HHS Public Access

Author manuscript

Cancer Epidemiol. Author manuscript; available in PMC 2019 October 01.

Published in final edited form as:

Cancer Epidemiol. 2018 October ; 56: 140–145. doi:10.1016/j.canep.2018.08.008.

Trends in Cervical Cancer Incidence and Mortality in Oklahoma and the United States, 1999-2013

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Abstract

Background: The twin prevention strategies of HPV vaccination and cervical cancer screening reduce new cases and averts deaths, yet women still develop or die from cervical cancer. To assess and better understand the burden of cervical cancer in Oklahoma, we analyzed incidence and mortality trends in Oklahoma from 1999 to 2013.

Methods: We obtained age-adjusted cervical cancer incidence and mortality rates and calculated standardized rate ratios (RR) for women in Oklahoma compared to the US. To evaluate temporal changes in annual age-adjusted incidence and mortality, we calculated the annual percent change (APC) using the Joinpoint Regression Program.

Results: We observed higher age-adjusted incidence (RR: 1.2; 95% CI: 1.1, 1.3) and mortality (RR: 1.2; 95% CI: 1.1, 1.2) rates among women in Oklahoma compared to the US. The overall incidence and mortality rates in Oklahoma were 9.7 and 2.9 per 100,000 women, respectively. In Oklahoma, the highest age-adjusted incidence rates were in American Indian/Alaska Native (AI/AN) (14.8 per 100,000 females) and Asian or Pacific Islander (API) (11.7 per 100,000 females) women and the highest mortality rates were in AI/AN (4.5 per 100,000 females) and African American (AA) (3.9 per 100,000 females) women. Incidence rates decreased for AA women (APC: −4.0; 95% CI: −7.7, −0.2), but were stable for all other races and ethnicities in Oklahoma (APC: −0.8; 95% CI: −2.2, 0.7). A stable trend for mortality was observed in Oklahoma (APC: 0.1; 95% CI: −2.2, 2.5) each year.

Conclusion: Women in Oklahoma had a higher cervical cancer incidence and mortality rate than the US. A disproportionately higher incidence of cervical cancer among AI/AN and API women and deaths among AI/AN and AA women were observed signaling continuing racial disparities.

Keywords

Cancer epidemiology; cancer trends; cervical cancer; disease burden; health disparities; incidence; mortality; Oklahoma; United States

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Contribution of Authors

All authors participated in designing the study, analyzing and interpreting data, and writing and approving the final version of the manuscript.

Conflict of Interest

The authors have no conflicts of interest to declare.

1. INTRODUCTION

Cervical cancer is the fourth most common cancer globally[1] with low- and middle-income countries disproportionately bearing 85% of the global burden and 88% of deaths.[2] In the US, due to use of screening programs based on the Papanicolaou (Pap) smear and pelvic examination,[3] cervical cancer is less common affecting over 12,000 women annually and accounting for 1.5% of all new cancer cases.[4] The burden of cervical cancer is higher in Southern states, which have eight of the top ten US states and territories with the highest cervical cancer incidence and mortality rate.[5] During 2010 to 2014, the state of Oklahoma ranked sixth and tenth for highest cervical cancer incidence (9.4 per 100,000 females) and mortality (2.7 per 100,000 females) among all states, respectively.[6] Both incidence and mortality rates in Oklahoma were considerably greater than the Healthy People (HP) 2020 target of 7.3 cases per 100,000 females and 2.2 deaths per 100,000 females.[7]

Persistent infection with oncogenic human papillomavirus (HPV) types is an established cause of cervical cancer, which makes it the most important risk factor.[8] Other risk factors for cervical cancer include smoking[9] and co-infection with HIV and some sexually transmitted infections,[10] among others.[11] To prevent most HPV-related cervical cancers, prophylactic HPV vaccines have been available and recommended for women aged 9 to 26 years since 2006;[12] however, their uptake (at least one dose) among female adolescents has been low in Oklahoma (58%) compared to the US (63%).[13] For screening, the Pap test (or Pap smears) and HPV DNA test can help prevent cervical cancer or find it early.[14] The U.S. Preventive Services Task Force recommends population-based screening among adults at average risk.[14] Screening tests can detect both precancerous lesions and cancer at an early stage, and aid in preventing its progression to cervical cancer. Currently, the Pap test is recommended for all women older than 21 years and HPV co-testing in conjunction with Pap tests for routine cervical screening of women 30 years of age and older.[14]

Cervical cancer screening programs, such as the National Breast and Cervical Cancer Early Detection Program (NBCCEDP), have reduced mortality among uninsured low-income women.[15,16] The Oklahoma Breast and Cervical Cancer Act (63 O.S. §1 554–558) was established in 1994 to implement plans to decrease cervical cancer morbidity and mortality in the state.[17] However, from 2010–2012, only 6.5% and 10.9% of the eligible population nationally and in Oklahoma, respectively, received NBCCEDP-funded Pap tests.[18] Additional resources for cervical cancer screening include SoonerPlan, Oklahoma's family planning program for men and women not enrolled on the state's Medicaid plan (SoonerCare);[17] family planning programs at the Oklahoma State Department of Health; and Planned Parenthood.

In this study, we analyzed incidence and mortality trends in Oklahoma and the US for all racial and ethnic groups, which addresses a gap in the literature. We also aimed to identify racial disparities in trends among minority populations, such as American Indian/Alaska Native (AI/AN). The study analyzed data from Oklahoma as the state has a relatively higher incidence and mortality rate[6] and also contains the second largest AI/AN population of all states in the US,[19] which provides a unique study setting.

2. MATERIALS AND METHODS

2.1. Data Source

Cervical cancer incidence and mortality data for Oklahoma were collected by the Oklahoma Central Cancer Registry (OCCR) and obtained from the publicly available website, OK2SHARE (http://www.health.state.ok.us/ok2share/).[20] OCCR is a population-based cancer registry that includes information on all cases of reportable cancers among Oklahoma residents beginning January 1, 1997. Based on quality, completeness, and timeliness of data, OCCR has received the silver or gold certification from the North American Association of Central Cancer Registries (NAACCR) since 2001.[21] For the US, we obtained data from the Centers for Disease Control and Prevention (CDC) National Program of Cancer Registries (NPCR) and the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) program, which we accessed through CDC WONDER (https://wonder.cdc.gov/).[22] Incidence and mortality data for both Oklahoma and the US were analyzed from 1999 through 2013.

2.2. Cervical Cancer Codes

For incidence, we included cervical cancer cases classified according to the *International Classification of Diseases for Oncology, 3rd Edition* (ICD-O-3) (sites C530-C539, excluding histology types 9050–9055, 9140, 9590–9992).[23,24] For mortality, the underlying cause of death was classified according to the 10th revision of the *International Statistical Classification of Diseases and Related Health Problems* (ICD-10) as C53.[25]

2.3. Study Population

Women diagnosed with cervical cancer, irrespective of stage at diagnosis, and women who have died from cervical cancer in Oklahoma and the US were included in this study. We classified race as white, African American (AA), AI/AN, and Asian or Pacific Islander (API). Ethnicity was classified as Hispanic or non-Hispanic.

2.4. Statistical Analysis

We obtained age-adjusted rates for cervical cancer by the direct method of adjustment using the 2000 US standard population.[26] All rates are expressed per 100,000 females. We calculated standardized rate ratios (RRs) and the 95% confidence intervals (CI) to determine whether incidence and mortality rates for Oklahoma differed from that in the US. A RR was significant if the 95% CI did not include 1.0. We also calculated RR and 95% CI to compare racial differences in incidence and mortality within Oklahoma.

We estimated age-adjusted incidence and mortality trends in Oklahoma using Joinpoint Regression Program (version 4.5.0.1; National Cancer Institute, Bethesda, Maryland). A log-linear model was used to approximate a normal distribution for rates from a small population and to interpret trends in terms of a rate change at a constant percent per year through annual percent change (APC).[27] Up to two joinpoints, or inflections, were allowed in the model due to the small number of cases (in certain racial and ethnic groups), and the resulting trends were characterized according to APC.[28] An APC estimate was reported to increase or decrease if the slope of the trend was significantly different from zero; otherwise, the trend

was reported as stable. Fewer than 10 cases or deaths annually were suppressed in OK2SHARE to protect confidentiality. Thus, we were unable to run this analysis for API or Hispanic women. Statistical tests were two-sided at $P < .05$ level.

The study used publicly available cancer data and did not meet the criteria for human subjects research as determined by the Institutional Review Board of the University of Oklahoma Health Sciences Center.

3. RESULTS

From 1999 to 2013 in Oklahoma, 2,648 women were diagnosed with and 847 women died from cervical cancer with an average of about 177 cases and 57 deaths per year. The overall incidence and mortality rates in Oklahoma were 9.7 and 2.9 per 100,000 women, respectively (Table 1). Age-specific incidence rates rose sharply from 20–24 years and peaked in the 40–44 age group (Figure 1). Thereafter, the rates of cervical cancer gradually declined with age, except for a small peak in the 60–64 age group. Mortality rates gradually increased with age with the highest rates among women 85 years and older.

From 1999 to 2013, the overall age-adjusted incidence rate in Oklahoma was significantly higher than the US (RR: 1.2; 95% CI: 1.1, 1.3) (Table 1). Similarly, Oklahoma had a significantly higher age-adjusted mortality rate than the US (RR: 1.2; 95% CI: 1.1, 1.3). In Oklahoma, both incidence (14.8 per 100,000 females) and mortality (4.5 per 100,000 females) rates were highest among AI/AN women. Hispanic women had higher incidence rates (12.9 per 100,000 females), but lower mortality rates (2.4 per 100,000 females) than non-Hispanic women in Oklahoma. For the US, both incidence and mortality were highest in AA (10.8 and 4.4 per 100,000 females, respectively) and Hispanic (11.8 and 3.0 per 100,000 females, respectively) women. The age-adjusted incidence rate was higher in Oklahoma compared to the US for both AI/AN (RR: 2.1; 95% CI: 1.9, 2.3) and API (RR: 1.6; 95% CI: 1.2, 2.1). Within Oklahoma, AI/AN women had a significantly higher cervical cancer incidence rate than white (RR: 1.6; 95% CI: 1.5, 1.8) and AA (RR: 1.5; 95% CI: 1.3, 1.8) women. Age-adjusted mortality was also higher in Oklahoma than the US for these racial groups (AI/AN: RR: 1.9; 95% CI: 1.5, 2.4; API: RR: 1.8; 95% CI: 1.1, 3.0). In Oklahoma, AI/AN (RR: 1.6; 95% CI: 1.3, 2.0) and AA (RR: 1.4; 95% CI: 1.1, 1.8) women had significantly higher cervical cancer mortality rates than white women. No significant differences were observed between the US and Oklahoma by Hispanic ethnicity. Compared to the US, women in Oklahoma had higher incidence (RR: 1.3; 95% CI: 1.2, 1.4) and mortality (RR: 1.5; 95% CI: 1.3, 1.8) rates among those aged 25–44 at diagnosis.

In our analysis of time trends in Oklahoma, incidence rates have remained stable (APC: 0.8%; 95% CI: −2.2, 0.7) from 1999 to 2013 (Table 2). We also observed a stable trend in incidence for all racial groups, with the exception of AA women, who had a significantly decreasing APC of −4.0% (95% CI: −7.7, −0.2). For mortality, a stable trend was observed overall from 1999 to 2013 (APC: 0.1%; 95% CI: −2.2, 2.5) each year. However, due to small numbers, APC was not calculable for AI/AN and AA women. For white and non-Hispanics of all races, incidence rates were also stable. Although we allowed for up to two Joinpoints in our analysis, we observed no Joinpoints for any of trends.

4. DISCUSSION

The overall incidence trend for cervical cancer in Oklahoma remained stable from 1999 to 2013. The State also had a significantly higher age-adjusted incidence rate than the US, and had not yet met the HP 2020 objectives. The relatively higher incidence rate in Oklahoma reflects regional disparity and could stem from a variety of factors which warrant investigation, including social and public health services,[29] insurance coverage,[30] health policies,[31] and screening.[31] For the latter, 20.7% of eligible women in the Behavioral Risk Factor Surveillance System survey from Oklahoma aged 18 years and older reported not receiving a Pap test in the past three years as opposed to 20.1% nationally.[32] However, a meta-analysis found that national survey data are overestimating cancer-screening utilization for Pap smears.[33] Overreporting for self-reported Pap smear could be related to forward telescoping of dates or if a woman mistakes a routine gynecologic exam without a Pap test as including the Pap test.[33,34]

The age-adjusted cervical cancer incidence was highest among AI/AN women in Oklahoma, which was twice as high as the rate for AI/AN women in the US. This finding needs to be investigated further as the difference in rates for AI/AN women has been shown to differ by region of the US and may stem from cervical cancer screening practices in the Indian Health Service (IHS) or due to differences in the use of IHS revised race categories, which may result in misclassification of AI/AN race in some areas.[35] Also, contrary to the national trend,[36] AI/AN women in Oklahoma had a higher cervical cancer incidence rate than white and AA women. Studies in the Northern Plains have identified that AI/AN women have a higher HPV burden and different HPV genotyping profile, which may contribute to higher rates of cervical cancer.[37,38] In the three years prior to 2016, more non-Hispanic women (81.9%) were screened compared to Hispanic women (76%) in Oklahoma.[32] Consistent with prior findings, higher incidence rates were observed in Hispanic as compared to Non-Hispanic women in Oklahoma and the US.[36] This has been largely driven by low rates of screening,[39] which may result from low levels of health care coverage,[40] health literacy,[41] and cultural and socioeconomic factors.[41]

Regarding mortality, the trend in Oklahoma was stable with a nonsignificant increase of 0.1% (95% CI: −2.2, 2.5) over the last 15 years. This stable trend differed from the US overall, which exhibited a decreasing trend during the same period.[42] Similarly, the age-adjusted mortality rate in Oklahoma was significantly higher than the US (RR: 1.2; 95% CI: 1.1, 1.3), and both Oklahoma and the US had not yet met the HP 2020 objective of 2.2 deaths per 100,000 females.[7] In Oklahoma, AI/AN women had the highest age-adjusted mortality rate followed by AA women. Both AI/AN and AA women had significantly higher mortality rates than white women. The racial disparity in death rates observed in Oklahoma is concerning; nevertheless, it is in line with findings from previous studies which have identified significantly higher incidence and mortality rates among minority women.[43–45] Minority women are more likely to present at an older age and later stage of cervical cancer diagnosis, and thus, access to timely screening is a likely factor impacting higher mortality in these populations.[46] Although this study did not explore reasons for racial disparities, future studies must address this gap.

To increase cervical screenings, recommended evidence-based strategies need to be implemented. Some of these strategies include provider practice and system change strategies such as client reminders,[47] provider reminder, and recall systems[48]; education through videos and printed materials[49]; and policy, systems or environmental approaches that increase access to screening.[50] In addition, comparatively lower rates of vaccine uptake in Oklahoma precludes the opportunity to reduce the HPV-related cancer burden. To prevent cervical cancer cases, HPV vaccination strategies and efforts need to be strengthened. Strategies to increase HPV vaccination rates in the state could include recommendation from a health-care provider,[51] reminder/recall systems,[52] standing orders for vaccination,[53] and education of patients.

Racial disparities were present in Oklahoma, with AI/AN, API, and AA women continuing to bear a disproportionate burden of cervical cancer. The high rates of cervical cancer are an indicator of problems in access to health care, and could reflect unequal access.[46] To address this issue, improving client-based interventions,[54] supporting culturally competent communication, removing cultural and economic barriers,[46] and decreasing structural barriers are needed. Closing the gap will not only reduce disparities, but also accelerate progress on the HP 2020 objectives for cervical cancer incidence and mortality.[7]

This study had a few limitations that merit consideration. First, results of groups with fewer than 10 cases or deaths were suppressed for confidentiality purposes and could not be included in the analysis. This limited our ability to evaluate mortality trends in some racial and ethnic groups such as API, AA, and Hispanics, which had fewer cases or deaths annually due to their relatively small population in Oklahoma. Second, the capacity to analyze data by strata such as narrower age groups or race and ethnicity was limited due to the small number of cases and deaths. Third, racial misclassification among the AI/AN population could still exist despite the IHS linkage process, particularly in states with few IHS facilities.[55] This may contribute to an underestimation among AI/AN women and lead to inaccuracies in characterizing cervical cancer burden for this population.[56,57] Finally, incidence and mortality rates were calculated from a relatively small number of cases and deaths. Despite these limitations, the study used high quality, population-based data for analysis.

This study provides insight in the incidence and mortality burden and trends for cervical cancer in Oklahoma for the past 15 years. Future studies are needed to evaluate the impact of screening programs and the recent implementation of HPV vaccination on cervical cancer incidence and mortality in Oklahoma. Future studies could also evaluate the impact of HPV vaccination on HPV prevalence as an intermediate step. Also, an assessment of cervical cancer survival statistics is needed to better understand the overall burden in Oklahoma. The racial disparities in incidence and mortality found in Oklahoma warrant further research, and failing to do so may inhibit the opportunity to understand and attenuate disparities.

Acknowledgments

Funding Support

JC was partially supported by grants NU58DP005513 from the Centers for Disease Control and Prevention (CDC). JC was partially supported by grants AIAMP120011 from the Office of Minority Health (OMH). AJ was partially supported by sub award number U1B1IHS0009-13-00 from Indian Health Service (IHS). The content is solely the responsibility of the authors and does not necessarily represent the official views of the CDC, OMH or IHS.

Abbreviations:

AA	African American
AI/AN	American Indian/Alaska Native
APC	annual percent change
API	Asian or Pacific Islander
HPV	human papillomavirus
NBCCEDP	National Breast and Cervical Cancer Early Detection Program
RR	rate ratio

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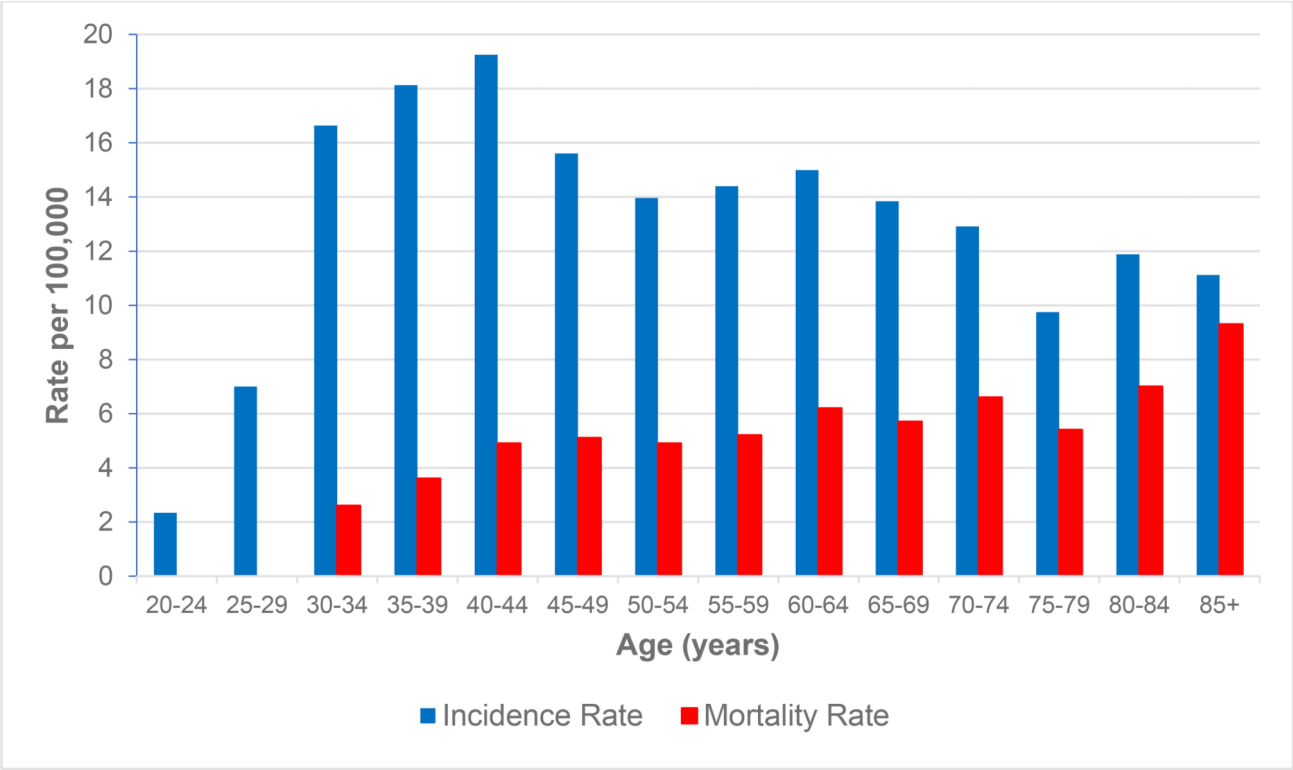

FIGURE 1.

Incidence and mortality rates for cervical cancer by age groups, Oklahoma, 1999–2013

Note: Fewer than 10 deaths observed in 20–24 and 25–29 age groups, respectively.

TABLE 1.

Cervical Cancer Incidence and Mortality Rates by Age, Race, and Ethnicity for women in Oklahoma and the United States, 1999–2013.

	Incidence					Mortality				
	Oklahoma		United States			Oklahoma		United States		
Characteristic	**Count (%)**	**Rate* (95% CI)**	**Count (%)**	**Rate* (95% CI)**	**OK:US RR(95% CI)**	**Count (%)**	**Rate* (95% CI)**	**Count (%)**	**Rate* (95% CI)**	**OK:US RR(95% CI)**
Overall	2,648	9.7 (9.3, 10.0)	189,000	8.2 (8.2, 8.3)	1.2(1.1, 1.3)	847	2.9(2.7, 3.1)	60,377	2.5(2.4, 2.5)	1.2(1.1, 1.3)
Age group (years)										
<25	51 (1.9)	0.5 (0.4, 0.7)	2,497 (1.3)	0.3(0.3, 0.3)	1.6(1.1, 2.2)	-**	-	207(0.3)	0.0(0.0, 0.0)	-
25–44	1,089 (41.1)	15.7 (14.8, 16.6)	72,387 (38.3)	12.0 (12.0, 12.1)	1.3(1.2, 1.4)	212(24.9)	3.1(2.7, 3.5)	12,215(20.2)	2.0(2.0, 2.1)	1.5(1.3, 1.8)
45–64	1,003 (37.9)	14.8 (13.9, 15.7)	75,377 (39.9)	13.5(13.4, 13.6)	1.1(1.0, 1.2)	359(42.2)	5.24(4.7, 5.8)	26,811(44.4)	4.7(4.6, 4.7)	1.1(1.0, 1.3)
65–84	437 (16.5)	12.3 (11.1, 13.5)	33,615 (17.8)	12.3 (12.2, 12.4)	1.0 (0.9, 1.1)	217(25.5)	6.11(5.3, 7.0)	17,045(28.2)	6.1(6.0, 6.2)	1.0(0.9, 1.2)
≥85	68 (2.6)	11.1 (8.6, 14.1)	5,124 (2.7)	10.2 (9.9, 10.5)	1.1(0.9, 1.4)	57(6.7)	9.32(7.1, 12.1)	4,099(6.8)	8.0(7.8, 8.3)	1.2(0.9, 1.5)
Race										
White	2,054(77.6)	9.1(8.7, 9.5)	146,454(77.5)	7.9(7.9, 7.9)	1.2(1.1, 1.2)	663(78.3)	2.7(2.5, 2.9)	45,609(75.5)	2.3(2.2, 2.3)	1.1(1.0, 1.2)
African American	179(6.8)	9.7(8.3, 11.2)	30,060(15.9)	10.8(10.7, 11.0)	0.9(0.8, 1.0)	73(8.6)	3.9(3.0, 4.8)	12,122(20.1)	4.4(4.3, 4.5)	1.0(0.8, 1.2)
American Indian/Alaska Native	328(12.4)	14.8(13.2, 16.5)	1,630(0.9)	7.1(6.7, 7.4)	2.1(1.9, 2.3)	99(11.7)	4.5(3.6, 5.4)	498(0.8)	2.3(2.1, 2.6)	1.9(1.5, 2.4)
Asian or Pacific Islander	57(2.2)	11.7(8.7, 15.4)	7,940(4.2)	7.1(7.0, 7.3)	1.6(1.2, 2.1)	12(1.4)	3.3(1.4, 5.2)	2,148(3.6)	2.0(2.0, 2.1)	1.8 (1.1, 3.0)
Ethnicity										
Hispanic	163(6.2)	12.9(10.8, 15.3)	29,981(15.9)	11.8(11.7, 12.0)	1.1(1.0, 1.2)	18(2.1)	1.7(2.8, 3.2)	6,764(11.2)	3.0(2.9, 3.1)	0.6(0.4, 0.9)
Non-Hispanic	2,485(93.8)	9.5(9.3, 10.0)	158,588(83.9)	7.8(7.8, 7.9)	1.2(1.1, 1.3)	827(97.6)	3.0(0.9, 2.5)	53,481(88.6)	2.4(2.4, 2.4)	1.2(1.1, 1.4)
Unknown or Missing	0	-	431 (0.2)	-	-	2(0.2)	-	132 (0.2)	-	-

Abbreviation: CI, confidence interval; RR, rate ratio.

*Rates are per 100,000 females and are age adjusted to the 2000 U.S. standard population.

**Fewer than 10 deaths observed.

TABLE 2.

Trends in age-adjusted cervical cancer incidence and mortality rates by race/ethnicity, Oklahoma, 1999–2013.

	Annual Percent Change*					
	Incidence			Mortality		
Race/Ethnicity**	**Year Range**	**Estimate (%) 95% CI**	**Direction**	**Year Range**	**Estimate (%) 95% CI**	**Direction**
All races/ethnicity	1999–2013	−0.8 (−2.2, 0.7)	Stable	1999–2013	0.1 (−2.2, 2.5)	Stable
Race						
White	1999–2013	−0.8 (−2.1, 0.5)	Stable	1999–2013	−0.5 (−2.8, 2.0)	Stable
American Indian/ Alaska Native	1999–2013	−2.0 (−5.2, 1.3)	Stable	-***	-	-
African American	1999–2013	−4.0**** (−7.7, −0.2)	Decreasing	-***	-	-
Ethnicity						
Non-Hispanic	1999–2013	−0.8 (−2.2, 0.6)	Stable	1999–2013	0.4 (−1.9, 2.8)	Stable

Abbreviation: CI, confidence interval

*Although we allowed for up to two Joinpoints in our analysis, we observed no Joinpoints for any of trends.

**Asian/Pacific Islander and Hispanic women could not be included due to fewer than 10 deaths occurring annually.

***Annual percent change could not be calculated due to fewer than 10 deaths annually.

****Annual percent change is significantly different from zero at $P < .05$.