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# The Impact of Racial, Geographic and Socioeconomic Risk Factors on the Development of Advanced Stage Cervical Cancer

**T. Clark Powell, MD, MPH**[1], **Sarah E. Dilley, MD, MPH**[2], **Sejong Bae, PhD**[3], **J. Michael Straughn Jr., MD**[2], **Kenneth H. Kim, MD**[2], and **Charles A. Leath III, MD, MSPH**[2]

[1]University of Alabama at Birmingham Department of Obstetrics & Gynecology

[2]University of Alabama at Birmingham Division of Gynecologic Oncology

[3]University of Alabama at Birmingham Division of Preventative Medicine

## Abstract

**Objectives:** Despite screening, disparities exist in cervical cancer incidence and outcomes. Demographic factors are associated with diagnosis at advanced stage (AS), but less is known about geographic factors. We sought to investigate risk factors for developing AS cervical cancer in Alabama.

**Methods:** We identified women treated for cervical cancer from 2005–2015 at our institution. Stages II-IV were considered AS. ZIP codes were categorized by federal Rural-Urban Commuting Area (RUCA) Codes, and 16 historically underserved counties were categorized as Black Belt Rural (BBR). Utilizing data from the American College of Obstetricians and Gynecologists (ACOG), we identified women's health provider locations. We explored associations between stage and multiple factors using logistic regression.

**Results:** Of 934 patients, 29.2% were black, 52.7% had AS cancer and 63.4% lived in urban areas. Average distance to nearest ACOG Fellow in urban, rural and BBR areas was 5.0, 10.6 and 13.7 miles, respectively. Black race, public insurance and age >65 were associated with increased risk of AS cancer. Living in a rural area trended towards higher risk but was not significant. When stratified by race, insurance status and age were associated with AS cancer in white women only.

**Conclusions:** Living further from a women's health provider or in a rural area was not associated with a higher risk of AS cervical cancer. Black women had a higher risk of AS than white women regardless of age, insurance status and geography. Disparities in cervical cancer are multifactorial and necessitate further research into socioeconomic, biologic and systems causes.

## Précis:

Black race remains a significant risk factor for development of advanced stage cervical cancer, while geography was not shown to affect stage at diagnosis.

**Corresponding Author:** T. Clark Powell, MD, MPH University of Alabama at Birmingham, 619 19th Street South, 176F Room 5329, Birmingham AL, 35249 thomaspowell@uabmc.edu Phone: 205-934-7873 Fax: 205-975-6174.

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**Keywords**

cervical cancer; racial disparity; geographic disparity; health disparities; rural health; public health

## Introduction

Cervical cancer is a worldwide public health problem causing significant morbidity and mortality. It is the second most common cancer among women and accounts for almost 300,000 deaths worldwide per year [1, 2]. In the United States, more than 12,000 new women are diagnosed annually [3, 4]. Despite widespread screening and increasing uptake of human papillomavirus (HPV) vaccination, over half of new diagnoses are advanced stage (AS) which carries high rates of morbidity and mortality as well as increased risk of recurrence [4, 5].

Similar to other healthcare disparities, the contributing factors to disparities in cervical cancer outcomes are multifactorial [2, 6]. Poverty, insurance status and race have all been shown to negatively affect HPV vaccination series completion rates, Pap screening rates and follow-up and treatment of abnormal Pap smear results [7–10]. Furthermore, disparities in stage at diagnosis, guideline-adherent care and outcomes have been demonstrated for cervical cancer [10–13]. Low socioeconomic status (SES), lack of access to reliable transportation, lack of health insurance and minority race have been shown to be associated with a diagnosis of AS cervical cancer [2, 14, 15]. In the United States, there is wide geographical variation in cervical cancer incidence and mortality rates with the highest rates seen in Appalachia, the South Atlantic, and lower Mississippi Valley. Alabama occupies the southernmost part of Appalachia [16, 17]. We have previously demonstrated the impact of distance from a comprehensive cancer center on overall survival in women diagnosed with cervical cancer, which highlights the importance of geographic location in obtaining and completing high quality cancer treatment [11]. Geographic measures such as the distance to nearest women's health provider and residing in a rural area are potentially modifiable barriers to both prevention and treatment of cervical cancer; however, less is known about the effects of these factors on stage at diagnosis and their interaction with other factors that impact cervical cancer outcomes. Thus, we evaluated the geographic and sociodemographic risk factors for development of AS cervical cancer in our state.

## Methods

Our institutional tumor registry was queried to identify a cohort of women treated for cervical cancer from 2005–2015 at the University of Alabama at Birmingham. Patients diagnosed with American Joint Committee on Cancer (AJCC) Stages II-IV were considered to have AS cervical cancer. ZIP codes were defined as rural or urban based on 2010 federal Rural-Urban Commuting Area (RUCA) Codes [18]. ZIP codes were further categorized as Black Belt Rural (BBR) if they were in one of 16 Black Belt counties, which are particularly medically underserved and rural with demonstrated disparities in other health outcomes whose population is approximately 50 percent African American (Figure 1) [19–23]. Utilizing data from the American College of Obstetricians and Gynecologists (ACOG), we

identified practice locations of ACOG Fellows in the state. A total of 442 ACOG Fellows were identified including 383 Fellows, 44 Junior Fellows, 8 Associate Members and 7 Senior Status Fellows. This was used as a proxy for women's health care providers. Estimated patient travel distance individually and combined with RUCA Codes have been used by other investigators to evaluate geospatial effects of residence on cancer outcomes [24]. Insurance status was classified as public, private or uninsured. Public insurance included Medicaid, Medicare, Tricare and Indian Health Services. There were 29 patients excluded from analysis due to unknown insurance status. Associations between stage and multiple factors including age, race, minimum distance between patient and nearest provider in miles, rurality, income and insurance status were explored using logistic regression using an alpha level of 0.05 for significance. SAS statistical software was used for analysis (SAS v9.4, SAS Institute, Cary, NC). This project was approved by our Institutional Review Board.

## Results

After exclusions, we identified 934 patients for the analysis. Of these, 273 (29.2%) patients were black and 661 (70.8%) were white. Mean age at diagnosis was 49.8 (SD 14.7). There were 493 patients with AS cervical cancer including: 197 (21.1%) Stage II, 210 (22.5%) Stage III and 86 (9.2%) Stage IV. 592 (63.4%) lived in urban areas and 342 (36.6%) in rural areas, including 85 in BBR areas (Table 1). Mean distance to the nearest women's health provider for patients in urban, rural and BBR areas was 5.0, 10.6 and 13.7 miles, respectively. Black women were significantly more likely to have public insurance compared to white women ($P$ <0.001) (Table 2).

In the crude analysis, black race (OR 1.46; 95% CI 1.09–1.94), public insurance (compared to private, OR 1.80; 95% CI 1.35–2.40) and age >65 years (OR 1.95; 95% CI 1.34–2.85) were associated with increased risk of being diagnosed with AS cervical cancer. A shorter minimum distance to nearest women's health provider did not have a significant effect on risk of AS disease (OR 0.995; 95% CI 0.98–1.01). Living in a rural (including BBR) area trended towards a higher risk of AS but was not statistically significant (OR 1.19; 95% CI 0.91–1.56) (Table 3). A significant interaction between race and insurance status on the outcome ($P$ = 0.03) was noted; therefore, we conducted a stratified analysis by race. When stratified by race and adjusted for multiple factors in multivariate analysis, insurance status (both uninsured and public insurance) and older age were both associated with AS cancer in white women but not black women (Table 4).

## Discussion

In our analysis, AS cervical cancer was diagnosed in over half of cases, which indicates that there are ample opportunities for improvement in both prevention and early detection. We examined distance to nearest women's health provider with the hypothesis that this can affect both primary and secondary prevention leading to delayed diagnosis. As expected, distance to nearest women's health provider was greater in both rural and BBR ZIP codes. Interestingly, this longer distance was not associated with a higher risk of AS disease, with neither closer distance to the nearest provider or rurality associated with AS disease.

Previous studies have shown that women who live in rural areas live farther from Pap screening and treatment services, and that lack of access to reliable transportation is associated with a higher likelihood of AS disease [2, 14, 15]. Furthermore, other studies have demonstrated the negative impact of distance from treatment facility for patients after diagnosis of both ovarian and cervical cancer [11, 25, 26]. However, this analysis indicates that other factors, namely race, age and insurance status, had a stronger influence on outcomes than did geography in our population.

When stratified by race, having public insurance and being uninsured were associated with AS cancer in white women but not black women. However, black women had a higher risk of AS cancer than white women regardless of age, insurance status, or geography. Our analysis is consistent with previous data showing that significant racial disparities exist, and that black race remains one of the strongest predictors of worse outcomes for women with cervical cancer [13, 27]. This is important in the context of recent analyses that demonstrate that racial disparities in cervical cancer are historically underestimated [13, 17]. The high rate of public insurance or lack of insurance among women diagnosed with cervical cancer in our series, as well as the association of insurance status with AS cervical cancer in white women reinforces the fact that funding status is an influential determinant of health disparities. Eliminating racial disparity, improving access to care and increasing insurance coverage are key determinants to the success in prevention and treatment of cervical cancer [8, 9, 28].

The strengths of our study include a large number of cases from a high-volume cancer center, minimal changes in management of AS disease over the study period and a wide range of variables available for analysis [29]. However, there are several limitations. While our tumor registry accounts for about 30% of the population in our state with cervical cancer, use of a single institution tumor registry may limit the sociodemographic distribution of patients and does not identify those treated elsewhere within the state. Further, histologic cancer type was not available for this analysis, which could affect results as non-squamous cancers are more likely to present at advanced stage. The use of ACOG data to identify women’s health providers may underestimate the number of medical professionals who provide preventive treatment for women, especially in rural areas. However, abnormal screening results require referral to physicians who offer biopsy or excisional procedures. These providers should be best identified by ACOG data. Our data do not include information regarding patient or provider mobility during the study period which could alter the geographic relationships between providers and patients over time. Women of racial/ethnic groups other than white and black were excluded due to their low numbers, and data were not available to control for individual medical comorbidities. Generalizability of these results may be limited as our results are representative of the outcomes resulting from screening, diagnosis and treatment within our state’s healthcare delivery system.

## Conclusion

Our study demonstrates that access to care is a complex concept that cannot be equated solely to distance to care. There are other person-level mediators of access to care such as access to transportation which may make distance more or less important depending on the

population in question. Furthermore, there may be a threshold above or below which distance becomes a vital mediator of access. Such evaluations are outside the scope of our investigation. However, this concept underlines the fact that attempts to identify and eliminate outcomes disparities must involve multiple disciplines including basic science, public health, epidemiology and clinical medicine and be specific to the target population. For example, HPV subtype and histologic differences by race have been demonstrated in cervical cancer, highlighting the importance of promoting racially diverse models for investigation of tumor biology and response to treatments [30, 31]. Improvements in public health infrastructure to eliminate barriers to screening, early diagnosis and high-quality cancer therapy must be advocated for at the local, state and national levels. Race, socioeconomic status and insurance status are determinants of initiation of HPV vaccination, adherence to screening guidelines and access to appropriate treatment. All of these should be targets for reducing incident cancer cases [7–9]. Stage at diagnosis, rates of guideline-adherent care and mortality are worse for non-white women [32]. Eliminating health disparities will require committed investigation to elucidate more targeted sources of inequitable care and outcomes [2, 6, 33].

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## Abbreviations:

| | |
|---|---|
| **AS** | Advanced Stage |
| **HPV** | human papillomavirus |
| **RUCA** | Rural-Urban Commuting Area Code |
| **BBR** | Black Belt Rural |
| **ACOG** | American College of Obstetricians and Gynecologists |
| **SES** | Socioeconomic Status |
| **AJCC** | American Joint Committee on Cancer |

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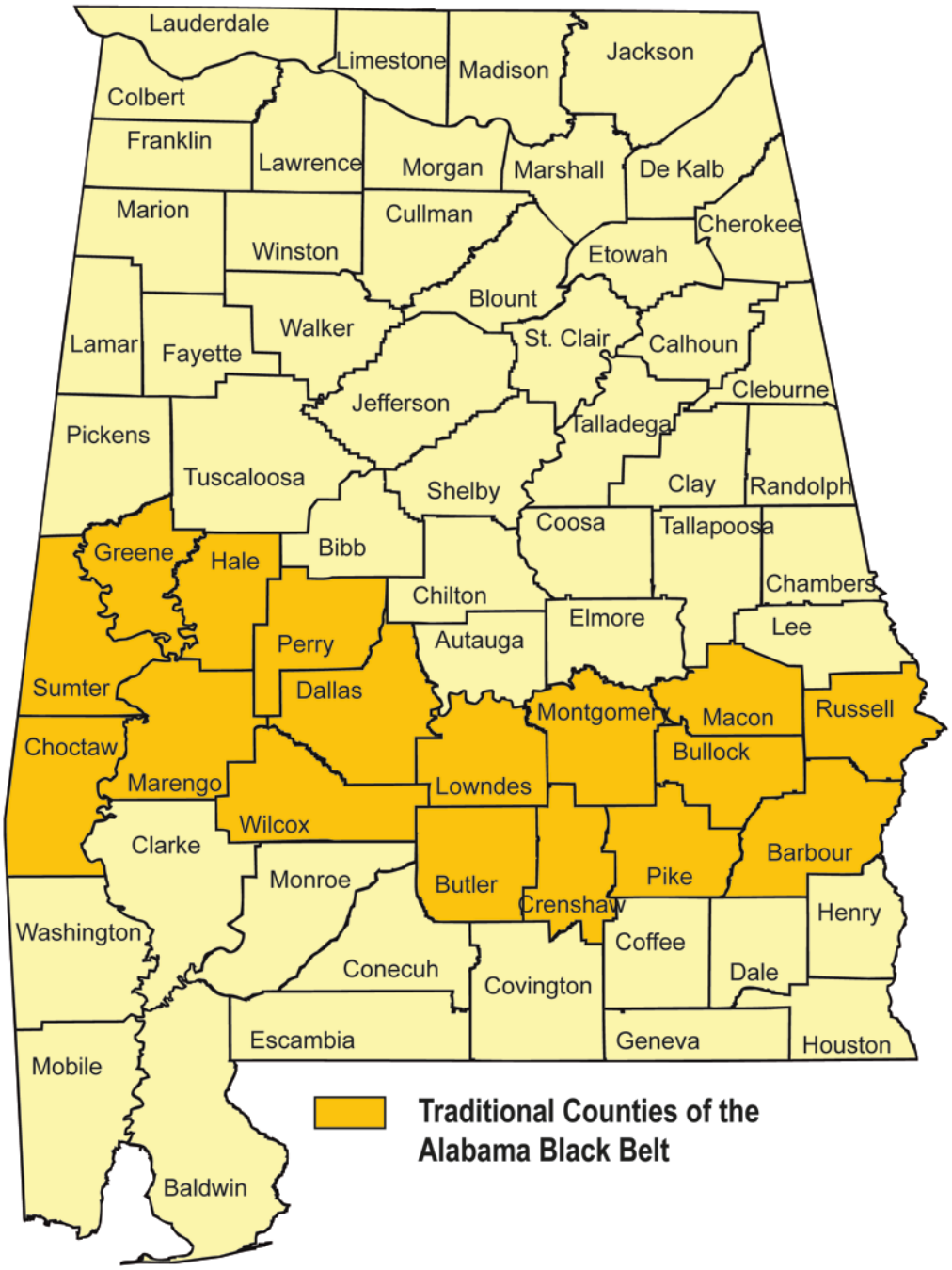


**Figure 1. Traditional Counties of the Alabama Black Belt**
Source: Center for Business and Economic Research, The University of Alabama

**Table 1.**

Patient Characteristics

| | Stage 1 | Stage II-V | Total |
|---|---|---|---|
| Counts, N (%) | 441 (47) | 493 (53) | 934 |
| Age, mean (SD) | 47 (14.7) | 52 (14.3) | |
| Race | | | |
| Black, N (%) | 125 (45) | 150 (55) | 273 |
| White, N (%) | 401 (61) | 260 (39) | 661 |
| Region | | | |
| Urban, N (%) | 278 (48) | 296 (52) | 592 |
| Rural, N (%) | 125 (45) | 150 (55) | 342 |
| BBR, N (%) | 38 (45) | 47 (55) | 85 |
| Mean Income | $42,013 | $40,700 | |

BBR – black belt rural

**Table 2.**

Insurance Status by Age, Race, and Rurality

| | Private N (%) | Public N (%) | Uninsured N (%) | Total | *P* value |
|---|---|---|---|---|---|
| | 346 (37) | 431 (46) | 128 (14) | 905 | |
| Race | | | | | <0.0001 |
| Black | 71 (27) | 160 (61) | 32 (12) | 263 | |
| White | 275 (43) | 271 (42) | 96 (15) | 642 | |
| Age | | | | | <0.0001 |
| Age ≤50 | 239 (47) | 183 (36) | 91 (18) | 513 | |
| Age 50–65 | 88 (35) | 130 (52) | 34 (13) | 252 | |
| Age >65 | 19 (14) | 118 (84) | 3 (2) | 140 | |
| Rurality | | | | | 0.02 |
| Rural | 117 (33) | 187 (53) | 47 (13) | 351 | |
| Urban | 229 (41) | 244 (44) | 81 (15) | 554 | |

**Table 3.**

Odds of Being Diagnosed with Advanced Stage Cervical Cancer

| | Crude OR | 95% CI |
|---|---|---|
| Age >65 vs. ≤50 | 1.95*** | 1.34–2.84 |
| Black vs. White | 1.46* | 1.09–1.94 |
| Rural vs. Urban | 1.19 | 0.91–1.56 |
| Shorter distance to provider | 0.99 | 0.98–1.01 |
| Uninsured † | 1.40 | 0.93–2.10 |
| Public Insurance † | 1.80*** | 1.35–2.4 |
| Higher income | 0.93 | 0.85–1.03 |

†: compared to women with private insurance

*P*-value:

*** = < 0.001

* = < 0.05

**Table 4.**

Adjusted Odds of Being diagnosed with Advanced Stage Cervical Cancer – Stratified by Race

| | Adjusted OR | 95% CI |
|---|---|---|
| White | | |
| Age >65 vs. ≤50 | 1.70 * | 1.03–2.83 |
| Rural vs. Urban | 0.99 | 0.68–1.46 |
| Uninsured † | 1.69 * | 1.05–2.71 |
| Public insurance † | 1.93 * | 1.34–2.69 |
| Black | | |
| Age >65 vs. ≤50 | 1.18 | 0.57–2.43 |
| Rural vs. Urban | 1.70 | 0.75–3.86 |
| Uninsured † | 0.77 | 0.32–1.82 |
| Public insurance † | 0.83 | 0.46–1.52 |

†: compared to women with private insurance

*P*-value:

* = < 0.05