Treatment of superficial bladder cancer with intravesical BCG. In: Terry, WT.; Rosenberg, SA., editors. Immunotherapy of human cancer. New York: Plenum Press; 1980.
18. Sylvester RJ, van der MA, Lamm DL. Intravesical bacillus Calmette-Guerin reduces the risk of progression in patients with superficial bladder cancer: a meta-analysis of the published results of randomized clinical trials. J Urol. 2002; 168(5):1964–70. [PubMed: 12394686]
19. Solsona E, Iborra I, Ricos JV, Monros JL, Casanova J, Dumont R. Effectiveness of a single immediate mitomycin C instillation in patients with low risk superficial bladder cancer: short and long-term followup. J Urol. 1999; 161(4):1120–3. [PubMed: 10081851]
20. Sylvester RJ, Oosterlinck W, van der Meijden AP. A single immediate postoperative instillation of chemotherapy decreases the risk of recurrence in patients with stage Ta T1 bladder cancer: a meta-analysis of published results of randomized clinical trials. J Urol. 2004; 171(6 Pt 1):2186–90. [PubMed: 15126782]
21. Ali-el-Dein B, Nabeeh A, el-Baz M, Shamaa S, Ashamallah A. Single-dose versus multiple instillations of epirubicin as prophylaxis for recurrence after transurethral resection of pTa and pT1 transitional-cell bladder tumours: a prospective, randomized controlled study. Br J Urol. 1997; 79(5):731–5. [PubMed: 9158511]
22. Berrum-Svennung I, Granfors T, Jahnson S, Boman H, Holmang S. A single instillation of epirubicin after transurethral resection of bladder tumors prevents only small recurrences. J Urol. 2008; 179(1):101–5. discussion 05-6. [PubMed: 17997459]
23. Gudjonsson S, Adell L, Merdasa F, et al. Should all patients with non-muscle-invasive bladder cancer receive early intravesical chemotherapy after transurethral resection? The results of a prospective randomised multicentre study. Eur Urol. 2009; 55(4):773–80. [PubMed: 19153001]
24. Oosterlinck W, Kurth KH, Schroder F, Bultinck J, Hammond B, Sylvester R. A prospective European Organization for Research and Treatment of Cancer Genitourinary Group randomized trial comparing transurethral resection followed by a single intravesical instillation of epirubicin or water in single stage Ta, T1 papillary carcinoma of the bladder. J Urol. 1993; 149(4):749–52. [PubMed: 8455236]
25. Rajala P, Kaasinen E, Raitanen M, Liukkonen T, Rintala E. Perioperative single dose instillation of epirubicin or interferon-alpha after transurethral resection for the prophylaxis of primary superficial bladder cancer recurrence: a prospective randomized multicenter study--FinnBladder III long-term results. J Urol. 2002; 168(3):981–5. [PubMed: 12187204]
26. Rajala P, Liukkonen T, Raitanen M, et al. Transurethral resection with perioperative instilation on interferon-alpha or epirubicin for the prophylaxis of recurrent primary superficial bladder cancer: a prospective randomized multicenter study--Finnbladder III. J Urol. 1999; 161(4):1133–5. discussion 35-6. [PubMed: 10081854]
27. Cropper, CM. The robot is in — and ready to operate. Business Week; March 14. 2005 p. 110-12.

28. Bowa K, Wood C, Chao A, Chintu C, Mudenda V, Chikwenya M. A review of the epidemiology of cancers at the University Teaching Hospital, Lusaka, Zambia. Trop Doct. 2009; 39(1):5–7. [PubMed: 19211410]

29. Schrag D, Mitra N, Xu F, et al. Cystectomy for muscle-invasive bladder cancer: patterns and outcomes of care in the Medicare population. Urology. 2005; 65(6):1118–25. [PubMed: 15922428]

30. Strope SA, Ye Z, Hollingsworth JM, Hollenbeck BK. Patterns of care for early stage bladder cancer. Cancer. 2010; 116(11):2604–11. [PubMed: 20310051]

31. van der Meijden AP, Sylvester RJ, Oosterlinck W, Hoeltl W, Bono AV. Maintenance Bacillus Calmette-Guerin for Ta T1 bladder tumors is not associated with increased toxicity: results from a European Organisation for Research and Treatment of Cancer Genito-Urinary Group Phase III Trial. European urology. 2003; 44(4):429–34. [PubMed: 14499676]

32. Ries, LAGEM.; Kosary, CL.; Hankey, BF.; Miller, BA.; Clegg, L.; Mariotto, A.; Feuer, EJ.; Edwards, BK. SEER Cancer Statistics Review, 1975–2002. National Cancer Institute; Bethesda, MD: 2005. http://seer.cancer.gov/csr/1975_2002/, based on November 2004 SEER data submission, posted to the SEER web site 2005

33. Federal Interagency Forum on Aging-Related Statistics. Older Americans update 2006: Key indicators of well-being. Washington, DC: U.S. Government Printing Office; July. 2006

34. Rosenthal MB, Landon BE, Normand SL, Frank RG, Epstein AM. Pay for performance in commercial HMOs. N Engl J Med. 2006; 355(18):1895–902. [PubMed: 17079763]

35. Cancer Statistics 1984–2009. American Cancer Society Surveillance Research;

Table 1

Cohort characteristics (*n*=4545)

Variables	Number	%
Age-group		
66–69	649	14.3%
70–74	1189	26.2%
75–79	1175	25.8%
≥80	1532	33.7%
Gender		
Male	3497	76.9%
Female	1048	23.1%
Race		
White	4151	91.3%
Black	109	2.4%
Hispanic	122	2.7%
Other	163	3.6%
Marital		
Not Married	1588	34.9%
Married	2957	65.1%
Charlson Score		
0	3181	70.0%
1	932	20.5%
2	303	6.7%
≥3	129	2.8%
% Of Subjects in ZIP code ≥25 years of age with ≥4 years of college education		
<15%	958	21.1%
15–25%	1171	25.8%
25%–35%	938	20.6%
>35%	1478	32.5%
Median ZIP code household income		
<$35,000	751	16.5%
$35,000–$45,000	1094	24.1%
$45,000–$55,000	1171	25.7%
>$55,000	1530	33.7%
Region		
West	2329	51.2%
Midwest	897	19.7%
South	420	9.2%
Northeast	899	19.8%
Year		
1992–1997	1698	37.4%
1998–2002	2847	62.6%

Variables	Number	%
Surgeon Volume		
Low (<4)	718	15.8%
Medium (4–11)	2373	52.2%
High (>11)	1454	32.0%
Hospital Volume		
Low (<11)	1487	32.7%
Medium (11–25)	1533	33.7%
High (>25)	1525	33.6%
Institution Type		
Non-Academic Non-Cancer Center	3217	70.8%
Academic Non-Cancer Center	979	21.5%
Academic Cancer Center	85	1.9%
Unknown	264	5.8%
Grade		
Poorly Differentiated	3622	79.7%
Undifferentiated	923	20.3%
Stage		
Ta	1727	38.0%
Tis	458	10.1%
T1	2360	51.9%

Table 2

Patient and provider compliance (on at least one occasion) stratified by year the NCCN guidelines for non-muscle-invasive bladder cancer was established.

Quality-of-Care Measure	Subjects Compliant (%)			Providers Compliant to at least one patient (%)		
	1992–1997 (*n*=1698)	1998–2002 (*n*=2847)	p-value	1992–1997 (*n*=725)	1998–2002 (*n*=1272)	p-value
≥8 Cystoscopy	93 (4.6%)	131 (4.7%)	0.89	70 (9.7%)	126 (9.9%)	0.86
≥8 Cytology	98 (5.5%)	143 (4.6%)	0.19	**80 (11.0%)**	**106 (8.3%)**	**0.04**
≥2 Upper tract Image	801 (47.2%)	1446 (50.8%)	0.18	491 (67.7%)	909 (71.5%)	0.08
Perioperative mitomycin C	48 (2.8%)	92 (3.2%)	0.44	43 (5.9%)	73 (5.7%)	0.86
≥6 Instillations of BCG, 1st dose within 90 days	**349 (20.5%)**	**824 (28.9%)**	**<0.001**	**240 (33.1%)**	**564 (44.3%)**	**<0.001**

Table 3

Progressive relaxation of guidelines depicting the number of subjects in receipt of compliant care and the number of providers who delivered compliant care to at least one patient.

Compliance criteria	Subjects (*n*=4545) n (%)	Providers (*n*=1536) n (%)
≥8 Cystoscopy and ≥8 Cytology and ≥6 BCG	19 (0.4%)	16 (1.0%)
≥8 Cystoscopy and ≥8 Cytology and ≥1 BCG	23 (0.5%)	22 (1.4%)
≥8 Cystoscopy and ≥4 Cytology and ≥6 BCG	42 (0.9%)	40 (2.6%)
≥4 Cystoscopy and ≥4 Cytology and ≥6 BCG	597 (13.1%)	398 (25.9%)
≥4 Cystoscopy and ≥4 Cytology and ≥1 BCG	799 (17.6%)	479 (31.2%)
≥4 Cystoscopy and ≥1 Cytology and ≥1 BCG	1527 (33.6%)	823 (53.6%)
≥1 Cystoscopy and ≥1 Cytology and ≥1 BCG	1703 (37.5%)	891 (58.0%)
≥1 Cystoscopy and ≥1 BCG	2437 (53.6%)	1148 (74.7%)
≥1 Cystoscopy	4373 (96.2%)	1510 (98.3%)

Cancer. Author manuscript; available in PMC 2012 December 1.

Table 4

Multilevel model predicting compliance with individual measures

Variables	≥8 Cystoscopy OR (95% CI)	≥8 Cytology OR (95% CI)	≥2 Imaging OR (95% CI)	≥1 Perioperative Mitomycin C OR (95% CI)	≥6 Postoperative BCG OR (95% CI)
Age-group					
66–69	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)
70–74	1.39 (0.86–2.25)	0.94 (0.56–1.56)	1.02 (0.83–1.26)	1.35 (0.72–2.50)	0.94 (0.73–1.21)
75–79	1.04 (0.63–1.72)	0.78 (0.45–1.33)	0.97 (0.79–1.20)	0.78 (0.40–1.53)	0.78 (0.60–0.99)*
≥80	0.89 (0.54–1.45)	0.39 (0.23–0.68)*	0.77 (0.63–0.94)*	1.25 (0.67–2.33)	0.52 (0.40–0.67)*
Gender					
Male	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)
Female	1.48 (1.03–2.11)*	1.11 (0.70–1.75)	0.94 (0.80–1.11)	0.98 (0.58–1.65)	1.00 (0.81–1.23)
Race					
White	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)
Black	0.62 (0.18–2.16)	1.58 (0.57–4.36)	0.91 (0.60–1.40)	0.24 (0.03–2.08)	0.40 (0.21–0.77)*
Hispanic	0.95 (0.35–2.55)	0.58 (0.15–2.20)	1.15 (0.77–1.72)	0.53 (0.11–2.49)	0.81 (0.48–1.37)
Other	1.08 (0.49–2.38)	0.44 (0.11–1.71)	1.16 (0.81–1.67)	2.78 (1.18–6.56)*	1.06 (0.67–1.68)
Marital					
Not Married	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)
Married	1.07 (0.76–1.50)	1.37 (0.91–2.08)	0.99 (0.86–1.15)	1.30 (0.82–2.05)	1.22 (1.02–1.47)*
Charlson Score					
0	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)
1	0.85 (0.59–1.24)	0.87 (0.56–1.37)	1.19 (1.02–1.40)*	1.14 (0.71–1.83)	0.99 (0.81–1.21)
2	0.48 (0.23–1.03)	0.84 (0.40–1.74)	1.41 (1.09–1.82)*	1.42 (0.69–2.92)	1.03 (0.75–1.42)
≥3	0.15 (0.02–1.10)	1.40 (0.51–3.88)	1.39 (0.94–2.05)	1.62 (0.56–4.67)	0.74 (0.45–1.21)
ZIP code Education					
<15%	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)
15%–25%	1.24 (0.74–2.07)	1.23 (0.68–2.21)	1.13 (0.92–1.38)	1.45 (0.77–2.71)	1.03 (0.79–1.34)
25%–35%	1.15 (0.64–2.07)	1.19 (0.58–2.45)	0.99 (0.78–1.25)	1.42 (0.68–2.96)	0.99 (0.72–1.34)
>35%	1.45 (0.79–2.67)	2.64 (1.27–5.50)*	0.94 (0.73–1.21)	0.67 (0.29–1.55)	1.21 (0.87–1.68)
ZIP code Income					
<$35,000	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)

Variables	≥8 Cystoscopy OR (95% CI)	≥8 Cytology OR (95% CI)	≥2 Imaging OR (95% CI)	≥1 Perioperative Mitomycin C OR (95% CI)	≥6 Postoperative BCG OR (95% CI)
$35,000–$45,000	1.00 (0.57–1.75)	0.81 (0.42–1.56)	0.80 (0.64–1.01)	0.72 (0.37–1.43)	0.83 (0.62–1.10)
$45,000–$55,000	1.06 (0.59–1.90)	0.82 (0.41–1.67)	1.02 (0.80–1.29)	0.89 (0.43–1.83)	0.87 (0.64–1.18)
>$55,000	1.09 (0.57–2.06)	0.54 (0.24–1.18)	1.24 (0.95–1.62)	1.16 (0.51–2.61)	0.93 (0.66–1.31)
Region					
West	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)
Midwest	0.87 (0.52–1.46)	2.60 (1.31–5.16)*	1.84 (1.47–2.30)*	1.09 (0.55–2.16)	0.79 (0.57–1.09)
South	0.65 (0.33–1.30)	1.31 (0.57–2.98)	1.69 (1.31–2.19)*	1.03 (0.44–2.40)	1.60 (1.15–2.22)*
Northeast	1.32 (0.85–2.05)	1.81 (0.94–3.47)	1.19 (0.97–1.46)	0.42 (0.20–0.89)*	1.48 (1.12–1.95)*
Year					
1992–1997	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)
1998–2002	1.02 (0.73–1.42)	0.72 (0.48–1.08)	1.19 (1.03–1.37)*	1.17 (0.75–1.83)	1.67 (1.39–2.01)*
Surgeon Volume					
Low (<4)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)
Medium (4–11)	1.00 (0.64–1.57)	0.98 (0.55–1.74)	0.82 (0.67–0.99)*	2.65 (1.24–5.65)*	0.83 (0.65–1.07)
High (≥12)	0.97 (0.57–1.65)	0.85 (0.42–1.71)	0.73 (0.58–0.92)*	2.95 (1.23–7.04)*	0.86 (0.63–1.18)
Hospital Volume					
Low (<11)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)
Medium (11–25)	0.81 (0.52–1.25)	1.00 (0.57–1.75)	1.11 (0.92–1.33)	1.09 (0.59–2.01)	1.00 (0.79–1.28)
High (>25)	0.81 (0.50–1.31)	0.82 (0.44–1.56)	1.11 (0.89–1.37)	1.23 (0.61–2.48)	1.14 (0.86–1.51)
Institution Type					
Non-Academic Non-Cancer	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)
Academic Non-Cancer	1.68 (1.11–2.54)*	3.27 (1.88–5.70)*	1.05 (0.87–1.28)	1.16 (0.62–2.15)	0.96 (0.74–1.25)
Academic Cancer	1.80 (0.67–4.85)	7.81 (2.60–23.53)*	0.91 (0.55–1.49)	2.28 (0.51–10.18)	0.65 (0.33–1.29)
Unknown	1.66 (0.90–3.06)	1.28 (0.52–3.13)	1.03 (0.76–1.39)	1.99 (0.84–4.75)	0.87 (0.59–1.28)
Grade					
Poorly Differentiated	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)
Undifferentiated	1.32 (0.92–1.89)	1.31 (0.83–2.06)	1.12 (0.95–1.32)	0.96 (0.58–1.57)	1.49 (1.22–1.82)*
Stage					
Ta	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)
Tis	1.36 (0.83–2.23)	2.50 (1.41–4.43)*	1.18 (0.94–1.49)	0.55 (0.23–1.35)	1.86 (1.39–2.48)*
T1	0.93 (0.67–1.28)	0.94 (0.63–1.41)	1.18 (1.03–1.36)*	1.26 (0.83–1.91)	2.03 (1.70–2.43)*

Table 5

Patient, tumor and surgeon contributions to variation in compliance with established measures

Partitioning of Variance	≥8 Cystoscopy	≥8 Cytology	≥2 Imaging	≥1 Perioperative Mitomycin C	≥6 Postoperative BCG
Surgeon-Attributable Variance (*null* model)	26.6%	58.3%	12.2%	47.7%	26.2%
Unexplained Surgeon Variance (full model)	25.1%	59.3%	9.9%	45.4%	26.3%
Patient Sociodemographic Characteristics	2.5%	3.6%	1.0%	4.1%	2.5%
Severity of Illness	4.5%	0.3%	0.6%	1.5%	2.9%
Provider Characteristics	2.9%	5.4%	1.8%	4.7%	2.1%
Year of Diagnosis	3.5%	0.6%	0.3%	2.8%	3.1%