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ORIGINAL RESEARCH

Distance from cancer facility as a barrier to timely treatment among patients with non-metastatic cervical cancer

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Abstract

Globally, cervical cancer remains the leading cause of cancer death in women in many countries and in the United States it is the second most common cause of cancer death in younger women age 20–39 years. Distance from treatment facility may contribute to treatment delay and ultimately, disease outcomes. We hypothesize that greater distance from the treating facility results in a treatment delay among women with non-metastatic cervical cancer. Data for 36,986 subjects with non-metastatic cervical cancer treated with definitive radiation or surgery between 2004 and 2015 were selected from the National Cancer Database. Subjects were excluded if they had missing information, variant histology, treatment >180 days from diagnosis, or lived >1000 miles from their facility. Univariate comparisons were performed using chi-square and analysis of variance. Multivariable linear regression was used to investigate the effect of distance quartile on time to treatment while adjusting for significant patient and disease characteristics. Results: The mean age was 49.5 years, 16.2% of women were black, 14.2% were Hispanic, 48.7% had private insurance, 98.4% lived in urban/metro counties, and 56.1% received surgery versus radiation as initial treatment. Multivariable analysis identified a treatment delay of 1.1 days for distance quartile 2 ($p = 0.008$), 2.0 days for quartile 3 ($p < 0.001$), and 4.0 days for quartile 4 ($p < 0.001$) compared to women in the closest quartile. Other patient and disease characteristics were significantly associated with treatment delay. Interestingly, women living in rural counties were treated over 8.5 days earlier than those from the most populous metropolitan counties ($p < 0.001$). In conclusion: Greater distance from treatment facility resulted in a statistically significant delay in treatment.

Keywords

Cervical cancer; Treatment disparity; Time to treat; Distance; National cancer database; Urbanization

1. Introduction

The incidence of cervical cancer has been declining in developed countries due to screening and vaccination efforts, but in 2020 cervical cancer remained a common cause of cancer mortality in women and was the leading cause of female cancer death in 36 countries around the world [1, 2]. Despite screening and vaccination, it is estimated that in 2022 in the United States about 14,100 people were diagnosed and over 4000 died of cervical cancer [1]. While the overall mortality from cervical cancer has improved in the past century, it is still the second most common cause of cancer death among women aged 20 to 39 years in the United States [1].

Multiple recent studies in the United States and globally have evaluated the travel burden for patients with cervical cancer, yet the effect of distance from treating facility on outcomes for patients with cervical cancer remains poorly understood [3, 4]. Greater distance to cancer facility has been correlated with decreased receipt of standard of care treatment, stage at diagnosis, and has been shown to impact the primary treatment modality among cancer patients [5–8]. Similarly, cervical cancer patients who traveled farther to their academic center had decreased survival [9]. One possible mechanism for this detrimental effect of distance is a delay in initiating definitive treatment.

Delays in curative treatment can be experienced by patients with cervical cancer for a variety of reasons: Pregnancy, fertility preservation, as well as various psycho-social factors [10–13]. At a population level, patient age, stage at diagnosis, and ethnicity have been associated with longer wait times before initiating treatment [11–13]. While studies are mixed regarding the actual impact of treatment delays on oncologic outcomes there is evidence that longer delay can be associated with worse outcomes [14, 15].

The objective of this study is to investigate the effect of distance from treatment facility on the time from diagnosis to the initiation of treatment in persons with non-metastatic cervical cancer.

2. Methods

2.1 Source of data

Data from the National Cancer Database (NCDB), the largest cancer registry in the United States, were used and institutional review board approval was officially waved due to the nature of the data. The NCDB captures medical and disease-specific information, patient-level demographic information, and information about the reporting facility. Clinical stage is reported in the NCDB using the American Joint Committee on Cancer staging manual appropriate for the year of diagnosis for each subject. The database details the first course of treatment and reports the time from diagnosis to initiation of treatment (overall, surgery, radiation, chemotherapy). Distance, education, income and urbanization are based on residential address (zip codes). Deidentified demographic data available from the database include age, sex, race, ethnicity, insurance status, and Charlson/Deyo Comorbidity Score.

2.2 Patient cohort

We included women with clinical stage IA–IVA cervical cancer diagnosed between 2004 and 2015 (N = 70,855). Participants were excluded if they did not receive local therapy (N = 12,114), were treated with palliative intent (N = 1313), had missing demographic or patient information (N = 6490), variant histology (N = 2179), received treatment at a site other than the reporting facility or had their case reported by multiple facilities (N = 11,417), started treatment >180 days after diagnosis (N = 276), initiated surgery and radiation on the same day (N = 18), and lived greater than 1000 miles from the treatment facility (N = 62).

Distance from treatment facility is reported in the database as the point to point distance from facility street address to the centroid of the participants' zip code of residence [16]. Women were stratified into distance quartiles with a distance of 5.0, 11.2 and 29.4 miles representing the 25th, 50th and 75th percentiles respectively. As a sensitivity analysis, distance was also examined as a continuous variable.

2.3 Statistical analysis

Descriptive statistics were used to report baseline patient characteristics and analysis of variance and chi-square were used to report differences between distance groups. For differences in time from diagnosis to treatment by categorical distance from treatment facility homogeneity of variances was violated using Levene's Test of Homogeneity of Variance, so a Welch's analysis of variance and Games-Howell *post hoc* analysis were used. Variables were included in the multivariable model if they were significant to $p < 0.1$ on univariable analysis or had previously been associated with treatment disparity in cervical cancer [17, 18]. A multivariable linear regression model was created to investigate differences in time from diagnosis to treatment by categorical distance from facility while adjusting for age, insurance status, race and ethnicity, income quartile and high school graduation rate of zip code of residence, urbanization, Charlson Comorbidity Score, year of diagnosis, stage of disease, and initial treatment modality. Facility type was not included in the multivariable model since this information is censored for persons younger than 40 years (27.5% of the cohort), eliminating a large and important cohort of cervical cancer patients.

Sensitivity analysis was performed with distance as an interval variable from 0 to 1000 miles. In our cohort 23.6% of women (N = 8715) reportedly received treatment on the same day as diagnosis, indicating that their diagnosis was captured at surgical resection or initiation of radiation therapy. To investigate the effect of these women on our study, an additional multivariable linear regression was performed with these women excluded as sensitivity analysis.

All statistics were performed using SPSS Statistics 25 (IBM Corporation, Armonk, NY, USA). For all statistical analyses, 2-sided p values were used with level < 0.05 considered statistically significant.

3. Results

A total of 36,986 subjects were included with a median age at diagnosis of 48 years and most subjects were without comorbid conditions (Charlson score of 0 in 86.4%; Table 1). The cohort was ethnically diverse with 16.2% of the cohort identifying as Black and 14.2% Hispanic. Participants lived in predominantly metropolitan counties (84.0%) with only 1.6% of patients living in rural counties. Most were insured (48.7% private, 22.9% Medicaid, 17.1% Medicare) and surgery was the initial treatment modality in 56.1% of participants.

On univariate analysis distance quartiles varied significantly by age (mean age 51.1, 49.9, 48.6 and 48.4 years for distance quartiles 1–4 respectively; $p < 0.001$; Table 1), racial diversity (52.5% white in quartile 1 compared to 77.4% white in quartile 4; $p < 0.001$), Charlson Comorbidity Scores (84.8% score zero in quartile 1, 87.3% in quartile 4; $p < 0.001$), urbanization of residence (98.2% in quartile 1 compared to 49.4% in quartile 4; $p < 0.001$), and initial treatment modality (48.3%, 45.4%, 41.9% and 39.9% received radiation first in quartiles 1–4 respectively; $p < 0.001$). Insurance status, income quartile, education, facility type, and clinical stage were also unequally distributed by distance quartile ($p < 0.001$ for all comparisons).

The mean time to treatment for the entire cohort was 30.6 days with standard deviation of 29.8 days. Mean time to treatment of 30.7, 31.1, 30.1 and 30.4 days was noted for distance quartiles 1–4 respectively and this was not statistically significant on univariate analysis ($p = 0.111$). *Post hoc* pairwise analysis confirmed that time to treatment did not significantly differ between any two distance groups.

TABLE 1. Patient characteristics overall and between distance groups.

Characteristics	Total	Distance Quartile 1 (0–5.0 miles) N = 9368	Distance Quartile 2 (5.1–11.2 miles) N = 9143	Distance Quartile 3 (11.3–29.4 miles) N = 9251	Distance Quartile 4 (≥29.5 miles) N = 9224	
	n (%)	n (%)	n (%)	n (%)	n (%)	*p*
Time to Treatment mean (d)	30.6	30.7	31.1	30.1	30.4	0.111
Age mean (yr)	49.5	51.1	49.9	48.6	48.4	<0.001
Race/Ethnicity						
White	23,766 (64.3)	4920 (52.5)	5102 (55.8)	6606 (71.4)	7138 (77.4)	
Black	5997 (16.2)	2218 (23.7)	1790 (19.6)	1007 (10.9)	982 (10.6)	<0.001
Hispanic	5259 (14.2)	1646 (17.6)	1665 (18.2)	1177 (12.7)	771 (8.4)	
Other	1964 (5.3)	584 (6.2)	586 (6.4)	461 (5.0)	333 (3.6)	
Charlson Comorbidity Score						
0	31,966 (86.4)	7942 (84.8)	7855 (85.9)	8115 (87.7)	8054 (87.3)	
1	4224 (11.4)	1170 (12.5)	1085 (11.9)	966 (10.4)	1003 (10.9)	<0.001
≥2	796 (2.2)	256 (2.7)	203 (2.2)	170 (1.8)	167 (1.8)	
Urbanization						
Metro (population >1 million)	20,359 (55.0)	6353 (67.8)	6675 (73.0)	5645 (61.0)	1686 (18.3)	
Metro (population 250,000 to 1 million)	7588 (20.5)	2146 (22.9)	1948 (21.3)	1985 (21.5)	1509 (16.4)	
Metro (population <250,000)	3109 (8.4)	706 (7.5)	399 (4.4)	652 (7.0)	1352 (14.7)	
Urban (population ≥20,000, adjacent to metro)	1691 (4.6)	82 (0.9)	64 (0.7)	352 (3.8)	1193 (12.9)	
Urban (population ≥20,000, not adjacent to metro)	515 (1.4)	56 (0.6)	29 (0.3)	44 (0.5)	386 (4.2)	<0.001
Urban (population 2500 to 19,999, adjacent to metro)	2108 (5.7)	14 (0.1)	13 (0.1)	434 (4.7)	1647 (17.9)	
Urban (population 2500 to 19,999, not adjacent to metro)	1027 (2.8)	10 (0.1)	10 (0.1)	76 (0.8)	931 (10.1)	
Rural (completely rural or <2500 urban population, adjacent to metro)	266 (0.7)	1 (0)	4 (0)	50 (0.5)	211 (2.3)	
Rural (completely rural or <2500 urban population, not adjacent to metro)	323 (0.9)	0 (0)	1 (0)	13 (0.1)	309 (3.3)	

TABLE 1. Continued.

Characteristics	Total	Distance Quartile 1 (0–5.0 miles) N = 9368	Distance Quartile 2 (5.1–11.2 miles) N = 9143	Distance Quartile 3 (11.3–29.4 miles) N = 9251	Distance Quartile 4 (≥29.5 miles) N = 9224	
	n (%)	n (%)	n (%)	n (%)	n (%)	*p*
Insurance Status						
Not Insured	3678 (9.9)	965 (10.3)	1017 (11.1)	938 (10.1)	758 (8.2)	
Private Insurance/Managed Care	18,018 (48.7)	3997 (42.7)	4469 (48.9)	4919 (53.2)	4633 (50.2)	
Medicaid	8462 (22.9)	2431 (26.0)	2029 (22.2)	1844 (19.9)	2158 (23.4)	<0.001
Medicare	6340 (17.1)	1882 (20.1)	1513 (16.5)	1420 (15.3)	1525 (16.5)	
Other Government	488 (1.3)	93 (1.0)	115 (1.3)	130 (1.4)	150 (1.6)	
Income (Zip Code)						
Quartile 1 (lowest)	9240 (25.0)	3224 (34.4)	1889 (20.7)	1126 (12.2)	3001 (32.5)	
Quartile 2	9255 (25.0)	2123 (22.7)	2054 (22.5)	1940 (21.0)	3138 (34.0)	<0.001
Quartile 3	9348 (25.3)	2064 (22.0)	2469 (27.0)	2810 (30.4)	2005 (21.7)	
Quartile 4 (highest)	9143 (24.7)	1957 (20.9)	2731 (29.9)	3375 (36.5)	1080 (11.7)	
Education (% without high school diploma by zip code)						
21% or more	9776 (26.4)	3097 (33.1)	2280 (24.9)	1736 (18.8)	2663 (28.9)	
13%–20.9%	10,595 (28.6)	2566 (27.4)	2422 (26.5)	2441 (26.4)	3166 (34.3)	<0.001
7%–12.9%	10,493 (28.4)	2318 (24.7)	2621 (28.7)	3031 (32.8)	2523 (27.4)	
Less than 7%	6122 (16.6)	1387 (14.8)	1820 (19.9)	2043 (22.1)	872 (9.5)	
Clinical Stage Group						
IA	6756 (18.3)	1680 (17.9)	1715 (18.8)	1775 (19.2)	1586 (17.2)	
IB	14,042 (38.0)	3136 (33.5)	3274 (35.8)	3603 (38.9)	4029 (43.7)	
IIA	1691 (4.6)	468 (5.0)	436 (4.8)	389 (4.2)	398 (4.3)	
IIB	5312 (14.4)	1430 (15.3)	1386 (15.2)	1245 (13.5)	1251 (13.6)	<0.001
IIIA	519 (1.4)	149 (1.6)	144 (1.6)	108 (1.2)	118 (1.3)	
IIIB	7604 (20.6)	2172 (23.2)	1928 (21.1)	1881 (20.3)	1623 (17.6)	
IVA	1062 (2.9)	333 (3.6)	260 (2.8)	250 (2.7)	219 (2.4)	

TABLE 1. Continued.

Characteristics	Total	Distance Quartile 1 (0–5.0 miles) N = 9368	Distance Quartile 2 (5.1–11.2 miles) N = 9143	Distance Quartile 3 (11.3–29.4 miles) N = 9251	Distance Quartile 4 (≥29.5 miles) N = 9224	
	n (%)	n (%)	n (%)	n (%)	n (%)	*p*
Initial Treatment Modality						
Surgery First	20,758 (56.1)	4846 (51.7)	4990 (54.6)	5379 (58.1)	5543 (60.1)	<0.001
Radiation First	16,228 (43.9)	4522 (48.3)	4153 (45.4)	3872 (41.9)	3681 (39.9)	
Facility Type						
Community Cancer Program	1211 (3.3)	498 (5.3)	273 (3.0)	296 (3.2)	144 (1.6)	<0.001
Comprehensive Community Cancer Program	9627 (26.0)	2471 (26.4)	2425 (26.5)	2517 (27.2)	2214 (24.0)	
Academic/Research Program	13,182 (35.6)	3333 (35.6)	3227 (35.3)	3032 (32.8)	3590 (38.9)	
Integrated Network Cancer Program	2799 (7.6)	790 (8.4)	777 (8.5)	726 (7.8)	506 (5.5)	
Censored	10,167 (27.5)	2276 (24.3)	2441 (26.7)	2680 (29.0)	2770 (30.0)	
Year of Diagnosis						
2004	2256 (6.1)	652 (7.0)	563 (6.2)	507 (5.5)	534 (5.8)	0.001
2005	2368 (6.4)	652 (7.0)	556 (6.1)	553 (6.0)	607 (6.6)	
2006	2338 (6.3)	598 (6.4)	535 (5.9)	607 (6.6)	598 (6.5)	
2007	2569 (6.9)	685 (7.3)	659 (7.2)	628 (6.8)	597 (6.5)	
2008	3031 (8.2)	761 (8.1)	782 (8.6)	773 (8.4)	715 (7.8)	
2009	3301 (8.9)	817 (8.7)	810 (8.9)	854 (9.2)	820 (8.9)	
2010	3388 (9.2)	837 (8.9)	831 (9.1)	876 (9.5)	844 (9.2)	
2011	3421 (9.2)	853 (9.1)	812 (8.9)	853 (9.2)	903 (9.8)	
2012	3459 (9.4)	852 (9.1)	896 (9.8)	823 (8.9)	888 (9.6)	
2013	3540 (9.6)	876 (9.4)	864 (9.4)	940 (10.2)	860 (9.3)	
2014	3656 (9.9)	900 (9.6)	907 (9.9)	921 (10.0)	928 (10.1)	
2015	3659 (9.9)	885 (9.4)	928 (10.1)	916 (9.9)	930 (10.1)	

Multivariable analysis adjusted for age, race, ethnicity, income, education, insurance status, Charlson Comorbidity Score, urbanization, clinical stage, year of diagnosis, and initial treatment modality found a statistically significant delay in treatment for women living farther from treatment facility (quartile 2: 1.12 days, $p = 0.008$; quartile 3: 1.98 days, $p < 0.001$; quartile 4: 4.03 days, $p < 0.001$; Table 2). Black and Hispanic persons when compared to white non-Hispanics experienced a delay in treatment of 2.30 and 5.12 days respectively ($p < 0.001$); women with Medicaid (4.87 days; $p < 0.001$) and who were uninsured (4.72 days; $p < 0.001$) were treated later than women with private insurance; and persons receiving radiation therapy first started their treatment 16.47 days later than those receiving surgery ($p < 0.001$). Increasing age resulted in a treatment delay of 0.08 days per year ($p < 0.001$). Later year of diagnosis was associated with treatment delays with women diagnosed in 2015 starting treatment 6.33 days later than those diagnosed in 2004. Interestingly, persons living in rural counties were treated earlier than persons from the largest metropolitan counties.

Sensitivity analysis excluding women with a time to treatment of zero days (diagnosed at the time of surgery or starting radiation) did not significantly alter the effect of distance on time to treatment (**Supplementary Table 1**). Sensitivity analysis using distance as an interval variable confirmed increasing time to treatment with increasing distance (0.021 days per mile, $p < 0.001$; **Supplementary Table 2**).

4. Discussion

Using National Cancer Database data, which includes approximately 70% of all incident cancers in the United States, we found that there was a significant treatment delay for persons living at a greater distance from their treatment facility. Persons living in the farthest quartile from their facility experience a delay in treatment of 4.03 days compared to persons living closest. These findings are novel as this is the first study using a nationally representative dataset to evaluate the effect of distance from facility on time to treatment in cervical cancer. These results highlight a factor that could contribute to well documented outcome disparities in cervical cancer [9, 19–21].

There are mixed reports on the effect of treatment delay on outcomes in patients with cervical cancer. In patients diagnosed with early-stage cancer of the cervix while pregnant, it has been shown that waiting for delivery to initiate treatment is associated with favorable outcomes [22, 23]. The pregnant women evaluated in these small studies were young, largely had stage I–II disease, and were already engaged in the medical community through their pregnancy. While intentional delay was not detrimental in this healthy population, it is difficult to compare these persons with the likely overwhelmingly unintentional delays represented by the findings in the current study. A Canadian study of women with cervical cancer treated with radical radiotherapy found that delay in treatment of 5 weeks or more was significantly associated with increased overall and disease-related death [18]. Similarly, a Taiwanese study found that women with a delay of over 4 months more than doubled their risk of death (95% Confidence Interval (CI): 2.01–2.65) [17]. However, in a study of nationwide data in the Netherlands, a delay in treatment of more than 8 weeks was not associated with any decrease in overall survival [14]. Logically, additional time between diagnosis and treatment could allow the disease to progress and possibly escape its local environment. However, the above studies have dissimilar clinical and/or social reasons for delays in treatment, and this makes conclusions about the effect of delay difficult to make. The current study identifies distance and several other demographic factors that may contribute to treatment delay, but what this delay might mean for outcomes remains unclear.

Because of a shortage of gynecologic oncologists as well as the centralized nature of resources such as brachytherapy, patients with cervical cancer commonly travel to complete their care [3, 4]. The literature is also mixed regarding the impact of distance from facility on outcomes in cervical cancer. A study conducted in Virginia found that women traveling farther to their treatment facility did not demonstrate a difference in progression free survival or overall survival relative to women with a short commute [24]. This study was conducted among a largely rural population with median travel of 72 miles, and as discussed in greater detail below, rural patients may not be negatively impacted by distance in the same way as urban patients. A similar study from the University of Alabama, however, found that subjects living >100 miles from their treatment facility demonstrated an increased risk of death with hazard ratio of 1.68 (95% CI 1.11–2.54) [9]. The study population in Alabama also traveled greater distances (median travel distance 58.9 miles) compared to the 11.2 miles in our study. The above studies were conducted among a largely rural population that may face different barriers to transportation compared to the largely urban population in the current study. Considerations related to transportation such as access to a personal vehicle, availability of public transportation, travel time and cost of travel likely exert a variable impact on rural and urban populations.

Investigations of a relationship between distance and outcomes in other disease sites are also variable. A recently published study found that among counties in the United States, greater distance from a radiation treatment facility was associated with an overall increase in cancer mortality-incidence ratio [25]. Among persons with muscle invasive bladder cancer, outcomes were equivocal between travel distance groups; however, greater travel distance was associated with care at high volume centers [26]. Similarly, men traveling greater distances for treatment of prostate cancer are more likely to receive treatment at academic and high volume centers, and among those treated at academic or high volume centers, men who traveled farther demonstrated improved survival outcomes [27]. Treatment at high volume centers has been shown to improve outcomes among women with locally advance cervical cancer, so the harmful effect of distance may be clouded by a group of people willing and able to travel to seek care at tertiary centers [28]. Certain behaviors such as seeking out an academic or referral center and traveling longer distances for consultation and treatment could understandably be associated with affluence and increased health literacy. The effect of travel distance on survival in a large national sample is therefore likely to be clouded by the differential effect of travel distance for those who travel

TABLE 2. Results of multivariable analysis.

Variable	Beta-Coefficient	95% Confidence Interval	*p*-value
Distance			
Quartile 1 (0–5.0 miles)	Referent	--	--
Quartile 2 (5.1–11.2 miles)	1.119	(0.297–0.941)	0.008
Quartile 3 (11.3–29.4 miles)	1.980	(1.134–2.826)	<0.001
Quartile 4 (≥29.5 miles)	4.034	(3.054–5.014)	<0.001
Age	0.079	(0.053–0.105)	<0.001
Race/Ethnicity			
White	Referent	--	--
Black	2.295	(1.430–3.160)	<0.001
Hispanic	5.118	(4.182–6.055)	<0.001
Other	1.631	(0.311–2.951)	0.015
Charleson Comorbidity Score			
0	Referent	--	--
1	−0.604	(−1.524–0.315)	0.198
≥2	0.411	(−1.596–2.418)	0.688
Urbanization			
Metro (population >1 million)	Referent	--	--
Metro (population 250,000 to 1 million)	−2.594	(−3.370–−1.817)	<0.001
Metro (population <250,000)	−3.101	(−4.247–−1.955)	<0.001
Urban (population ≥20,000, adjacent to metro)	−3.306	(−4.851–−1.760)	<0.001
Urban (population ≥20,000, not adjacent to metro)	−2.185	(−4.737–0.366)	0.093
Urban (population 2500 to 19,999, adjacent to metro)	−5.387	(−6.845–−3.930)	<0.001
Urban (population 2500 to 19,999, not adjacent to metro)	−5.728	(−7.668–−3.877)	<0.001
Rural (completely rural or <2500 urban population, adjacent to metro)	−8.576	(−12.070–−5.082)	<0.001
Rural (completely rural or <2500 urban population, not adjacent to metro)	−8.798	(−12.021–−5.576)	<0.001
Insurance Status			
Private Insurance/Managed Care	Referent	--	--
Medicaid	4.866	(4.101–5.632)	<0.001
Medicare	1.131	(0.138–2.123)	0.026
Other Government	0.993	(−1.551–3.538)	0.444
Uninsured	4.719	(3.674–5.765)	<0.001
Income (Zip Code)			
Quartile 1 (lowest)	Referent	--	--
Quartile 2	−0.381	(−1.268–0.505)	0.399
Quartile 3	−0.525	(−1.513–0.462)	0.297
Quartile 4 (highest)	−0.638	(−1.840–0.563)	0.298

TABLE 2. Continued.

Variable	Beta-Coefficient	95% Confidence Interval	*p*-value
Education (% without high school diploma by zip code)			
21% or more	Referent	--	--
13%–20.9%	−1.915	(−2.763–−1.067)	<0.001
7%–12.9%	−2.287	(−3.271–−1.303)	<0.001
Less than 7%	−3.429	(−4.667–−2.190)	<0.001
Year of Diagnosis			
2004	Referent	--	--
2005	1.313	(−0.316–2.942)	0.114
2006	1.698	(0.063–3.332)	0.042
2007	3.748	(2.151–5.346)	<0.001
2008	3.241	(1.700–4.782)	<0.001
2009	4.346	(2.831–5.860)	<0.001
2010	4.119	(2.612–5.626)	<0.001
2011	3.895	(2.390–5.399)	<0.001
2012	4.751	(3.249–6.252)	<0.001
2013	4.268	(2.775–5.762)	<0.001
2014	6.054	(4.568–7.540)	<0.001
2015	6.325	(4.840–7.811)	<0.001
Stage at Diagnosis			
IA	Referent	--	--
IB	8.052	(7.212–8.892)	<0.001
IIA	5.952	(4.334–7.571)	<0.001
IIB	2.544	(1.331–3.756)	<0.001
IIIA	0.630	(−1.997–3.256)	0.638
IIIB	−0.418	(−1.548–0.713)	0.469
IVA	−6.068	(−8.014–−4.122)	<0.001
Initial Treatment Modality			
Surgery	Referent	--	--
Radiation	16.474	(15.672–17.276)	<0.001
Intercept (Beta_0)	11.073	(9.116–13.030)	<0.001

Example calculation for the estimated time from diagnosis to treatment for a 68 years old black patient who is diagnosed in 2006 with stage T2A disease, lives 6 miles from their treatment facility, has no comorbid conditions, is insured by Medicare, receives definitive surgery, and lives in a completely rural zip code not adjacent to a metropolitan area that is at the 2nd quartile for both income and education: 11.073 +1.119 + (68 years) × 0.079 + 2.295 + 0 − 8.798 + 1.131 − 0.381 − 1.915 + 1.698 + 5.952 + 0 = 17.546 days.

greater distance out of necessity versus by choice.

Patients living in rural environments may have unique barriers to care and have been shown to have lower adherence to cervical cancer screening recommendations [29]. Interestingly, in our study women living in rural zip codes, who presumably often travel to urban or metropolitan zip codes to receive treatment, demonstrated decreased time to treatment. Previous literature has noted that the effect of distance is complicated by a paradoxical effect of urbanization on treatment outcomes. Our results suggest a strong effect of degree of urbanization on time from diagnosis to treatment with increasingly urban counties being treated later than rural counties. Residents of the most remote rural counties received treatment an average of 8.80 days earlier than those who reside in the most populated metropolitan counties. While rural residents only account for 1.6% of our total sample, this result is striking and in line with previous studies that have proposed a disparate impact of distance among rural compared to urban patients. A previous study by Spees *et al.* [6], found similar results that greater distance was detrimental among urban residents but protective among rural residents. They proposed that transportation may provide a greater barrier among urban residents since rural residents are more likely to own personal transportation which has been associated with improved access to healthcare [30, 31].

The participants in the current study were treated at Commission on Cancer accredited cancer centers which may disproportionately represent centralized centers localized in metropolitan areas, so the rural residents included in the National Cancer Database may select for those willing and able to travel longer distances to receive care. In men with prostate cancer, Vetterlein *et al*. [27] found that traveling longer distances to receive treatment at academic or very high volume centers was associated with improved survival relative to those traveling short distances. We were unfortunately not able to further explore the interplay of treatment facility and distance traveled due to censoring of facility information in a large portion of our population.

We identify greater time from diagnosis to treatment associated with later years of diagnosis. Increasing complexity of care including the widespread adoption of advanced imaging to aid in diagnosis and plan treatment could be a factor contributing to increasing delays in treatment [32–36]. The logistical struggle of scheduling advanced imaging is a plausible explanation for the increasing time from diagnosis to treatment with increasing year.

This study found a delay in treatment of 4.03 days for women living in the furthest quartile from their treatment facility. An average delay in treatment of 4 days may be modest, but it indicates an important effect of distance that may be unequally impacting subgroups among more remote patients. Women in the first and fourth distance quartile could be separated by as little as 24.4 miles, a distance that is unlikely to act as a barrier to care among people with reliable transportation. It is also important to note that the average delay by distance is adjusted for other variables that are unlikely to be evenly distributed among persons in different distance quartiles. For instance, two neighbors with the same disease characteristics living 50 miles from their treatment facility, a 70-year-old, black, uninsured woman would be estimated to experience a 10.2-day delay compared to her 30-year-old, white neighbor with private insurance. However, both of these neighbors would be estimated to experience an average of a 4-day delay relative to two similar neighbors living close to their facility. The results of this analysis are important in that they provide evidence of a potentially clinically relevant treatment disparity among women based on distance from facility when controlling for other variables.

Our study has several limitations worth mentioning. First, this is a retrospective study and we were not able to adjust for facility information. Second, distance defined by zip codes can be problematic when performing spatial analysis [37]. However, the use of zip code centroids as a proxy for travel distance is an accepted methodology for spatial studies and allows large databases to maintain patient anonymity [7, 27, 38]. Categorization of distance by quartile was performed to limit the bias introduced by selecting artificial distance thresholds, however, as discussed above there can be as little as 24.4 miles separating patients in the first and fourth quartiles. This relatively small difference in distance between groups could partially explain the small magnitude of delay experienced by subjects in the fourth quartile relative to those in the first quartile. Sensitivity analysis using a linear distance variable help reinforce the overall conclusion that greater distance is associated with a modest delay in treatment. Finally, complex social/system issues that are impossible to capture in a large database likely effect time to starting treatment, and for this analysis we are necessarily reducing this complexity into a single variable of time to treatment.

5. Conclusions

In conclusion, using a large and nationally representative sample we found that women with cervical cancer living farther from their treatment facility experience a modest, but statistically significant delay in treatment. There are likely subgroups for whom distance acts as a substantial barrier and further research to identify factors that synergize with distance to lead to delays and adverse outcomes is needed.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are widely available through the National Cancer Database upon request.

AUTHOR CONTRIBUTIONS

EMS and JAH—were integral in conception, design, data analysis, interpretation and drafting the final article; SER—was heavily involved in interpretation of results and provided a detailed review of the article. All authors approve the final transcript for submission.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the Indiana University Institutional Review Board #20083. All data were deidentified and consent from subjects was not required.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at https://oss.ejgo.net/files/article/1846063950923218944/attachment/Supplementary%20material.docx.

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