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# 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.

## 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 2010–2014, 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 9–26 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

*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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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 to 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, 2648 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 to 24 years and peaked in the 40–44 age group (Fig. 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 1999–2013, 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