Locoregional prostate cancer treatment pattern variation in independent cancer centers: policy effect, patient preference, or physician incentive?

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ABSTRACT: Surveillance, Epidemiologic, and End Results (SEER) registry data abstracted from a priority 2 or higher reporting source from 2006 to 2008 were used to compare treatment patterns in 45–64-year old men diagnosed with locoregional prostate cancer (LRPC) across states with or without radiation therapy-directed certificate of need (CON) laws and across independent cancer centers (ICCs) compared to large multi-specialty groups (LMSGs). Adjusted treatment percentages for the five most common LRPC treatments (surgery, external beam radiation therapy (EBRT), combination brachytherapy with EBRT, brachytherapy, and observation) were compared using cross-sectional logistic regression between CON-unregulated and -regulated states and between LMSGs and ICCs. LRPC EBRT rates were no different across CON regions, but are increased in ICCs compared to LMSGs (37.00% vs. 13.23%, P < 0.001). Variation in LRPC treatment patterns by reporting source merits further scrutiny under the Affordable Care Act of 2010, considering the intent of incentivized accountable care organizations (ACOs) established by the Patient Protection and Affordable Care Act of 2010 (PPACA) and the implications of early descriptions of these new healthcare provider organizations on prostate cancer treatment patterns.

KEYWORDS: certificate of need, prostate cancer, Affordable Care Act, accountable care organizations, treatment patterns

Introduction
Locoregional prostate cancer (LRPC), the most common solid malignancy treated with healthcare intervention in the United States, has increasingly diverse initial treatment options with broad differences in initial treatment cost and was identified as an initial priority by the Institute of Medicine after 1.1 billion dollars from the American Recovery and Reinvestment Act of 2009 was invested to promote healthcare comparative effectiveness research (CER).

For initial treatment of LRPC, the National Comprehensive Cancer Network (NCCN) clinical practice guidelines recommend three broad categories of initial treatment: (1) radical prostatectomy, (2) radiation therapy, and (3) active surveillance. Radiation therapy can be delivered with external beam radiation therapy (EBRT), brachytherapy (brachy), or a combination of EBRT with a brachytherapy boost (combo). These interventions have been shown to have equivalent oncologic outcomes. Ideally, the delivered intervention is chosen through a shared-decision model to preserve the patient’s comfort and quality of life in consideration of clinical factors (eg, age, comorbidities, lifestyle preferences, or presenting prostate specific antigen (PSA)). However, in previous studies, non-clinical factors have been shown to be associated with variations in prostate cancer treatment. Among the nonclinical factors associated with variation in LRPC treatment, a patient’s state of residence remains significant when socioeconomic and urban–rural variables are controlled, suggesting that a state’s healthcare regulatory environment might contribute to variation in a physician-recommended prostate cancer treatment patterns.

Over the past decade, there has been increasing national interest in physician referral patterns leading to increased use of a new and expensive initial treatment for LRPC, intensity-modulated radiation therapy (IMRT). IMRT is a type of EBRT that has become widely adopted for LRPC treatment since Medicare reimbursement began in 2002. The central component of the new construction required for an IMRT center is the medical linear accelerator (LINAC) used to deliver the EBRT. A New England Journal of Medicine article found that 58% more EBRT is performed in free-standing radiation therapy centers owned by the referring non-radiation oncologist physicians in Florida. The overuse or misuse of new and expensive technology, such as IMRT in prostate cancer, by self-referring (SF) healthcare systems is the type of poor healthcare that state-run certificate of need (CON) programs are intended to prevent.

Integrated prostate cancer centers (IPCC) are urology groups that own LINACs and offer EBRT at free-standing
radiation therapy centers. *Wall Street Journal (WSJ)* in collaboration with the Center for Public Integrity (CPI) published an investigative article in 2010, initially reviewing a 5% sample of all Medicare billing in 37 IPCCs, but was unable to form an accurate picture of SF urology group practice patterns from the sample. *WSJ* subsequently obtained 100% of identified self-referral IPCC billing records from the US Department of Health and Human Services (DHHS) and analyzed groups of 10 or more physicians, finding that self-referral-based IPCCs prescribed more IMRT than the national average.\(^\text{13}\) In response to the *WSJ* article, a Surveillance, Epidemiologic, and End Results (SEER)-Medicare study was published exploring utilization trends in prostate cancer treatment over the same time period as our current study (2006–2008) showing no difference in prostate cancer treatment based on site of service, outpatient versus inpatient.\(^\text{14}\) These results were generated using the 5% Medicare sample that *WSJ* determined to be inadequate to characterize practice patterns of SF urology groups. Medicare billing records do not account for the referral source or ownership structure of the site of service delivering care.

In addition to the *WSJ* article, Congress requested that the Government Accountability Office (GAO) investigate Medicare self-referral trends among radiation oncology services. The GAO used publicly unavailable data from the Center for Medicare & Medicaid Services (CMS) to define SF prostate cancer IMRT by meeting minimum numbers of SF treatments. SF treatments were defined as any IMRT billed within one year of a prostate biopsy under the same taxpayer ID number. All remaining groups were considered non-self-referring (NSF). Furthermore, the GAO report used publicly available data to classify providers as limited-specialty groups.\(^\text{15}\) The subsequent GAO report (GAO report 13-525), titled “Higher Use of Costly Prostate Cancer Treatment by Providers Who Self-Refer Warrants Scrutiny,” showed IMRT use increased in SF groups from 2006 to 2010 relative to NSF groups, attributed the growth in SF IMRT services entirely to limited-specialty groups, and suggested “financial incentives were likely a major factor driving the increase of IMRT referrals among SF providers in limited-specialty groups.”\(^\text{15}\)

To increase patients’ awareness of providers’ financial interest in a particular prostate cancer treatment, the GAO report urged Congress to require providers who self-refer to disclose their financial interest in the service. The GAO also specifically recommended that providers indicate whether IMRT services are self-referred so that CMS can monitor the effects that self-referral has on costs and Medicare beneficiary treatment selection. The U.S. DHHS did not agree with the GAO recommendations in lieu of “other payment reforms” better suited to address over-utilization.\(^\text{15}\) Congress has not enacted the recommendations put forth by the GAO, but the DHHS response suggested that forthcoming policy or policy implementation, likely referring to the Patient Protection and Affordable Care Act of 2010 (PPACA), would address the misalignment of physician financial incentives leading to increases in SF IMRT in limited-specialty groups treating prostate cancer.

The GAO report is the most comprehensive published analysis of SF IMRT in the US, but the report is limited by the scope of the Congressional request. With variation in state healthcare policy, a commentary on differences in SF IMRT practices across states with different policy climates might have provided insight into policies associated with consistent IMRT treatment patterns across SF and NSF groups. Also, there is no comment on the contribution of limited-specialty groups to prostate cancer treatment patterns other than in SF IMRT. It is possible that limited-specialty groups are associated with the rise in not only SF IMRT but also NSF IMRT. In this article, we describe initial recommended treatment for LRPC using the publicly available SEER data from 2006 to 2008. We examined these patterns of care in two sets of two cohorts: states with versus states without CON programs, inclusive of medical LINACs, and large multi-specialty groups (LMSGs) versus independent cancer centers (ICCs). We hypothesized that states regulated by CON policy covering medical LINACs will have lower rates of EBRT and that ICCs will have higher rates of EBRT than LMSGs. We will discuss the results compared to the GAO report findings, the treatment patterns associated with CON-regulated versus CON unregulated states, and the results in context of two PPACA initiatives intended to align patient preference and physician incentives: the Patient-Centered Outcomes Research Institute (PCORI) and a policy device with political enthusiasm similar to CON programs in the 1960s and early 1970s, the incentivized accountable care organizations (ACOs).

**Materials and Methods**

The public access SEER data (2006–2008) were queried for cases of 45–64-year-old men diagnosed with localized prostate cancer (C61.9), abstracted from a priority 2 or higher reporting source.

Mode of initial treatment was coded into five categories based on initially recommended intervention: radical prostatectomy (surgery), EBRT, combination brachytherapy and EBRT (combo), brachytherapy (brachy), and no treatment (none) (Supplementary File 1). Surgery includes any prostate cancer-directed surgical procedure intended to remove the prostate without regard to technique. EBRT refers to any prostate-directed radiation teletherapy delivered to the prostate without regard to technique. Codes are not available in the SEER database to distinguish conventional 2D radiation therapy, 3D conformal radiotherapy, and IMRT. However, many articles have established IMRT as the dominant technique for delivering EBRT in prostate cancer treatment since 2006.\(^\text{14,16–19}\) Combo refers to any combination of EBRT and brachy delivered as a single course of treatment. Brachy refers to any brachytherapy delivered to the prostate, including low-dose rate (LDR) brachytherapy and high-dose...
rate (HDR) brachytherapy. None refers to all SEER prostate cancer cases with “no treatment” recorded as the first course of therapy. This category is defined as active surveillance or watchful waiting with other prostate cancer-directed therapy initiated within one year of the prostate cancer diagnosis.\textsuperscript{20} Forty-four patients who received both surgery and radiation, with radiation before surgery, intraoperative radiation, or unknown sequence, were excluded because these therapies are uncommon recommended initial prostate cancer therapies based on sequencing.

In order to evaluate a prostate cancer patient population not captured in previously published Medicare-based studies, the SEER database was queried for men aged 45–64 years old. By selecting a younger population than studied in the GAO report, relatively higher rates of surgery are expected because of patient preference.\textsuperscript{3}

By selecting cases limited to a priority 1 or priority 2 reporting source, cases abstracted from information in a stand-alone medical record kept at a lower priority reporting source (laboratory only, private medical practitioner not affiliated with a large practice, nursing home/hospice, autopsy only, death certificate only, and other outpatient unit/surgery centers) were not included in the initial query. Lower priority cases were excluded from the query to ensure that each case collected was seen in a setting with intent to treat, as opposed to found at autopsy or other nonclinical setting. SEER rates reporting sources based on the best available information.\textsuperscript{20} If information is not available in a priority 1 reporting source, the SEER-reported case is abstracted from a priority 2 reporting source. Reporting source is defined as the highest priority source of documents used to abstract the case. SEER reporting source identified type of provider, large HMO-affiliated reporting sources or multi-specialty groups (LMSGs) and ICCs. LMSGs include all SEER priority 1 reporting sources (HMO-affiliated and large multi-specialty physician groups with a comprehensive, unified medical record) with all group-affiliated hospital inpatient and outpatient facilities, clinics, free-standing laboratories, surgery centers, and oncology treatment centers. ICCs include all priority 2 reporting sources (radiation treatment facilities and medical oncology centers with a stand-alone medical record).

Age at diagnosis, race, and year of diagnosis were also reported.

Data were then divided into two cohorts, regulated and unregulated, based on radiation therapy CON policy identified through the National Conference of State Legislatures and the American Health Planning Association.\textsuperscript{21} All cases from a state with a CON policy, including coverage of LINACs, were assigned to the regulated cohort, and all cases from states without a CON policy or with a CON policy that does not include LINACs were assigned to the unregulated cohort.

Statistical analysis was conducted using SAS version 9.3. Descriptive statistics were reported for all variables. The unadjusted association of each demographic with CON policy was assessed using the chi-square test for categorical covariates and ANOVA for numerical covariates. EBRT use was modeled using logistic regression and generalized estimating equations to cluster on state in order to account for possible correlations within states. An exchangeable correlation structure was used. The regression model included CON policy, age, race, reporting source, and year of diagnosis. Since California made up the majority of the unregulated cohort, the models were repeated, excluding California for sensitivity analysis.

Additionally, adjusted treatment percentages for all five treatments were compared between unregulated and regulated states and between LMSGs and ICCs. Logistic regression was used to model each of the treatment outcomes separately, including CON policy, age, race, reporting source, and year of diagnosis, and clustering on state. Percentages were calculated at the mean of the covariates in the sample. In order to see if treatment patterns differed between unregulated and regulated states within each reporting source, the models were repeated with the addition of an interaction term between CON policy and reporting source. Differences in practice patterns between two states with a high number of ICC reported cases (New Jersey and Georgia) were also explored within each reporting source. Logistic regression models were used on the subgroup of New Jersey and Georgia cases. The models included state, reporting source, age, race, year of diagnosis, and an interaction between state and reporting source.

Results
The initial query returned 46,398 cases with complete treatment modality information, and these cases were equally distributed across the study period (14,983 cases in 2006, 16,076 cases in 2007, and 15,339 in 2008). A total of 13 states were represented in the SEER-reported cases. In all, 7 of the 13 states were in the regulated cohort (Alaska, Connecticut, Georgia, Hawaii, Iowa, Kentucky, and Michigan) and 5 were in the unregulated cohort (California, Louisiana, New Jersey, New Mexico, Utah, and Washington). The resulting cohorts included 13,645 regulated cases and 32,753 unregulated cases. There were 1079 cases from ICCs (491 in unregulated states and 588 in regulated states). There were 45,319 cases from LMSGs (32,262 in unregulated states and 13,057 cases in regulated states). Table 1 details the demographics across each cohort. While differences across each cohort were small in magnitude, they were statistically significant in race, age, reporting source, and year of diagnosis.

Multivariable analysis revealed no difference in recommendation rates of EBRT across the regulated and unregulated states (\( OR = 0.83, 95\% CI 0.52–1.53 \)) or year of diagnosis. Lower rates of EBRT were associated with younger age at diagnosis (\( P < 0.001 \)) and LMSG reporting source (\( OR = 0.26, 95\% CI 0.12–0.56 \)). Higher rates of EBRT were associated with non-white race (\( P < 0.001 \)). Complete results of the multivariate analysis for EBRT are shown in Table 2. California represented the majority of cases in the unregulated cohort.
Table 1. Demographics by CON policy.

<table>
<thead>
<tr>
<th>COVARIATE</th>
<th>LEVEL</th>
<th>TOTAL N = 46398 (%)</th>
<th>CON POLICY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>UNREGULATED N = 32753 (%)</td>
<td>REGULATED N = 13645 (%)</td>
</tr>
<tr>
<td>Age at Dx</td>
<td>Mean (Std)</td>
<td>57.97 (4.60)</td>
<td>58.03 (4.59)</td>
</tr>
<tr>
<td></td>
<td>45–49</td>
<td>2666 (5.7)</td>
<td>1828 (5.58)</td>
</tr>
<tr>
<td></td>
<td>50–54</td>
<td>7828 (16.9)</td>
<td>5434 (16.59)</td>
</tr>
<tr>
<td></td>
<td>55–59</td>
<td>15476 (33.4)</td>
<td>10897 (33.27)</td>
</tr>
<tr>
<td></td>
<td>60–64</td>
<td>20428 (44.0)</td>
<td>14594 (44.56)</td>
</tr>
<tr>
<td>Race</td>
<td>White</td>
<td>36259 (79.5)</td>
<td>26231 (81.42)</td>
</tr>
<tr>
<td></td>
<td>Black</td>
<td>7359 (16.1)</td>
<td>4494 (13.95)</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>1973 (4.3)</td>
<td>1491 (4.63)</td>
</tr>
<tr>
<td>Reporting source</td>
<td>Large Multi-Specialty Group (LMSG)</td>
<td>45319 (97.7)</td>
<td>32262 (98.5)</td>
</tr>
<tr>
<td></td>
<td>Independent Cancer Center (ICC)</td>
<td>1079 (2.3)</td>
<td>491 (1.5)</td>
</tr>
<tr>
<td>Year of diagnosis</td>
<td>2006</td>
<td>14983 (32.3)</td>
<td>10457 (31.93)</td>
</tr>
<tr>
<td></td>
<td>2007</td>
<td>16076 (34.6)</td>
<td>11377 (34.74)</td>
</tr>
<tr>
<td></td>
<td>2008</td>
<td>15339 (33.1)</td>
<td>10919 (33.34)</td>
</tr>
</tbody>
</table>

Notes: *The P-value is calculated by ANOVA for numerical covariates and chi-square test for categorical covariates.

Sensitivity analysis, excluding California, from the unregulated cohort showed similar results.

In addition to not finding significant differences in external beam radiotherapy rates in states with CON regulation on LINACs versus unregulated states (12.66% vs. 14.00%, P = 0.675), no differences in any of the treatment modalities were found between CON-regulated and -unregulated cohorts as detailed in Figure 1A. However, practice patterns differed between ICCs and LMSGs for all treatment modalities other than brachy as detailed in Figure 1B. All analyses revealed no difference in EBRT rates across the regulated and unregulated states in the total cohort, in LMSGs, or in ICCs (Figs. 1A and 2A and B). In ICCs, higher surgery rates were associated with unregulated states (14.17% vs. 5.35%, P < 0.001) (Fig. 2B).

In the total cohort, rates of combo and EBRT were higher in ICCs compared to LMSGs, while none and surgery rates were lower (Fig. 1A). Most of the ICC cases (56%) were...
from only two states, New Jersey (unregulated) and Georgia (regulated). In the unregulated states, 52.1% of the ICC cases were from New Jersey. In the regulated states, 58.8% of the ICC cases were from Georgia. Practice patterns were different in all modalities, except none between Georgia and New Jersey in LMSGs ($P < 0.001$, Fig. 2C) and in ICCs ($P < 0.001$, Fig. 2D). Brachy was associated with lower use in New Jersey LMSGs and higher use in New Jersey ICCs. Otherwise, lower use of Combo and higher use of EBRT and surgery were associated with New Jersey concordantly in LMSGs and ICCs. (Fig. 2B and C).

**Discussion**

The overall treatment patterns reported in this study are consistent with previously reported patterns for LRPC in a similar age group. This study reports overall lower rates of surgery, lower rates of EBRT (including IMRT), lower rates of brachy, and lower rates of no initial treatment (including active surveillance and watchful waiting) than the reported LRPC treatment patterns in the youngest cohort (66–69 years old) from 2009 in GAO report 13-525. Our algorithm for coding initial therapy categorized patients based on initial recommended treatment only, for example a prostatectomy patient who received adjuvant IMRT after prostatectomy based on surgical findings, such as a positive surgical margin, would be classified as *surgery* in our study and as both *radical prostatectomy* and *IMRT* in the GAO report, leading to higher relative rates of EBRT compared to surgery in the GAO report. Our study did not consider hormone therapy use. It is also possible that increased EBRT reflects LRPC treatment trends in 2009 compared to 2006–2008. Most likely, we think that the overall differences in LRPC practice patterns between the GAO LRPC practice patterns and our LRPC practice patterns are a function of physician recommendation and patient preference based on age differences in our patients and the GAO patients.

When considering all reported LRPC cases, CON programs are not associated with different treatment patterns.
at the state level. Our hypothesis assumed that a LINAC-specific CON program would affect LRPC practice patterns by limiting the ability of limited-specialty groups to construct ICCs in regulated states, as suggested by the *WSJ* article with a LINAC-specific CON program in only one of five states harboring a high number of IPCCs. Contrary to our assumption, a higher percentage of ICC cases were reported from regulated states compared to unregulated states (*P* < 0.001, Table 1).

With only 2.3% of reported cases from ICCs, the impact of prostate cancer treatment patterns from these sites of service on the national cost and quality of care might be presumed to be small or insignificant. However, ICCs have an increase in EBRT when compared to LMSGs (37.00% vs. 13.23%, *P* < 0.001), consistent with previously published increased use of EBRT in free-standing radiation therapy centers owned by the referring non-radiation oncologist physicians, GAO SF limited-specialty groups compared to SF LMSGs, and IPCCs when compared to non-self-referral radiation centers.12,13,15,22 It is possible that SEER IPCCs have a higher portion of self-referred patients, leading to the similar increase in the rate of EBRT in previously published studies of self-referral prostate cancer treatment centers.13,15,22 but the taxpayer ID numbers and Medicare billing records were not available for inclusion in our study, so SEER reporting sources could not be identified as SF by the GAO criteria. However, the GAO description of limited-specialty groups is consistent with the SEER description of ICCs, “facilities with a stand-alone medical record such as radiation treatment centers or medical oncology centers (hospital affiliated or independent).”20 GAO report 13-525 included only non-hospital-affiliated services, and the SEER reporting sources do not differentiate between hospital- and non-hospital-affiliated services. However, a previous publication showed similar rates of IMRT for prostate cancer across all sites of service over the same time period as our study,14 indicating that site of service is unlikely to be the reason for the association of higher rates of EBRT and ICCs.

ICC practice patterns might maximize a fee-for-service physician incentive for the specific procedure offered, or they might be shifting to current patterns of patient preference more quickly than the larger managed care organizations.23–26 In the analysis of SEER reporting source across New Jersey and Georgia, the portion of cases treated with surgery in the LMSGs is largely redistributed to EBRT in the model CON-unregulated state (New Jersey) and to combo in the model CON-regulated state (Georgia). If the patterns of care reflect patients treated according to fee-for-service incentives, owners of ICCs in New Jersey have a profit interest in EBRT and owners of ICCs in Georgia have a profit interest in combo therapy. New Jersey is the only SEER reporting state with a high number of urology-owned SF IPCCs identified in the *WSJ* article.13 In Georgia, there is a high-volume-independent radiation oncology group that uses a proprietary combination brachytherapy with EBRT to treat LRPC.27 Several studies have shown that physician recommendation influences patient decisions in prostate cancer and variation in treatment patterns is likely more indicative of the information patients receive than actual patient
preference. 28 Rather than representing a strict fee-for-service physician profit incentive, treatment patterns in ICCs, with less diversity of physician experience and fewer treatment options compared to LMSGs, possibly indicate that patients do not receive information or recommendations regarding prostate cancer treatment options available outside the ICC.

The PPACA contains provisions to encourage development of comprehensive clinical decision aids through the PCORI.29 However, in order to allow patients to choose a treatment based on comprehensive and high-quality information, the chosen treatment must be available in the healthcare coverage purchased by the patient. If a patient is referred (or physician self-referred) to a limited-specialty group, a patient’s preferred treatment might not be available because of the limited scope of practice or a group’s preference to offer only certain treatments. So, the PPACA encourages the availability of all appropriate courses of treatment through incentivizing ACOs, an integrated group of providers agreed to comprehensively care for a defined patient population (eg, LRPC patients). If ACOs are successful in integrating ICCs with a limited scope of LRPC treatments, quality and cost evaluations of the ACOs and ACO participants must include data regarding LRPC treatments available in the ACO, patient education regarding each treatment, and patient preference.

Conclusions

This is the first published study of LRPC treatment patterns, considering SEER reporting source. Among all reported prostate cancer cases, there were no differences in prostate cancer treatment patterns across CON regions, consistent with previous studies of CON and prostate cancer treatment patterns. However, without consideration of self-referral practices, we found that ICCs have an increase in EBRT (including IMRT) compared to LMSGs (37.00% vs. 13.23%, P < 0.001), similar to the increased rates of IMRT seen in the self-referral groups in GAO report 13-525. After reporting increases in IMRT for LRPC entirely because of SF limited-specialty groups (report 13-525), the GAO made policy recommendations that were not enacted by Congress because of DHHS suggestion that pending policy, likely referring to the PPACA of 2010, would suffice. The GAO report did not comment on the growth of IMRT services contribution in limited-specialty groups outside of self-referral systems. The GAO report also did not comment on the effect of state CON policy on IMRT treatment patterns. With the failure of CON to control healthcare costs and DHHS suggesting that the PPACA will address the issues of increasing IMRT use by self-referral limited-specialty groups identified in GAO report 13-525, variation in prostate cancer treatment patterns by reporting source must be monitored as participation in ACOs increases.

Author Contributions

Conceived and designed the experiments: AC, PR. Analyzed the data: AC, DN, AJ, PR. Wrote the first draft of the manuscript: AC, DN, AJ, PR. Contributed to the writing of the manuscript: AC, DN, AJ, PR. Agree with manuscript results and conclusions: AC, DN, AJ, PR. Jointly developed the structure and arguments for the paper: AC, PR. Made critical revisions and approved final version: AC, DN, AJ, PR. All authors reviewed and approved of the final manuscript.

Supplementary Data

Supplementary file 1. Initial Treatment Coding and relevant SEER Program Coding and Staging Manual Guidelines.

REFERENCES

1. Institute of Medicine (U.S.); Committee on Comparative Effective Research Prioritization; Institute of Medicine (U.S.). Initial National Priorities for Comparative Effectiveness Research. Washington, D.C.: Institute of Medicine of the National Academies; 2009.