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Author manuscript *Urology*. Author manuscript; available in PMC 2019 August 14.

Published in final edited form as: Urology. 2013 March ; 81(3): 540–546. doi:10.1016/j.urology.2012.09.058.

## Place of Residence and Primary Treatment of Prostate Cancer: Examining Trends in Rural and Nonrural Areas in Wisconsin

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## Abstract

**OBJECTIVE**—To determine whether rural residents were at a disadvantage compared with urban residents with regard to the receipt of curative therapy for prostate cancer.

**MATERIALS AND METHODS**—Using the Breast and Prostate Cancer Data Quality and Patterns of Care Study II, patients with prostate cancer who were diagnosed in 2004 were identified. Registrars reviewed the medical records of randomly selected patients with incident prostate cancer (n = 1906). The patients' residential address was geocoded and linked to the census tract from the 2000 U.S. Census. The place of residence was defined as rural or nonrural according to the census tract and rural-urban commuting area categorization. The distance from the residence to the nearest radiation oncology facility was calculated. The odds ratio and 95% confidence intervals associated with receipt of noncurative treatment was calculated from logistic regression models and adjusted for several potential confounders.

**RESULTS**—Of the incident patients, 39.1% lived in urban census tracts, 41.5% lived in mixed tracts, and 19.4% lived in rural tracts. Hormone-only or active surveillance was received by 15.4% of the patients. Relative to the urban patients, the odds ratio for noncurative treatment was 1.01 (95% confidence interval 0.59–1.74) for those living in mixed tracts and 0.96 (95% confidence interval 0.52–1.77) for those living in rural tracts. No association was found for noncurative treatment according to the Rural-Urban Commuting Area categorization. The linear trend was null between noncurative treatment and the distance to nearest radiation oncology facility (P .92).

**CONCLUSION**—The choice of curative treatment did not significantly depend on the patient's place of residence, suggesting a lack of geographic disparity for the primary treatment of prostate cancer.

Prostate cancer is the most common cancer among men in the United States. During 2011, an estimated 240,890 new cases of prostate cancer were diagnosed and 33,720 deaths

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Presented at the 2011 American Society of Clinical Oncology Annual Meeting, June 1-5, Chicago, Illinois.

occurred from the disease.<sup>1</sup> Most patients present with localized disease and therefore are curable.<sup>2</sup> Because of insufficient evidence, no consensus has been reached on the optimal treatment of localized prostate cancer, and curative treatment—radical prostatectomy, external beam radiotherapy and brachytherapy therapy—are considered to have equivalent therapeutic outcomes.<sup>3</sup> The choice between these options depends on a number of factors, including pretreatment risk classification; the patient's health status, knowledge, and preferences; the physician's preferences and skills; and the patient's socioeconomic status. <sup>4–6</sup> Available evidence suggests that noncurative treatments—in particular, active surveillance—might be important treatment considerations for some men diagnosed with localized disease,<sup>7,8</sup> depending on patient age, comorbidities, cancer stage, and other tumor characteristics.<sup>9</sup>

In the absence of strong scientific evidence to support decision making, studies have revealed large variations in the treatment of localized prostate cancer.<sup>10</sup> However, limited evidence is available on the effect of geography-where a patient lives-on treatment. particularly in North America. One hypothesis is that men living in rural areas have greater difficulty accessing care, such as radiation facilities, than their nonrural counterparts<sup>11</sup> and, thus, are less likely to receive curative therapy and more likely to receive noncurative treatment. The evidence that exists is inconsistent. A Virginia study found that neither the distance to the radiation facility nor the residence (rural or urban) affected receipt of surgery vs radiation for prostate cancer but that living in an urban area decreased the likelihood of receiving any curative treatment.<sup>12</sup> The same study found that the receipt of hormonal therapy (compared with surgery or radiation) was less common in men living farther away from the radiation facilities. A recent Georgia study showed that rural patients with prostate cancer were more likely to receive external beam radiotherapy than surgery.<sup>13</sup> A study in the Lake Superior region (including parts of Minnesota, Wisconsin, and Michigan) showed that rural patients with prostate cancer were at a disadvantage in terms of undergoing disease staging, initial management procedures, and participation in cancer clinical trials, but the study did not compare treatment.<sup>14</sup>

Understanding the variation in the treatment of prostate cancer by patient residence is vital, especially in the context of evidence that prostate cancer mortality is greater in rural areas of the United States.<sup>15</sup> Using a statewide, population-based sample of patients with prostate cancer, we explored the relationship between geography and primary treatment of locoregional prostate cancer in Wisconsin men. Wisconsin as a state has a relatively large rural population in which nearly one third of the population lives in rural areas.<sup>16</sup>

## MATERIAL AND METHODS

#### Patients

As a part of the Breast and Prostate Cancer Data Quality and Patterns of Care Study II (a collaboration of the Centers for Disease Control and Prevention, the National Program of Cancer Registries, and cancer registries from 7 U.S. states).<sup>17</sup> Patients with prostate cancer diagnosed in 2004 with pathologically confirmed disease were identified through the Wisconsin Cancer Reporting System, a state statutory-mandated cancer registry. Patients previously diagnosed with cancer or treated at Veterans Affairs hospitals and cases reported

on autopsy or by death certificate only were ineligible for the present study. Of 3220 eligible subjects, 1169 patients were randomly selected and their medical records abstracted. Cases of invasive prostate cancer were randomly selected across strata defined by race/ethnicity and state-specific factors such as patient volume of the facility. Minorities were oversampled to increase the statistical power to compare factors by race and ethnicity. The institutional review board at the University of Wisconsin-Madison approved the present study.

#### **Data Collection**

Certified, trained cancer registrars reviewed and abstracted the inpatient and outpatient records from >60 medical facilities across Wisconsin in 2008 and 2009. Patient comorbidities (using the Adult Comorbidity Evaluation-27,<sup>18</sup> an index with a wide range of coexisting conditions relevant to cancer therapy choice and outcome), demographic data, diagnostics, tumor characteristics, primary treatment type, and follow-up data for 1 year starting from diagnosis were abstracted using the study protocol. Registrars entered the data into Abstract Plus (a comprehensive, standardized software program provided by the Centers for Disease Control and Prevention) while on-site at the medical facility.

#### **Statistical Analysis**

Patients with prostate cancer with a diagnosis of metastatic disease (n = 49) or with an unknown disease stage (n = 12) were excluded from the present analysis. An additional 12 patients with unknown treatment plans were also excluded. Thus, of the 1169 patients with abstracted data, 1096 were included in the final analysis. Curative treatment was defined as prostatectomy, external beam radiotherapy, brachytherapy, or cryotherapy as the first course of treatment of prostate cancer. Noncurative treatment was defined as receiving hormonal therapy only or active surveillance or watchful waiting. For the purposes of the present analysis, active surveillance and watchful waiting were considered equivalent and both categorized as active surveillance.

Several geographic variables were constructed according to the patient's residence at diagnosis. First, the residential addresses were geocoded and linked to the census tracts (2000 U.S. Census), and each address was assigned a value for the percentage of census tract classified as urban. Second, a code for the rural-urban commuting area (RUCA) was assigned to each patient by census tract. RUCA is a classification scheme developed by the Office of Rural Health Policy that characterizes each census tract according to the proportion of urbanized population from the U.S. Census and information on commuting flow.<sup>19</sup> Each patient's residence was further categorized as either urban focused, large rural/town focused, small rural town focused, or isolated small rural town focused, using the RUCA 4-tiered taxonomy.<sup>20</sup> Third, the radiation oncology facility locations in and bordering Wisconsin were geocoded. The distance from the patient's residence to the nearest radiation oncology facility was calculated using the North American Association of Central Cancer Registries' great circle distance calculator.<sup>21</sup>

A secondary analysis assessed the association of receiving radiotherapy vs surgery for patients with prostate cancer according to the urban-rural residential classification. Using multivariate logistic regression models, we calculated the odds ratios and 95% confidence

intervals to assess the association of noncurative treatment with the geographic variables. The percentage of census tracts classified as urban and the distance from the residence to the nearest radiation oncology facility were analyzed categorically and continuously in separate models. The RUCA classification was assessed categorically. The models were adjusted for covariates chosen a priori: age at diagnosis (20–54, 55–59, 60–64, 65–69, 70–74, and 75 years), race/ethnicity (Hispanic, non-Hispanic white, non-Hispanic black, non-Hispanic Asian or Pacific Islander, non-Hispanic Native American, or Alaskan Native), Adult Comorbidity Evaluation-27 overall comorbidity score (none, mild, moderate, severe, unknown), Gleason score (<5, 6, 7, 8, test not done, unknown), insurance category (no insurance, private insurance, Medicaid, Medicare, or other public insurance, unknown), disease stage (localized, regional), and prediagnosis prostate-specific antigen level (<10 vs 10 ng/mL). We accounted for the sampling design using sampling weights in logistic regression models and in the calculation of percentages. P trends represent ordinal terms in regression models. All analyses were performed using SAS, version 9.1, software (SAS Institute, Cary, NC).

#### Sensitivity Analysis

A sensitivity analysis was conducted using only patients with prostate cancer with localized disease (n = 877). The results did not change substantially from the results of the analysis of localized and regional disease; therefore, the sensitivity analysis results were not shown.

## RESULTS

Of the 1096 patients with locoregional prostate cancer, 55.3% elected prostatectomy (including cryotherapy, representing 2% of total cases), 29.3% radiotherapy (defined as either external beam radiotherapy or brachy-therapy), 5.4% hormonal therapy only, and 10.0% active surveillance. The clinical, socioeconomic, and geographic characteristics of the men in each treatment group are listed in Table 1. In general, men undergoing definitive therapy were younger, had fewer health problems, and had a later stage of prostate cancer than patients receiving noncurative therapy (hormonal therapy alone or active surveillance). With regard to definitive therapy, no difference was noted between the receipt of radiotherapy vs surgery relative to patients living in urban areas (odds ratio 1.00, 95% confidence interval 0.63–1.61 for urban-rural mixed cases; odds ratio 0.98, 95% confidence interval 0.53–1.82 for rural cases).

According to the census tract data, 39.1% of the patients with prostate cancer lived in an urban setting, 41.5% in a mixed urban-rural environment, and 19.4% in a rural setting. The results of the multivariate-adjusted model revealed little difference in the receipt of therapy by patient residence. Relative to urban patients, the odds ratio for noncurative treatment was 1.01 (95% confidence interval 0.59–1.74) for mixed cases and 0.96 (95% confidence interval 0.52–1.77) for rural cases (Table 2). Using the percentage of those living in an urban area as a continuous variables was not significant (P .84).

Using the RUCA classifications, 70.2% of the patients lived in urban-focused areas, 9.9% lived in large rural/town-focused areas, 8.8% in small rural town-focused area, and 11.0% in

isolated small rural town-focused areas. The odds ratios for noncurative treatment by RUCA categories were not significant (Table 2).

The median distance from the patient's residence to the nearest radiation oncology facility was 4.7 miles (mean 10.8, range 0.1–66.1). The distance from the residence to the nearest radiation oncology facility was not significantly associated with noncurative treatment, either continuously (P = .92) or categorically (Table 2).

## COMMENT

Men diagnosed with localized prostate cancer face a difficult dilemma—which definitive therapy, if any, to choose. The lack of randomized prospective data comparing treatment modalities has limited the ability to use evidence-based medicine as a decision making tool.<sup>3</sup> Thus, considerable variation exists in the primary treatment of prostate cancer. One relatively unexplored area of interest that might further explain the variation in primary treatment of prostate cancer is the effect of geography within a given region, specifically the effect of a rural vs nonrural place of residence.

Previously, research has recognized differences in health outcomes depending on geography. Extensive evidence has shown that living far from a population center creates unique health, and healthcare, needs.<sup>22</sup> Studies have documented that rural patients with cancer have poorer outcomes, a lower quality of cancer care, and limited access to cancer support services and clinical trials.<sup>23,24</sup> In Wisconsin, where the present study was conducted, a recent study found that rural patients with cancer in the state had lower health literacy and lower satisfaction with their cancer care than residents from nonrural counties.<sup>25</sup>

Therefore, it is conceivable that rural patients with prostate cancer might have limited access to certain medical technologies, such as availability to radiation oncology facilities. We hypothesized that compared with urban residents, rural residents would be less likely to undergo definitive therapy. This would then have the potential consequence of more rural patients receiving noncurative treatment such as primary androgen deprivation therapy or active surveillance. For example, because of advanced age or deleterious comorbidities, a rural patients with prostate cancer might not be surgical candidates and therefore would otherwise be referred for definitive radiotherapy, a therapy requiring daily treatment sessions for 8 weeks. However, we hypothesized that if no radiation facilities were nearby, a patient would, by default, receive noncurative treatment. However, our data showed quite the opposite—rural patients were just as likely to receive radiotherapy as urban residents, presumably because of ubiquitous radiation facilities.

Previous research has revealed a large amount of regional variation in the frequency of radical prostatectomy<sup>7,10,26</sup> and radiotherapy<sup>27</sup> within the United States. In our cohort, radical prostatectomy was the most frequent primary treatment (53%) and did not differ according to the patient's place of residence. In contrast, the 1999 Dartmouth Atlas of Health Care noted that the lowest prostatectomy rates in Wisconsin were in the major urban areas, including Madison and Milwaukee (1.9/1000 and 1.5/1000, respectively).<sup>26</sup> An additional 28% of patients in the present study underwent primary radiotherapy, significantly

less than that (57%) reported by Lai et al<sup>27</sup> for Iowa, a neighboring state, using an analysis of the Surveillance, Epidemiology, and End Results data.

One potential explanation for the lack of geographic disparities seen in our study might relate to the characteristics unique to Wisconsin. Wisconsin is a relatively homogenous state in which racial minority populations are relatively small and geographically clustered. These similarities might have then created a culture of similar beliefs, attitudes, and biases toward medical interventions, leading to little variation. Alternatively, perhaps Wisconsin has developed an efficient system of healthcare delivery that serves the needs of its residents, regardless of geography. The Wisconsin healthcare systems and hospitals provide access to essentially the entire state. Thus, 95% of the population reside within 15 miles of a hospital, <sup>28</sup> and Wisconsin has one of the lowest uninsured rates in the United States.<sup>29</sup> No remote or frontier-designated areas are present in the state. These facts support the findings that the access and quality of prostate cancer care in rural areas is comparable to that of urban areas. Also, when primary care providers identify abnormalities attributable to prostate cancer, the standards of care available to these patients are similar in rural and urban areas.

Others have demonstrated a significant variation in the treatment of localized prostate cancer among regions within the United States.<sup>10</sup> Our study is the first to analyze the effect of a patient's place of residence on treatment variations within a region, with the inclusion of noncurative treatment options such as primary androgen deprivation therapy and active surveillance. In addition, our study is the first to analyze the effect of geography on any medical condition within the state of Wisconsin.

An important caveat to our analysis should be noted—categorizing geographic regions as "urban" or "rural" can be described as challenging, elusive, and unstandardized.<sup>19</sup> For the purposes of the present study, we used 2 different definitions for urban and rural, using the census tract and RUCA codes, both well-accepted methods. These definitions are the same used by the Offices of Rural Health in determining grant eligibility for rural funding. Others have concluded that use of census tract data is appropriate for analyzing disparities in prostate cancer outcomes.<sup>30</sup> Other potential limitations to the present analysis included the lack of generalizability, no information regarding tobacco usage (which might influence eligibility for surgery), and no patient-level socioeconomic data. In addition, we did not have patient-level information on decision making nor physician level preferences.

Our analysis had several strengths. The Breast and Prostate Cancer Data Quality and Patterns of Care Study II data have extensive details regarding comorbidities and health history, because these were verified by professional cancer registrars who had access to each patient's medical charts. Therefore, we were able to accurately account and adjust for these patient-specific factors to the extent that the charts were complete. In addition, incident cases were randomly chosen from the state's cancer registry, and minorities were oversampled. To perform the analysis, we had access to the latitude and longitude of each patient's residence, allowing for accurate geocoding. Finally, we used >1 definition of rural and nonrural, all of which consistently showed the same lack of an association between the choice of therapy and residential location, increasing confidence in our findings.

## CONCLUSION

Our data did not demonstrate that rural patients with prostate cancer in Wisconsin are less likely to receive curative therapy. These results suggest that there is access to available treatment modalities within rural Wisconsin communities. The lack of variation with respect to geography suggests that the national trends in practice-level variation in the management of prostate cancer result from other factors such as physician training, payer mix, reimbursement patterns, culture, and patient preferences. Future research should examine other regions of the country with rural populations or an analysis of the difference in quality of care between different geographic areas, such has been investigated for other cancers.

## Acknowledgments.

To Julie McGregor, Jeanne Strickland, and Kathy Peck, University of Wisconsin Carbone Cancer Center, and to Nancy Sonnleitner and Laura Stephenson and the project abstractors and Shaun Golding at the Wisconsin Office of Rural Health, with thanks.

**Funding Support:** This project was funded by the American Cancer Society Institutional Research Grant disparities award to the University of Wisconsin Carbone Cancer Center (grant IRG-58-011-48). Data collection was funded by the Centers for Disease Control as a part of the Breast and Prostate Cancer Data Quality and Patterns of Care Study and WICARE (grant U01 DP0000261 to primary investigator J. F. W.).

Financial Disclosure: The authors declare that they have no relevant financial interests.

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Table 1.

General characteristics of 1096 prostate cancer cases by treatment type, Wisconsin 2004

		Pros	state Cancer	Treatment	*(%)
	Patients (n)	Surgery (n = 585)	$\begin{array}{c} RT \\ (n=310) \end{array}$	$\begin{array}{c} HT \\ (n=84) \end{array}$	Active Surveillance (n = 117)
Overall	1096	55.3	29.3	5.4	10.0
Age at diagnosis (y) $\dot{\tau}$					
20–54	144 (12.5)	85.7	8.2	1.2	5.0
55–59	171 (15.8)	80.8	10.9	0.5	7.8
60–64	209 (19.6)	68.9	24.9	1.1	5.1
65–69	211 (19.7)	54.9	37.3	1.9	5.9
70–74	181 (17.0)	35.5	50.8	3.8	6.6
75	180 (15.1)	8.5	37.3	26.1	28.2
Race/ethnicity					
Non-Hispanic white	924 (92.6)	55.8	29.0	5.3	10.0
Non-Hispanic black	131 (5.8)	48.1	35.9	6.9	9.2
Other	41 (1.6)	55.9	24.6	6.6	12.9
${\rm Comorbidities} ^{\not t}$					
None	410 (39.8)	65.9	20.2	3.3	10.6
Mild	528 (47.8)	52.3	34.2	5.3	8.2
Moderate	111 (8.6)	38.6	40.6	10.1	10.7
Severe	24 (2.1)	14.9	48.9	19.9	16.3
Unknown	23 (1.6)	24.9	23.7	16.0	35.3
Gleason score					
5	33 (3.7)	60.7	16.2	0.0	23.1
6	491 (45.2)	50.9	35.7	2.7	10.7
7	425 (39.0)	65.0	20.3	5.8	8.9
8	133 (11.0)	40.6	37.2	17.0	5.2
Not done/unknown	14 (1.1)	25.8	50.3	3.3	20.6
Insurance coverage $\dot{\tau}$					
Private	749 (68.4)	63.8	23.8	3.8	8.5

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		Pros	state Cancer	Treatment	.(%)
	Patients (n)	Surgery (n = 585)	$\begin{array}{c} RT \\ (n=310) \end{array}$	$\begin{array}{l} HT\\ (n=84) \end{array}$	Active Surveillance (n = 117)
Medicaid	34 (2.3)	24.8	50.2	10.6	14.4
Medicare and other public	281 (27.2)	38.6	41.1	8.2	12.1
None/unknown	32 (2.1)	28.1	31.4	16.1	24.3
Disease stage $^{\not{ au}}$					
Localized	877 (79.8)	46.3	35.6	5.9	12.1
Regional	219 (20.2)	90.9	4.5	3.3	1.4
Prediagnosis PSA (ng/mL) $^{\dagger\prime}$					
<10	770 (73.1)	60.0	29.9	2.4	7.8
10	307 (25.1)	44.2	28.1	14.2	13.5
Unknown	19 (1.8)	20.8	23.3	4.9	51.0
Urban/rural classification					
Urban (100% urban)	487 (39.1)	52.1	31.7	4.9	11.3
90%–99% Urban	114 (11.9)	58.5	29.8	5.6	6.1
50%–89% Urban	183 (18.2)	59.1	25.7	7.1	8.2
1%–49% Urban	112 (11.4)	58.4	27.8	5.5	8.3
Rural (100% rural)	200 (19.4)	54.6	28.5	4.5	12.4
HT, hormonal therapy; PSA, pr	ostate-specific ar	ntigen, RT, radiotheraj	py.		

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 $\stackrel{f}{\not\sim}$  Overall chi-square test of general characteristic by curative/noncurative treatment with P < 05.

\* Row percentages adjusted for sample weighting.

		Prostate Cance	er Treatment <sup>*</sup> (%)	- -			
Residential Location	Patients (n)	Surgery or RT (n = 895)	HT or Active Surveillance (n = 201)	Crude OR	95% CI	Multivariate-adjusted $\mathbf{OR}^{\dagger}$	95% CI <sup>†</sup>
Urban/rural classification							
Urban (100% urban)	487	83.8	16.2	1 (Reference)		1 (Reference)	
Urban-rural mix	409	86.1	13.9	0.83	0.55 - 1.25	1.01	0.59 - 1.74
Rural (100% rural)	200	83.1	16.9	1.06	0.66 - 1.70	0.96	0.52 - 1.77
Pvalue				.91		.84	
Ptrend				.37		.97	
RUCA							
Urban focused	793	84.9	15.1	1(Reference)		1 (Reference)	
Large rural/town ("micropolitan") focused	06	89.3	10.7	0.68	0.33 - 1.40	0.93	0.37 - 2.31
Small rural town focused	95	84.1	15.9	1.06	0.59 - 1.92	0.95	0.49 - 1.85
Isolated small rural town focused	118	79.2	20.8	1.48	0.87-2.50	1.30	0.69–2.44
Ptrend				.25		.56	
Distance from patient residence to nearest radiation oncology facility (miles)							
<2	265	81.3	18.7	1 (Reference)		1 (Reference)	
2-4.9	310	86.7	13.3	0.66	0.40 - 1.10	0.88	0.45 - 1.70
5-14.9	239	87.1	12.9	0.65	0.37 - 1.12	0.83	0.41 - 1.68
15-29.9	168	79.7	20.3	1.10	0.64 - 1.89	1.12	0.54 - 2.33
30	114	88.0	12.0	0.59	0.30 - 1.15	0.67	0.29 - 1.54
Pvalue				.96		.92	
Ptrend				.61		.71	
CI, confidence interval; OR, odds ratio; RUCA, rural-urban con * Row nercentages adiusted for sample weighting	nmuting area; oth	r abbreviations as in ]	lable 1.				
toon percentages adjusted for sumply invigations.							

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<sup>7</sup>/Adjusted for patient's age, race/ethnicity, comorbidity score, Gleason score, insurance coverage, disease stage, and prediagnosis prostate-specific antigen value.

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Table 2.