

Racial/Ethnic Disparities in Cervical Cancer Screening and Outcomes

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Key Words

Cervical cancer screening · Disparity · Race · Ethnicity

Abstract

Invasive cervical cancer disproportionately affects women without sufficient access to care, with higher rates among minority groups in higher-income countries and women in low-resource regions of the world. Many elements contribute to racial/ethnic disparities in the cervical cancer continuum – from screening and diagnosis to treatment and outcome. Sociodemographic factors, access to healthcare, income and education level, and disease stage at diagnosis are closely linked to such inequities. Despite the identification of such elements, racial/ethnic disparities persist, and are widening in several minority subgroups, particularly in older women, who are ineligible for human papillomavirus (HPV) vaccination and are underscreened. Recent studies suggest that racial/ethnic differences in HPV infection exist and may also have a role in observed differences in cervical cancer. In

this review, we provide an overview of the current literature on racial disparities in cervical cancer screening, incidence, treatment and outcome to inform future strategies to reduce persistent inequities.

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Introduction

Invasive cervical cancer (ICC) disproportionately affects women without sufficient access to care, with higher rates among minority groups in higher-income countries and women in low-resource regions of the world. More than 80% of deaths due to ICC are in low- and middle-income countries and the World Health Organization estimates that ICC cases are expected to increase 40% by 2030 [1–4]. In contrast, ICC incidence and related deaths are declining in high-income countries due to the widespread availability of cytology-based screening and access to early, curative treatment for precancer-

Table 1. Cervical cancer statistics [89]

Population	World	Less developed regions	More developed regions
Women at risk for cervical cancer (female population aged ≥ 15 years) in millions	2,716.830	2,174.580	542.250
Annual new cervical cancer cases, n	527,624	444,546	83,078
Standardized cervical cancer incidence rates per 100,000 population	14.0	15.7	9.9
Annual cervical cancer deaths, n	265,672	230,158	35,514
Standardized cervical cancer mortality rates per 100,000 population	6.8	8.3	3.3

Data were extracted from the 2016 Summary Report of Human Papillomavirus and Related Diseases in the World.

ous cervical lesions (table 1) [2, 5]. Much of the decline in ICC over the last 4 decades may be attributed to the adoption of effective cytology-based screening programs [6–8]. However, the availability of cervical cytology as a primary screening tool is mostly limited to high-income countries [6–8]. Efforts have been made to find more effective, low-cost strategies for cervical cancer screening, especially in low-income countries, such as the new independent states of the former Soviet Union [9], Brazil and Argentina [10], Haiti [11], China [12] and India [13]. In India, for example, which has the most cases of ICC of any country in the world, over 100,000 women are diagnosed annually. A large cluster-randomized study suggested that for rural settings in India, where screening rates are as low as 6% in several states, more ICC cases were identified and there was a mortality benefit to primary screening with human papilloma virus (HPV) testing compared to cervical cytology or visual inspection with acetic acid [14].

Despite the existence of effective primary (prophylactic vaccination against HPV infection) and secondary prevention tools, barriers continue to impede women from accessing these services, as attested by higher observed incidence rates of ICC and later stage at diagnosis in low-resource settings, and among women of minority groups in high-income countries [10]. The complexity of health disparities appears to not only be entwined in geographic and socioeconomic barriers to care, but also racial barriers [11]. Racial disparities are particularly apparent in high-income settings. For example, in the USA, ICC incidence, morbidity and mortality remain higher among black women as compared to whites (fig. 1, 2) [12].

Among American women diagnosed with ICC, African American women are twice as likely as Caucasian women to die from the condition [13]. Similarly, Hispanic women often present with more advanced stages of

ICC than women from the general population, which is linked to lack of access to screening and treatment services [14]. Racial disparities have been shown to undercut current cervical cancer prevention, treatment and survival strategies. Accordingly, the purpose of this review is to explore the most recent literature surrounding racial inequalities in cervical cancer screening and outcomes to inform future prevention strategies that may improve such disparities.

Screening Uptake and Disease Stage

Cytological screening has been an effective primary method to identify precancerous lesions [14, 15] and has led to a dramatic decline in ICC incidence and mortality [9]. Uptake of cytology screening varies substantially by country income. Gakidou et al. [16] estimated screening rates across 57 diverse countries. In developed countries, the proportion of eligible women (25–64 years old) who reported having had a pelvic exam in their lifetime was 93.6%, whereas in developing countries this proportion was 44.7% [2, 3, 17, 18].

In the most recent analysis of cervical cancer screening uptake by the Centers for Disease Control, 81% of women in the USA had undergone cytological screening within the last 3 years, and this rate was slightly higher in African American women, while rates were significantly lower among Asian and Hispanic women [19, 20]. However, African American women are more likely to be diagnosed with advanced disease compared to Caucasians [19–22]. A Texas study observed that 20% of Hispanic women presenting with stage IV disease had never had a Pap smear, compared to 3% of women presenting at a similar disease stage [20, 22, 23]. Data extracted from the Surveillance Epidemiology and End Results (SEER) database (1973–2009) showed that stages II to IV disease were higher

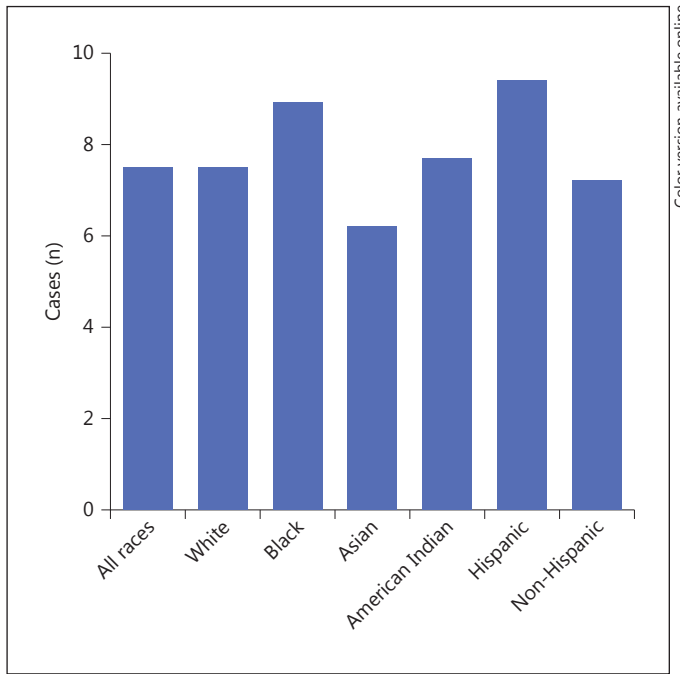


Fig. 1. Incidence of ICC stratified by age/ethnicity (SEER 2009–2013). Number of new cases per 100,000 individuals.

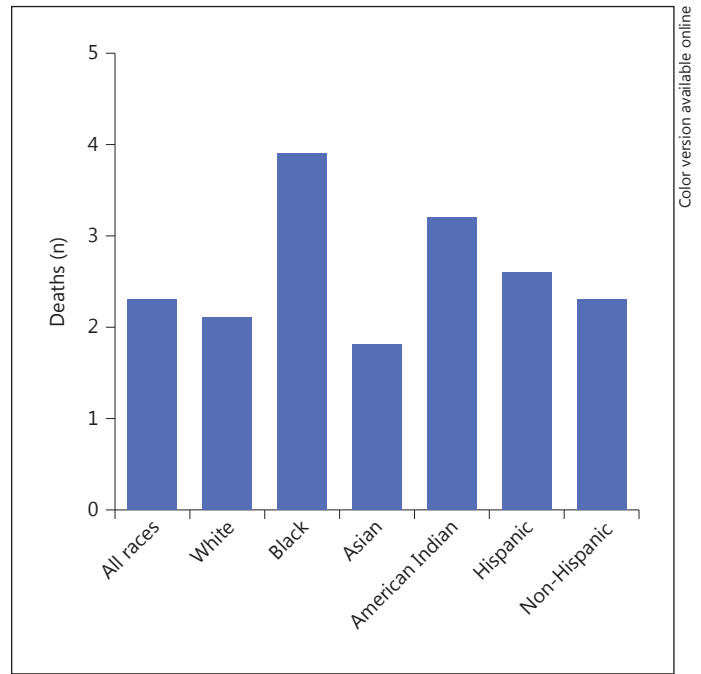


Fig. 2. ICC mortality rates stratified by race/ethnicity (SEER 2009–2013). Number of deaths per 100,000 individuals.

among white Hispanic than white non-Hispanic women, and there was a higher incidence of cervical cancer in white Hispanic women [24, 25]. Despite screening uptake differences between African American and Hispanic women, both groups are more likely to be diagnosed with later-stage disease than white women and generally have poorer treatment responses with increased morbidity and mortality [22]. Taken together, these data suggest that other factors in addition to screening uptake account in part for the disparate outcomes observed.

Minority women with a low socioeconomic status (SES) have much higher rates of ICC, are less likely to have undergone screening, and consequently more likely to present with advanced disease [26]. Increasing SES decreases the odds of delayed- versus early-stage diagnosis among all racial groups [16]. Among minority groups of low SES, black women are significantly more likely to have a delayed-stage diagnosis [27]. Furthermore, a recent study identified black and Hispanic women living in an area with a high proportion of black women to be at higher risk for high-grade cervical neoplastic disease, suggesting that the race-related social network may attribute to cervical cancer risk [16]. SES appears to influence the risk for advanced disease more when combined with race.

Age

The incidence of ICC, as with many other cancers, increases with age across all racial and ethnic groups studied. Older women make up a discrepant proportion of new ICC cases diagnosed and related deaths [16]. Age-specific incidences of cervical cancer stratified by race/ethnicity are shown in figure 3.

A recent nationwide analysis in the UK showed that women aged 65 years or older accounted for 20% of incident cases and half of all cervical cancer-related deaths [28–30]. Similar findings were reported in the USA [31].

With increasing age, racial disparities widen substantially, as seen in North Carolina and other American states. In black and Asian/Pacific Islander women compared to white and Hispanic women, those over the age of 60 years have a higher incidence of CC and account for disproportionate cervical cancer-related mortality [25]. Many women diagnosed with ICC in this age group have either never been screened or have not been screened in the 3 years prior to diagnosis [32]. This is especially true for elderly black women [20–22, 25]. The clinical significance of screening women for cervical cancer over the age of 65 years remains controversial [33]. The potential benefits of cancer screening include early diagnosis and treat-

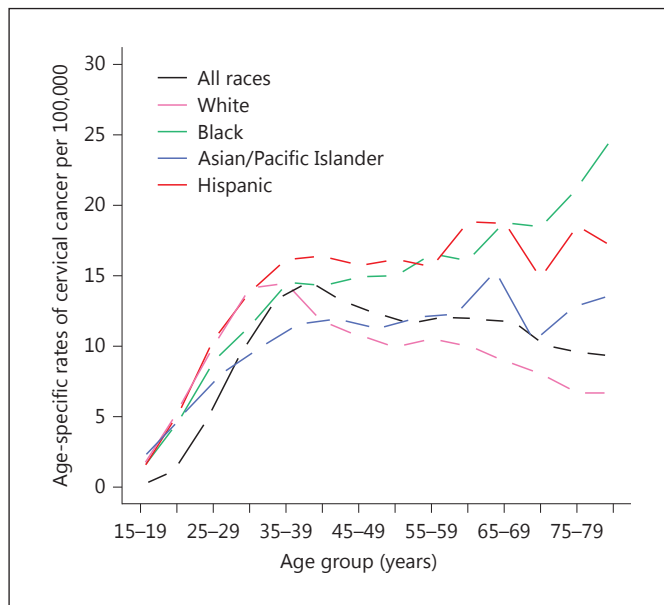


Fig. 3. Incidence of cervical cancer stratified by age and race/ethnicity (SEER 2009–2013).

ment, and improved survival, while a net benefit has not been definitively demonstrated for elderly women [34].

If the upper age limit of screening is increased, current literature suggests a greater potential benefit for black and Asian/Pacific Islander women. However, perhaps more importantly, disparate screening rates highlight a need to focus screening improvement efforts on older women from underscreened minority groups.

Linkage of Care

Cervical cytology screening is only effective if abnormal results are followed up by timely diagnosis and treatment. Women from minority racial/ethnic groups have been shown to have longer waiting times from the abnormal cytology screening result to being scheduled for a final diagnostic procedure. Furthermore, among women with abnormal cervical cytology screening results, Hispanic, Asian, and black women have significantly lower odds of being scheduled for treatment [21, 35]. In one study, loss to follow-up after an abnormal screening result was shown to be highest in Blacks (17.9%) and Native Americans (15%) compared to the general population and other racial/ethnic groups [36].

Women from racial/ethnic minority groups with cervical neoplasia are also more likely to have a delay be-

tween diagnosis and treatment initiation. This delay has also been shown to be improved, with reduced loss to follow-up in all racial/ethnic groups, when patient navigators are available [37, 38].

Mounting evidence continues to support the use of telephone support with navigation to improve screening rates and follow-up for racial/ethnic minorities [39, 40]. A recent study by Charlot et al. [41] demonstrated that in a Boston Patient Navigation Program, race and language concordance significantly increased the likelihood of having a timelier resolution in minority women with cervical cancer screening abnormalities [42]. In particular, black patients who had black navigators were 50% more likely to have a timelier resolution of cancer screening abnormalities after 3 months. Hispanic patients with Hispanic navigators were 80% more likely to have a timelier resolution of cancer screening abnormalities. These findings highlight the importance of recruiting a diverse healthcare workforce in primary care and oncology settings. The increased benefit for Hispanic compared to black patients, most whom spoke Spanish as their primary language, also pointed to the importance of communicating with racial/ethnic minority patients in a concordant language.

Treatment

Treatment differences between minority groups and white women have been demonstrated periodically and likely play a major role in racially disparate outcomes. Multiple studies have shown that among women of similar disease stage, black women with cervical neoplastic disease are less likely to receive treatment due to loss of follow-up and differences in treatment [43]. For example, a study by Bernard et al. [44] observed that, among women with low-grade cytological abnormalities, white women were more likely than comparison groups to be followed up by colposcopy rather than a repeat Pap test [27, 45]. Compared to white and Hispanic women, black women with ICC were less likely to receive surgery, less likely to have surgery recommended, and more likely to receive radiation therapy compared to other racial categories [46]. In another study of early-stage ICC management, minority women were less likely to undergo a hysterectomy and more likely to be treated with fertility-sparing, less definitive procedures. These discrepancies have been hypothesized to be related to increased comorbidities, patient choice to decline the recommended treatment, and provider bias in treatment recommendations

in minority patients [37, 47], which have also been observed in the treatment of other diseases [48].

In several studies performed in publicly insured populations with presumed equal access to care, a disparity between race and survival was not observed [44]. Although null findings do not equate to the absence of a relationship, they do suggest that racial gaps are greatly diminished when access to treatment improves.

Access to Healthcare

Access to healthcare in the context of cervical cancer screening is normally defined by health insurance status and the usual source of care. Individuals with private health insurance and a usual source of care are much more likely to be screened and to be diagnosed with early rather than late-stage cervical cancer and to receive guideline-based therapy compared to their counterparts [49]. Several studies have upheld this association even after controlling for SES [50]. A nationwide study conducted by the United States Center for Disease Control and Prevention found that, among women aged between 21 and 65 years who had not undergone a hysterectomy, 88.7% with private insurance, 81.9% with public insurance, and only 63.8% of the uninsured had undergone a PAP test within the last 3 years. Furthermore, among patients with a usual source of care compared to those who had none or went to the Emergency Department, there was a 20% difference in adherence to PAP testing (86.4 vs. 64.9%) [51]. Together, these findings suggest that insurance status among women acts as a barrier to accessing screening services.

Minorities including Blacks, Asians, and Hispanic individuals are less likely to have either health insurance or a usual source of care [41]. In a study of black women from an urban setting, the effectiveness of a culturally appropriate intervention to improve screening rates was significantly related to insurance status – those with private insurance were more likely to follow the intervention than those covered by Medicaid or Medicare than those with no insurance [52–55]. Several other studies concluded that the strongest predictors of cervical screening behaviors in multiethnic populations were having private health insurance and having a usual source of care [56].

A recent study in the USA compared states that improved access to public health insurance through Medicaid expansion to those that did not, and found that racial disparities in screening rates were higher in nonexpansion states and related to insurance status and a higher

prevalence of minorities residing there. Together, these data suggest that existing racial disparities are likely to widen with geographic differences in health insurance status [21, 27, 31].

Geography

Racial disparities may be related to the geographic location of racial groups with major geographic differences observed in cervical cancer incidence and mortality between and within countries [57–59]. Cervical cancer screening and incidence also varies substantially by urban and rural status, with women in rural areas having the lowest screening rates and highest incidences of advanced disease in low- and high-income countries. Rural areas have fewer healthcare providers per capita with alternate competing risk factors, including lower SES and interface with healthcare providers. To improve rural disparities in cervical cancer in some low- and middle-income countries, screening programs have been developed that utilize community health workers. In 2009 in China, which has the second most incident cases of cervical cancer annually, the government launched a national screening program using this model. Notably, a follow-up study to assess community health workers' knowledge of cervical cancer prevention, including risk factors and screening methods, was not found to be sufficient, highlighting a need to train a rural-based workforce to effectively address cervical cancer disparities [60, 61].

Among minorities who reside in rural compared to urban areas, screen rates for cervical cancer have also been demonstrated to be lower in Hispanic, American, Asian, and black women from developed and developing countries [52, 62]. In minority groups, geographic differences in screening uptake and cervical cancer incidence are resolved after correcting for SES and health insurance status.

Income

Cervical cancer screening uptake rates, incidence, cancer stage at disease presentation, treatment response, and mortality vary dramatically according to SES and household income. In particular, low-income, minority women are more likely to be diagnosed at later disease stages and have increased mortality [63–66]. Women with stage IA disease have a 93% 5-year survival, while women diagnosed with stage IIA and IIIA disease have 5-year sur-

vival rates of 63 and 35%, respectively [43, 67]. SES is frequently defined as the economic and social standing of an individual within a society and is highly associated with cancer screening rates. Multiple studies at the individual, community and census-tract levels suggest that minority women of lower SES have much lower screening rates, after extensive adjustments for cofounders [68]. One multilevel study of black women found that those living in census tracts with <5% poverty, compared to women living in high-poverty areas (defined by >20% poverty), were 1.2-fold less likely to have undergone cervical cytology screening within the last 2 years [65, 69].

Health Literacy and Immigration Status

Health literacy has been defined by the National Academy of Medicine as “the capacity to obtain, process and understand basic health information needed to make decisions” [70]. Low health literacy rates are commonly observed in women already at higher risk for cervical cancer, including ethnic minorities, the elderly, immigrants and nonnative speakers [71–73]. Although few studies have evaluated the role of health literacy on cervical cytology screening, a recent systematic review showed a positive correlation between health literacy and cancer knowledge and perceived barriers to care – all of which were implicated in cervical cancer screening adherence [74]. At present, few studies have examined cultural and language differences in the context of health literacy and cervical cancer screening adherence. With this in mind, further research is needed to effectively target low literacy groups at higher risk for cervical cancer, including minority groups.

Immigrants have unique barriers to accessing screening services, including linguistic, cultural, and socioeconomic obstacles [75, 76]. Cultural differences include lack of acceptance of receipt of care from male providers, including pelvic examination, and seeking healthcare for symptomatic disease rather than for preventative care. A lack of culturally sensitive and language-concordant screening environments may contribute to low rates of cervical cytology screening in immigrant women [13].

Within racial/ethnic groups, disparities in cervical cancer persist among foreign-born and native-born women. In one study of white women from Arab Nations, compared to women born in the USA, foreign-born women were less likely to receive preventative care, including cancer screenings, suggesting immigration status functions as a predictor of screening uptake independent

of ethnicity or race [13]. In a study conducted in Spain, cervical cancer screening coverage and the prevalence of abnormal cervical cytology was examined in Catalonia by immigration status in over 1 million women. The study showed that immigrants had higher screening rates than Spanish-born women, but were more likely to have abnormal cervical cytology (2.9 vs. 4.5%), highlighting an increased risk for cervical disease in immigrant populations [77, 78].

HPV Infection

ICC is caused by infection with a high risk (hr) type of HPV. Consequently, among women in low-resource areas, a high prevalence of hrHPV infection has been linked to a high burden of cervical cancer. One of the largest studies to highlight this relationship was conducted in Haiti, a country with one of the highest ICC rates in the world. Among over 9,000 asymptomatic women screened for cervical cancer, the prevalence of hrHPV infection was 19.0%. HPV-infected women were more likely to have CIN2+ (cervical intraepithelial neoplasia grade 2+) lesions compared to women without hrHPV. Of note, Haitian women with CIN2+ were most likely to be infected with hrHPV types 16 or 35. This differed from the most common types (HPV16 and 18) implicated in ICC studies that predominantly enrolled women that were not of African descent [79]. Racial/ethnic differences in HPV infection among women with CIN have been observed in other studies as well [80]. A multiethnic cohort study of women undergoing colposcopy demonstrated that European American women were twice as likely to be infected with HPV 16 or 18 compared to African American women. This relationship held true across similar grades of CIN. Furthermore, African American women were more likely to be coinfecting with multiple types of HPV compared to European American women for unclear reasons [79, 81–83]. Other studies have also demonstrated that black, Hispanic and Asian women are less likely to be infected by HPV16 or 18 compared to white women [84], whereas HPV58 and 45 are more commonly found in Hispanics than Whites [85]. Poverty has also been associated with a lower prevalence of HPV16/18 among infected women, after adjustment for race/ethnicity [43, 86]. Together, these studies suggest that women of African descent residing in low-resource areas may not be equally protected by vaccination against HPV types 16 and 18.

Persistent infection with hrHPV is a known risk factor for CIN and subsequent progression to ICC. Risk factors

for persistence include younger age of first sexual intercourse, a higher number of lifetime sexual partners, and coinfection with other sexually transmitted infections [87].

A recent study conducted in the southeastern United States has implicated race as a new risk factor for HPV persistence. Banister et al. [88] found that, among college-age women, African Americans compared to European Americans had a median clearance of carcinogenic HPV infection of 601 days compared to 316 days, and a higher prevalence of HPV infection despite a similar incident infection rate. Together, these results suggest that longer HPV infection times and harboring multiple high-risk HPV infections simultaneously may contribute to the increased risk for abnormal cervical cytology and progression to ICC in African Americans compared to other racial/ethnic groups [72].

Conclusion

As access to cervical cancer screening increases, individualized, molecular technologies emerge, and prevention strategies including HPV vaccination expand, the prevention and early diagnosis of cervical cancer will con-

tinue to save the lives of innumerable women worldwide. Simultaneously, racial/ethnic disparities in cervical cancer continue to persist, and are widening in several domains. There is strong evidence that addressing the gaps in access to care will narrow such disparities, but will likely not resolve them entirely. In this context, further research and policy changes in improving access to health-care, enhancing awareness and outreach to minorities within and between geopolitical borders, and further study on molecular and genetic mechanisms that may contribute to the differences in HPV pathogenesis and cervical cancer outcomes between racial groups, may be critical to eliminating such disparities.

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Disclosure Statement

The authors have no conflicts of interest to declare.

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