Original Article

Understanding the Variation in Treatment Intensity Among Patients With Early Stage Bladder Cancer

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BACKGROUND: Given the uncertainty surrounding the optimal management for early stage bladder cancer, physicians vary in how they approach the disease. The authors of this report linked cancer registry data with medical claims to identify the sources of variation and opportunities for improving the value of cancer care. **METHODS:** By using data from the Surveillance, Epidemiology, and End Results-Medicare database (1992-2005), patients with early stage bladder cancer were abstracted (n = 18,276). The primary outcome was the intensity of initial treatment that patients received, as measured by all Medicare payments for bladder cancer incurred in the 2 years after diagnosis. Multilevel models were fitted to partition the variation in treatment intensity attributable to patient versus provider factors, and the potential savings to Medicare from reducing the physician contribution were estimated. **RESULTS:** Provider factors accounted for 9.2% of the variation in treatment intensity. Increasing provider treatment intensity did not correlate with improved cancer-specific survival ($P = .07$), but it was associated with the subsequent receipt of major interventions, including radical cystectomy ($P < .001$). If provider-level variation was reduced and clinical practice was aligned with that of physicians who performed in the 25th percentile of treatment intensity, then total payments made for the average patient could be lowered by 18.6%, saving Medicare $18.7 million annually. **CONCLUSIONS:** The current results indicated that a substantial amount of the variation in initial treatment intensity for early stage bladder cancer is driven by the physician. Furthermore, a more intensive practice style was not associated with improved cancer-specific survival or the avoidance of major interventions. Therefore, interventions aimed at reducing between-provider differences may improve the value of cancer care. ***Cancer*** **2010;116;3587–94.** © *2010 American Cancer Society.*

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Because mortality from muscle-invasive bladder cancer is common, the goal of initial management for early stage (ie, superficial) disease is to prevent progression. Although this goal is clear, how best to achieve it is not. Contemporary practice guidelines for early stage bladder cancer reflect a view held by many authorities favoring intensive surveillance and treatment.[1,2] Implicit in such an approach is that more care prevents progression (and prolongs survival) or, at the very least, allows for the detection of recurrences early enough so that subsequent interventions are more successful and palatable.

However, the evidence base for these guidelines is limited and often relies on medical theory and expert opinion. For example, surveillance recommendations call for frequent and regular endoscopies. Yet data supporting such recommendations were derived from a single trial of less than 100 patients.[3] Moreover, the basis for the intensive treatment regimens promoted by current guidelines is extrapolated largely from intermediate outcomes. Although the use of intravesical therapy can lengthen the interval between recurrences,[4,5] its benefits for imperative outcomes (eg, progression) are less certain.

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Indeed, patients with early stage disease fare no better when treated by physicians who provide more intensive initial treatment.[6]

With the uncertainty on how best to manage early stage bladder cancer, physicians vary widely in their approach.[7-10] Given the spectrum of disease severity among this population, a "1-size-fits-all" approach is impractical. Insofar as patient factors explain the differences in physician practice, this variation may be appropriate. However, to the extent that the physician is a significant driver of this variation, efforts to decrease practice differences, especially those that add little benefit, are warranted. For this reason, we performed a study using Surveillance, Epidemiology, and End Results (SEER)-Medicare data to understand the sources of variation in the treatment of early stage disease as well as opportunities for improving the value of cancer care.

MATERIALS AND METHODS

Database and Patients

For this study, we used SEER-Medicare data for the years 1992 through 2002. Patients were followed using Medicare claims through December 31, 2005. The cancer-specific information collected by the SEER Program is generally representative of the entire United States population.[11] Data regarding tumor incidence, treatment, and mortality can be linked successfully with hospital, physician, and other medical service claims for greater than 90% of the Medicare beneficiaries who are tracked by SEER.[12] By using appropriate SEER site-specific codes (67.0-67.9), we abstracted data on all Medicare beneficiaries ages 65 to 99 years in the SEER Patient Entitlement and Diagnosis Summary file who had an incident case of early stage (modified American Joint Commission on Cancer[13] stages 0 and 1) bladder cancer. The study was limited further to fee-for-service patients who were eligible for both Part A and Part B of Medicare throughout the study interval.

To identify the physician primarily responsible for providing a patient's bladder cancer care, we examined all bladder cancer-related procedures (as described in detail by Schrag and colleagues[9]) performed in the first 2 years after diagnosis. By using a physician-specific identifier, we assigned each patient to the provider who performed the majority of these procedures. To ensure the reliability surrounding each provider's practice style, we limited our study to those providers who treated at least 10 patients during the study period. Our final cohort consisted of 18,276 patients with early stage bladder cancer who were cared for by 907 providers.

Outcomes

With the patient serving as the unit of analysis, our primary outcome was the initial treatment intensity received, as measured by all Medicare payments for bladder cancer incurred during the first 2 years after diagnosis.[14] First, we identified all claims associated with a primary diagnosis code for bladder cancer (*International Classification of Diseases, Ninth Revision* [ICD-9], *Clinical Modification* codes: 188.x [bladder cancer], 233.7 [carcinoma in situ of the bladder], and V105.4 [personal history of bladder cancer]) from the inpatient, outpatient, and carrier files. Next, we tallied the total payments for these claims, standardized these to 2005 US dollars, and price-adjusted them to account for regional differences in Medicare reimbursement.[15] Because these data were positively skewed, we applied a logarithmic transformation to normalize them.

For our secondary outcomes, we measured bladder cancer-specific survival using the cause-of-death field available in SEER. We assessed survival from January 1, 1992 through December 31, 2005. We also determined a patient's subsequent need for a major intervention (as evidenced by the receipt of radical cystectomy, systemic chemotherapy, or radiation treatment). We identified these procedures using appropriate ICD-9 procedure codes and Healthcare Common Procedure Coding System (HCPCS) codes.

Characterizing Patients and Providers

Subsequently, we constructed a variety of patient-level variables hypothesized to influence the intensity of care. In particular, we used the SEER records and Medicare claims to categorize patients by their age at diagnosis, sex, race/ethnicity (white, black, other), socioeconomic status, level of comorbidity, geographic region of residence (the hospital referral region [HRR] boundaries defined by the *Dartmouth Atlas of Health Care*[16]), tumor grade (low, medium, high, unknown), and tumor stage (Ta, tumor in situ [Tis], T1, Ta/T1 not otherwise specified). We assessed socioeconomic status at the patient zip code level using a composite measure.[17] With an adaptation of the Charlson index,[18] we examined patients' healthcare encounters in the 12-month period preceding their cancer diagnosis to determine their comorbid illnesses.[19] Through patients' Medicare claims, we also distinguished between those who experienced a bladder cancer recurrence and those who did not. Specifically, we defined a

patient as having recurrent disease if he underwent a transurethral bladder resection of bladder tumor (HCPCS codes 52234, 52235, and 52240) more than 60 days after his date of diagnosis.

To characterize the physicians who provided bladder cancer care, we linked their Medicare claims with the American Medical Association Masterfile through the providers' Unique Physician Identifier Numbers.[20] On the basis of the Masterfile data, we built variables that indicated each physician's sex, type of degree (Medical Doctor vs Doctor of Osteopathy), location of training (US graduate vs non-US graduate), and decade of medical school graduation. In addition, we identified those providers who were urologists using the Masterfile's primary specialty designation. We also determined the number of patients with early stage disease that each provider treated during the study period.

Statistical Analysis

We used multilevel models to examine our continuous dependent variable: treatment intensity. We fitted 2-level linear mixed models with random intercepts. Our level-1 unit was the patient, and our level-2 unit was the provider. Our initial model was a random intercept model with only the provider identifier as a random effect and no explanatory variables. This "empty" model allowed us to understand the basic partitioning of the variation in treatment intensity between the patient and the provider. From the empty model, we determined the percentage of the total variance that was caused by unmeasured between-provider differences (ie, the provider intraclass correlation[21]). We then proceeded to add in sets of independent variables as fixed effects (diagnosis year, patient characteristics, tumor features, recurrent disease status, provider factors, and HRR) and measured the degree to which each set changed the amount of between-provider variation in treatment intensity.

Next, we fitted another series of multilevel models from which the variance was partitioned further into contributions from the measured provider and patient characteristics. Each model included the provider identifier as a random effect and only 1 of the following independent variables: patient age, sex, race/ethnicity, socioeconomic status, level of comorbidity, geographic region, tumor grade and stage, whether the patient had a subsequent bladder cancer recurrence, and diagnosis year. We calculated the percentage of the total variance explained by each variable. This allowed us to understand the importance of each variable relative to the overall variation in treatment intensity.

Then, we estimated providers' average treatment intensity from our multilevel models (controlling for patient characteristics, tumor features, recurrent disease status, and diagnosis year) using empirical Bayes methods. Empirical Bayes estimates account for differences in the reliability of individual measures of provider treatment intensity that result from variations in the size of a physician's patient panel by adjusting each provider-specific measure toward the overall mean as a factor of the physician's panel size.[22] Because our linear mixed models were based on the log of total payments, it was necessary for us to retransform our predicted values back to their original scale.[23]

After ranking providers by their treatment intensity from lowest to highest, we sorted them into 20 equal quantiles. We measured the degree of correlation between a provider's treatment intensity quantile and patient median cancer-specific survival as well as subsequent need for major intervention, using the Kendall rank correlation coefficient. Finally, we determined the potential annual savings per patient from reducing physician variation in treatment intensity using parameters from our previous models and simulated datasets in which we changed all providers' practice habits to be similar to those of the physicians residing in 1 of the treatment intensity quantiles (beginning at the 5th percentile and ending with the 95th). We estimated possible implications for the Medicare program by reducing practice variation based on the assumption of 45,000 incident cases of early stage bladder cancer diagnosed annually.[24]

We carried out all analyses using the SAS statistical package (version 9.1; SAS Institute, Cary, NC). All tests were 2-tailed, and we set the probability of Type 1 error at 0.05. The Institutional Review Board of the University of Michigan approved this study.

RESULTS

Over the study interval, mean expenditures per patient were $4744. White men aged >74 years represented the majority of patients in our study population, as displayed in Table 1. Low-to-medium grade and stage Ta tumors were the most common cancers at diagnosis, and 49.4% of patients had recurrent disease. Figure 1 depicts the proportion of variation in treatment intensity explained by measurable patient demographics and tumor features. Subsequent bladder cancer recurrence explained the highest percentage of the total variance (16%). Patient age,

Table 1. Patient and Physician Characteristics

Characteristic	Percentage
Patients (N=18,276)	
Age, y	
65-69	17.6
70-74	26.1
75-79	25.7
80-84	17.6
≥85	13
Women	25.3
Race/ethnicity	
White	94.9
Black	2.8
Other	2.3
Socioeconomic status	
Low	32.5
Medium	34.4
High	33.1
Modified Charlson score	
0	43.9
1	29.8
2	14.8
≥3	11.5
Tumor grade	
Low	19.6
Medium	45.3
High	28.2
Unknown	6.9
Tumor classification	
Ta	57.1
T1	24.8
Carcinoma in situ	7
Ta/T1 not otherwise specified	11.1
Bladder cancer recurrence	49.4
Physicians (N=907)	
Received an MD degree	97.5
US trained	85.7
Decade of graduation	
Before 1960	4
1960-1970	11
1971-1980	32.1
1981-1990	31.7
After 1990	21.2
Primary specialty is urology	98.5
Bladder cancer volume	
Low (≤19 patients with early stage bladder cancer)	35.5
Medium (20-34 patients)	32
High (≥35 patients)	32.5
Women	1.9

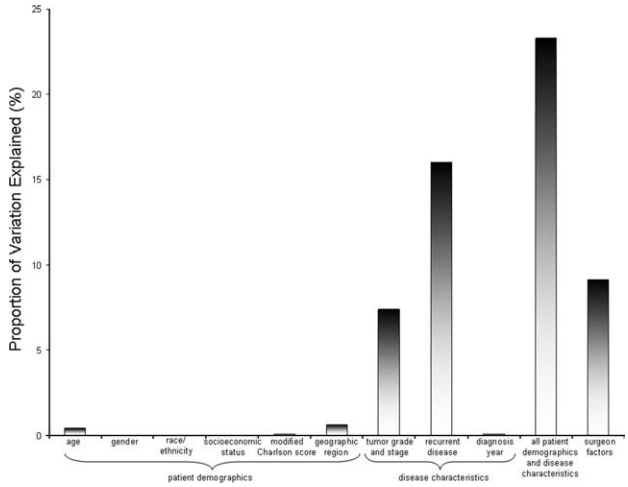

Figure 1. This chart illustrates the proportion of variation in treatment intensity explained by patient-level factors. A series of 2-level models was fitted that included the provider as a random effect and each of the following variables as a fixed effect: patient age, sex, race/ethnicity, socioeconomic status, comorbidity, tumor grade, tumor classification, recurrent disease status, and diagnosis year. A 2-level random effects model with a random intercept (provider in our analysis) and some predictor variables with fixed effects but no other random effects can be written as follows: $Y_{ij} = \gamma_O + \Sigma\gamma_h X_{hij} + U_{Oj} + R_{ij}$, in which the fixed part of the model is $Y_{ij} = \gamma_O + \Sigma X_{hij}$ and constitutes the linear predictor for Y with a variance of σ^2_F.[21] The percentage of total variance explained by each was calculated. The explained proportion of the level-1 (patient) variance (var) is defined as the proportional reduction in mean squared prediction error, which can be written as $1 - (\text{var}[Y_{ij} - \Sigma\gamma_h X_{hij}]/\text{var}[Y_{ij}])$. Intraclass correlation (or the proportion of the variance attributable to the provider) is equal to $\tau^2_O/(\tau^2_O + \sigma^2)$, in which τ^2_O is the level-2 variance, and σ^2 is the level-1 variance.

sex, race/ethnicity, socioeconomic status, level of comorbidity, and geographic region of residence contributed minimally to the observed variation, accounting for <2% of the total variance combined.

The majority of physicians in our cohort were US-trained, male urologists who completed their medical schooling before the 1980s (Table 1). On average, each provider cared for 17 patients with early stage bladder cancer during the study period, and the mean (±standard deviation) follow-up was 62.4 ± 38.4 months. According to our empty model, the estimated proportion of the unexplained variance that was accounted for by unmeasured provider factors was 9.2%. The size of the physician effect on initial treatment intensity exceeded that attributable to all measurable patient characteristics and tumor stage and grade (Fig. 1). In our final model, we were able to explain only 18.7% of the provider-level variation.

After sorting physicians into quantiles using their estimated per patient expenditures (Fig. 2A), we observed no significant correlation between increasing provider treatment intensity and patient median cancer-specific survival ($P = .07$). However, despite no measurable

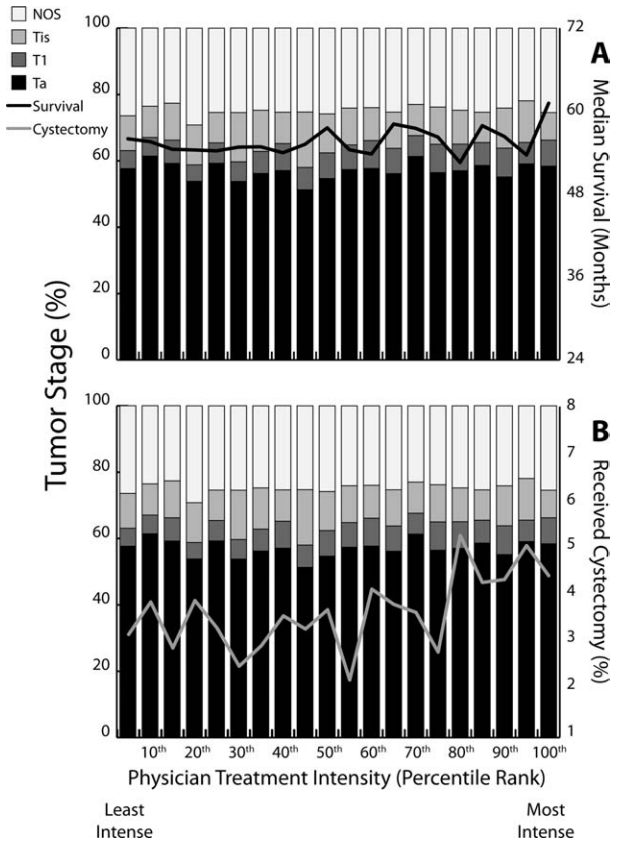

Figure 2. These charts illustrate the correlations between initial treatment intensity, (A) median cancer-specific survival, and (B) the use of radical cystectomy. Providers were ranked according to their treatment intensity from lowest to highest and were sorted into 20 quantiles. With respect to tumor classification (stacked bar chart), the level of disease severity was similar across quantiles ($P = 1$). Treatment intensity was not correlated with median cancer-specific survival ($P = .12$); however, it was associated with undergoing radical cystectomy ($P < .001$). NOS indicates not otherwise specified; Tis, carcinoma in situ.

differences in the level of disease severity treated ($P < .001$), there was a positive correlation, albeit small, between increasing provider treatment intensity and a patient's subsequent receipt of radical cystectomy (Fig. 2B) (tau = 0.019; $P < .001$), as well as radiation treatment (tau = 0.018; $P < .001$) and systemic chemotherapy (tau = 0.030; $P < .001$). Table 2 displays the cost savings achieved by eliminating the contribution of physician practice style to the variation in treatment intensity for the typical patient with early stage bladder cancer. For example, if all physicians' care was similar to that of the physicians in the 25th percentile of treatment intensity, then total payments would be lowered by a minimum of 18.6% ($832), which would translate into an annual savings of $18,720,000 for Medicare (Fig. 3).

Table 2. The Effect of Reducing Physician-Attributable Variation on Bladder Cancer Expenditures for Patients With Early Stage Disease

Percentile	Average Expenditures per Patient, $[a]	Reduction From Overall Mean, %[b]	Potential Savings per Patient, $
5th	2833	36.7	1641
10th	3103	30.6	1371
15th	3309	26	1165
20th	3489	22	985
25th	3642	18.6	832
30th	3790	15.3	684
35th	3877	13.3	597
40th	3978	11.1	496
45th	4127	7.8	347
50th	4233	5.4	241
55th	4379	2.1	95
60th	4549	−1.7	−75
65th	4677	−4.6	−203
70th	4865	−8.8	−391
75th	5048	−12.9	−574
80th	5306	−18.6	−832
85th	5637	−26	−1163
90th	5985	−33.8	−1511
95th	6507	−45.5	−2033

[a] Average expenditures per patient were predicted by running multilevel models on simulated datasets in which all providers' practice habits were changed to be similar to those of the physicians from 1 of the treatment-intensity quantiles (beginning at the 5th percentile and ending with the 95th percentile).
[b] The overall mean expenditures were $4474 per patient.

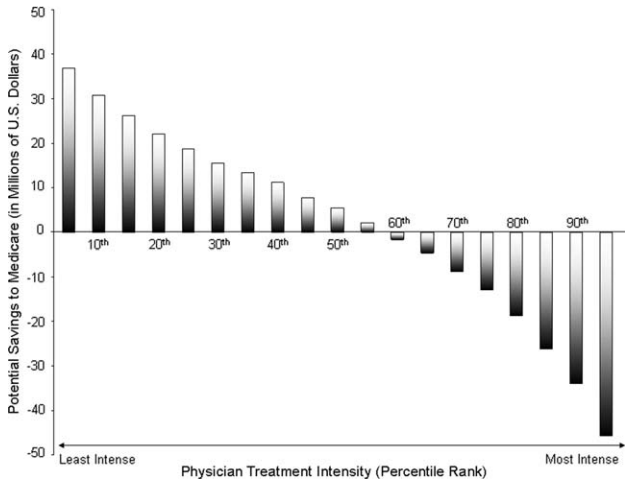

Figure 3. Potential annual savings for Medicare from reducing physician-attributable variation is shown. By using parameters from our multilevel models and simulated datasets, we changed all providers' practice styles to be similar to those of the physicians in 1 of the 20 treatment-intensity quantiles (beginning at the 5th percentile and ending with the 95th percentile). The figure illustrates the annual savings of these changes for Medicare.

DISCUSSION

A difference greater than 2-fold exists in expenditures for early stage bladder cancer care delivered between the highest and lowest intensity providers. Approximately 9% of this variation is attributable to physician factors. The size of this physician effect exceeded that attributable to all measurable patient characteristics and tumor stage and grade. We observed no measurable benefit associated with more intensive treatment for patients in terms of cancer-specific survival or in the avoidance of a major intervention. In fact, patients who received more intensive treatment were more likely to undergo subsequent radical cystectomy. If we reduced this potentially unwarranted variation and aligned clinical practice with that of physicians in the 25th percentile of treatment intensity, then per capita Medicare expenditures could be lowered by 19% in the first 2 years after diagnosis. Such a reduction would translate into an estimated annual cost savings of nearly $19 million to the Medicare program.

Although, on the surface, the provider contribution (9%) to treatment intensity variation that we observed may seem small, it is meaningful and, compared with other findings, relatively large. To provide some context, the size of this physician effect is 4 times greater than the corresponding effect for resource use at teaching hospitals,[25] 3 times greater than that for prescribing rates among general practitioners,[26] and 2 times greater than that in outpatient visits for diabetes care.[27] Sources of these between-provider differences in bladder cancer treatment intensity probably are multiple. We attempted to account for several physician factors (eg, provider case volume and year of medical school graduation) that demonstrably influence use[9]; however, their inclusion explained little of the physician effect.

One explanation for this persistent physician-attributable variation pertains to the lack of empiricism underlying current guidelines. In contrast to other chronic diseases like diabetes for which evidenced-based quality indicators exist to direct care,[28] consensus recommendations for early stage bladder cancer largely are limited to expert opinion or nonexperimental data, leaving providers with considerable "wiggle room" and, thereby, facilitating practice style variation. Alternatively, external forces that are not appreciable in the data may be fostering the observed variation. For example, the threat of medical liability may lead physicians to adopt assurance behavior, whereby they supply additional services of marginal or no medical value with the aim of deterring patients from filing malpractice claims.[29]

Our results must be viewed with several caveats. First, although we observed substantial physician-attributable variation, the majority of the variability in treatment intensity still resided at the patient level, and we were able to account for only 23% of these between-patient differences. Several yet unknown factors seem to influence the observed variability in treatment intensity. Although it is likely that patient preference and/or noncompliance contributes to some of this variability, other possible factors need to be explored. These factors may include the available supply of healthcare services (eg, the per capita number of urologists and medical oncologists for a given area or the number of endoscopy suites within a market) and local idiosyncrasies (ie, practices unique to a community or small group of physicians that a provider adopts).

Second, unmeasured patient differences between our physician quantiles might explain some of the practice variation that we observed. We addressed this limitation of observational data[30,31] using a well developed approach for measuring comorbidity[19] and clinical registry data linked with medical claims to ascertain cancer stage and grade and recurrent disease status—arguably the most important determinants of patient outcomes in the bladder cancer population.[32,33] Third, the SEER-Medicare linked data may not be generalizable to patients aged <65 years; however, nearly 75% of bladder cancer diagnoses occur among Medicare-aged patients.[34] So, our findings are relevant to the majority of the bladder cancer population. Finally, we chose to focus on the treatment intensity that a patient receives within the first 2 years of diagnosis. With more than 500,000 bladder cancer survivors in the United States (the majority of whom were diagnosed with early stage disease and still require some form of surveillance[35]), we probably are underestimating the magnitude of the physician effect on expenditures. Therefore, the decreases in total payments that we project after reducing physician-attributable variation are interpreted best as a floor, and the savings to the Medicare program are potentially much greater.

Having identified the provider level as a possible target, an examination of interventions to decrease practice variation in early stage bladder cancer care is warranted. Investigators have tried numerous strategies to alter physician behavior with variable succes.[36] The literature on colon polyp surveillance, an area in which considerable between-provider differences also exist,[37] illustrates the utility of a continuous quality-improvement approach.[38,39] These initiatives aim to be inclusive and involve all stakeholders in the process of system change

rather than identifying and punishing outliers.[40] With a focus on provider retraining, continuous quality-improvement programs can increase the uniformity of physician care while reducing costs.[38,39]

In conclusion, although much of the variation in initial treatment intensity is determined by patient-level factors, relatively little is accounted for by those factors that we commonly measure (eg, patient age, comorbid status, tumor grade and stage, and subsequent disease recurrence). Furthermore, physician practice style appears to contribute substantially to differences in treatment intensity absent a demonstrable benefit to the patient. With up to 33% of Medicare spending potentially wasted on unnecessary (or even harmful) care,[41] an intervention aimed at reducing between-provider differences in treatment intensity may improve the value of cancer care.

CONFLICT OF INTEREST DISCLOSURES

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