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# Surveillance of high-grade cervical cancer precursors (CIN III/AIS) in four population-based cancer registries, United States, 2009–2012

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## Abstract

Surveillance of cervical intraepithelial neoplasia grade III (CIN III) and adenocarcinoma in situ (AIS) is important for determining the burden of a preventable disease, identifying effects of vaccination on future diagnoses, and developing targeted programs. We analyzed population-based rates of high-grade cervical cancer precursor lesions using data from four central cancer registries (diagnosis years 2009–2012 from Louisiana, Kentucky, Michigan, and diagnosis years 2011–2012 from Los Angeles) by age, race, and histology. We also compared rates of precursors to invasive

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cancers. With 4 complete years of data from Michigan, we were able to conduct a trend analysis for that state. Data analysis was conducted in Atlanta during 2016. Kentucky reported the highest rate of CIN III/AIS (69.8), followed by Michigan (55.4), Louisiana (42.3), and Los Angeles (19.2). CIN III/AIS rates declined among women in Michigan by 37% each year for women aged 15–19, 14% for those aged 20–24, and 7% for those aged 25–29. Rates of CIN III/AIS vary by registry, and were higher than invasive cancer. In Michigan, declines in CIN III/AIS among women aged 15–29 are likely related in part to updated screening recommendations, and to the impact of human papillomavirus vaccination.

**Keywords**

cervical cancer; cervical intraepithelial neoplasia; HPV; HPV vaccines; population-based cancer registries

## INTRODUCTION

National population-based data on cancers are collected through central cancer registries (CCRs) at the state and regional level. These CCRs are supported by state public health agencies as well as by the Centers for Disease Control and Prevention's (CDC) National Program of Cancer Registries (NPCR) and the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program. In 1996, nearly all CCRs ceased collection of data on in situ cervical cancer lesions because of concerns about appropriate case definitions and changes in diagnostic terminology, especially introduction of the Bethesda system for reporting cervical cytology.[1, 2] In addition, surveillance for these lesions was complicated by increasing diagnosis and treatment of these lesions in outpatient settings.[1] One state, Michigan, continued to collect information on in situ cervical cancer lesions even though doing so was not required by federal cancer surveillance programs.

Two vaccines that protect against infection with two of the high-risk types of human papillomavirus (HPV) that cause most cervical cancers, HPV 16 and 18, have been available in the United States since 2006, with a third vaccine protecting against seven additional high-risk types becoming available in late 2014.[3, 4] Invasive cervical cancer usually takes decades to develop, so the effects of HPV vaccines on invasive cervical cancer rates in the US population will likely not be measurable for many more years.[5, 6] However, population-based surveillance of cervical cancer precursors has the potential to provide important information to evaluate intermediate endpoints of HPV vaccines and other cancer control activities.[7]

To better understand the burden of cervical cancers and the impact of cancer prevention and control activities, CDC currently supports collection of data on high-grade cervical cancer precursor lesions in four CCRs: the Kentucky Cancer Registry (KCR), the Louisiana Tumor Registry (LTR), the Michigan Cancer Surveillance Program (MCSP), and the Los Angeles Cancer Surveillance Program (LACSP). A previous report described feasibility and initial findings of this data collection activity.[7] The purpose of the current analysis is to provide population-based rates of cervical cancer precursor lesions over time, including information

on histology; a comparison of cervical cancer precursor rates to rates of invasive cervical cancer; and an examination of short-term trends in one state, Michigan.

# METHODS

## DATA COLLECTION

CDC provides support to the four participating CCRs specifically to collect data on CIN III/AIS. KCR and LTR receive support from both CDC and NCI through the NPCR and SEER programs, and conduct cancer surveillance for their entire states; these two registries began collecting data on CIN III/AIS in 2009. Although MCSP had been collecting CIN III/AIS data for many years prior to initiation of this project, the registry edited case selection criteria for consistency with other registries in 2009, when CDC funding for this project was available. MCSP is supported by state-level and CDC funds, and conducts cancer surveillance for all areas of Michigan. To accomplish this surveillance efficiently, MCSP collaborated with the Detroit Metropolitan Cancer Surveillance System, the NCI-funded SEER registry covering the tri-county Detroit area. LACSP is supported through SEER and collects data on cancers diagnosed in Los Angeles County. LACSP began collecting CIN III/AIS data in April 2010, so we only report on data from diagnosis years 2011–2012 for that registry (compared to 2009–2010 for the other three registries). Cases were defined as having one of the following pathologic classifications: cervical intraepithelial neoplasia grade III (CIN III), cervical carcinoma in situ, adenocarcinoma in situ (AIS), or severe dysplasia. These lesions will henceforth be referred to collectively as CIN III/AIS. More information on case inclusion criteria as well as case finding, follow-back, and data abstraction is described in Flagg et al.[7]

## DATA ANALYSIS

In 2016, we examined age-adjusted rates of cervical cancer precursors (CIN III/AIS) across reporting CCRs by year of diagnosis, 5-year age groups, and race [white, black, American Indian/Alaska Native (AI/AN), or Asian/Pacific Islander (API)]. We also examined data by histologic type. Glandular precursors were defined as ICD-O-3 histology code 8140, and squamous precursors were defined as 8010, 8050, 8052, 8070–8072, 8076, or 8077. All analyses of histologic type were limited to microscopically confirmed cases.

We examined annual percent change (APC) in rates for the Michigan cancer registry only. Change over time in other registries was complicated by the fact that Kentucky and Louisiana could not determine which 2009 cases were prevalent cases (i.e., cases diagnosed in a previous year) versus incident cases, leading to slightly inflated rates in that year; Los Angeles did not provide a complete year of data until 2011.

To provide a comparison with CIN III/AIS data, we also examined data on the age and histological distribution of invasive cervical cancer (ICC). ICC data from the same registries and years as precursor data were included (KCR, LTR, and MCSP for 2009–2012, and LACSP for 2011–2012). Invasive glandular adenocarcinomas were defined as ICD-O-3 histology code 8015, 8140–8149, 8160–8162, 8190–8221, 8260–8337, 8350–8551, 8560, 8570–8576, or 8940–8941, and invasive squamous carcinomas were defined as ICD-O-3

histology codes 8050–8084 or 8120–8131. All analyses of histologic type were limited to microscopically confirmed cases.

We used SEER*Stat version 8.2.1 to calculate age-adjusted rates for both CIN III/AIS and ICC. All rates are adjusted to the 2000 US Standard Population, expressed per 100,000 females, with 95% confidence intervals calculated using the Tiwari modification.[8]

## RESULTS

We identified a total of 21,770 CIN III/AIS cases, with an overall age-adjusted rate of 47.0 cases per 100,000 women (Table 1). Rates varied widely by registry, with Kentucky reporting the highest rate (69.8), followed by Michigan (55.4), Louisiana (42.3), and Los Angeles (19.2). Case counts in Kentucky and Louisiana were highest in the first year of the study (2009) and thereafter remained relatively stable, while counts in Michigan declined year to year during 2009–2012. Rates of CIN III/AIS were very low for women aged 15–19 years, and increased with age, peaking at age 25–29 in Kentucky, Louisiana, and Michigan, and at age 35–39 in Los Angeles. Rates of CIN III/AIS then declined, but remained higher than rates of ICC until about age 55–59 (Table 1, Figure 1). Median age at diagnosis also varied by registry, and was 29 years in Kentucky and Louisiana, 30 in Michigan, and 35 in Los Angeles (data not shown). The overall median age at diagnosis for CIN III/AIS was age 30, versus age 49 for ICC diagnosed in corresponding years and locations (data not shown).

Overall, white women had the highest rates of CIN III/AIS, followed by black women (41.6 and 37.5, respectively). White women had the highest rates of diagnosis in Kentucky and Louisiana ($P<0.05$), while rates were similar for black and white women in Michigan and Los Angeles. Race was “other, unspecified” (not white, black, AI/AN, or API) for 3% of cases.

Table 2 provides rates of CIN III and AIS, compared with rates of ICC by histology (adenocarcinoma and squamous carcinoma, respectively). The majority of precursor lesions were of squamous cell origin, consistent with the majority of invasive lesions. Overall, rates of AIS ranged from 0.8 in Louisiana to 2.4 in Michigan, while rates of CIN III ranged from 17.6 in Los Angeles to 67.7 in Kentucky. The ratio of CIN III to invasive squamous carcinoma varied from 3.5 in Los Angeles to 12.0 in Michigan. Less variety existed in the rate ratio of AIS to invasive adenocarcinoma (from 0.5 in Louisiana to 1.2 in Michigan).

We also examined APC for Michigan, overall and by age (Figure 2). The decline in CIN III/AIS diagnosed in Michigan was significant for all age groups combined during 2009–2012 (APC -8.1; $P<0.05$). Rates for the youngest age group (age 15–19) declined an average of 37% per year during 2009–2012, more than any other age group. Rates among women aged 20–24 and 25–29 also demonstrated statistically significant declines in Michigan (APC -13.7 and -6.6, respectively).

## DISCUSSION

Our study documents declines in CIN III/AIS among women aged 15–29 in Michigan, the state for which we have 4 complete years of data. Declines in the incidence rate of CIN

III/AIS are likely related, in part, to updated screening recommendations, especially age at screening initiation and 3-year Papanicolaou(Pap) test screening intervals. In the past decade, recommendations for cervical cancer screening have undergone multiple changes, including the following: raising the age for initiating screening to 21 years, increasing the screening interval to 3 years, and incorporating recommendations for HPV co-testing.[9, 10] For many years, key provider organizations differed on recommendations regarding age to initiate screening and screening intervals for Pap and HPV co-tests.[9, 11] In 2012, the American Collegeof Obstetricians and Gynecologists (ACOG), American Cancer Society (ACS), and US Preventive Services Task Force (USPSTF) aligned their screening guidelines to recommend that (1) screening by Pap test should not be performed for women aged <21 years, regardless of initiation of sexual activity, (2) a screening interval of 3 years should be maintained for women aged 21–30 years, and (3) HPV co-testing can be performed for women >30 years with a 5-year interval.[12] Provider practice often takes several years to catch up to recommendations, and evidence exists that adherence to recommendations differs by provider specialty.[9] A recent study describes declining Pap test rates over the past decade, especially for younger women.[13]

Declines in CIN III/AIS among the youngest groups of women may also be related in part to HPV vaccination.[14] Similar declines have been noted in other studies. The HPV IMPACT study collected data on CIN II–III/AIS from smaller populations, and also collected screening and vaccination data.[15] The study observed declines in HPV 16/18-attributable lesions among presumed-vaccinated young women age 18–39 between 2008 and 2012, while no significant decrease occurred in lesions among presumed-unvaccinated women.[16] National data have documented declines in vaccine-type HPV infections, as well as in anogenital warts among younger women in the United States since the introduction of the vaccine in 2006.[17–19]

We found lower rates of high-grade cervical precursors in Los Angeles than in other CCRs, as well as higher median age at diagnosis. Other studies of CIN III/AIS have also documented wide variations in the rate of precursor lesions by geographic area (county or state).[20–22] Variations in rates of CIN III/AIS by registry may be related to provider screening practices and adherence to screening guidelines, to HPV vaccination, or to population differences in other behavioral risk factors such as sexual behavior or smoking. Cervical cancer screening data from 2012 show that adherence to screening guidelines (i.e., screened within 3 years) varied among areas participating in our study (21.4% in Louisiana, 21.5% in Michigan, 24.7% in Kentucky, and 28.6% in Los Angeles).[23] Variations in cervical screening are associated with differences in underlying populations and related factors such as income, education, access to care, and acculturation.[24] Smoking prevalence also varied widely among participating registries; according to data from the Behavioral Risk Factor Surveillance System, in 2011, the smoking prevalence was 29.0% in Kentucky, 25.7% in Louisiana, 23.3% in Michigan, and 12.8% in the Los Angeles metropolitan statistical area.[25, 26] Although smoking approximately doubles risk of cervical cancer and pre-cancer, HPV infection and lack of recommended screening and follow-up are greater risk factors for this disease.[27–29]

In contrast with rates of ICC, which is more common among black women,[30] the highest rates of CIN III/AIS were statistically higher among white women in Kentucky and Louisiana, while rates among black and white women were similar in Michigan and Los Angeles (i.e. no statistically significant difference). The higher observed rates among whites in Kentucky and Louisiana could reflect differences in access to care by race in those states.

We found that an average of six cases of CIN III/AIS were diagnosed for every case of ICC. This ratio varied by histology, with about nine CIN III lesions diagnosed for every invasive squamous cell cancer, compared with fewer than one AIS diagnosed for each invasive glandular cell cancer. Because screening more readily detects squamous lesions than glandular lesions,[31] and because trends in glandular carcinomas have increased declines in the more common squamous carcinomas,[32] differences by registry in the ratio of squamous pre-cancers to invasive cancer may further support possible differences in screening in those areas.

This study has several limitations. First, we were not able to collect screening or vaccination history for these women, so we cannot determine what proportion of observed declines were related to changes in screening practice or to HPV vaccination. Future analyses in some areas may be able to address this issue by linking to vaccination and screening registries.[33] Also, during the first year of data collection, three of the four registries were unable to identify recurrent cancer precursors that should have been excluded, leading to higher rates in that year. Because Michigan had been collecting these cases for many years, this problem was avoided as recurrent cases were routinely excluded from the data, so we were able to examine trends for that state. In some states, case data were collected primarily from pathology laboratories via electronic reporting. Because many of these cases were diagnosed and treated in outpatient settings, it is possible that some cases were missed. However, an audit conducted specifically for this precursor study demonstrated that case collection appeared to be complete.[34]

Also, while the population included is relatively diverse and the data are population-based at the state or metro area level, we do not know the generalizability of these data to other areas. The frequency of cases of unknown race is another cause for concern with these data. Overall, 14.6% of cases were missing information on race, with variation across CCRs (from 4.3% of cases reported with unknown race in Louisiana to 20.0% in Michigan). Although registry staff attempted to find missing race information, the collection of these data outside the hospital-focused traditional CCR system makes obtaining complete race information more difficult. Cases of “other, unspecified” race were also common in some registries, and could affect race-specific rates. Finally, the lack of information on Hispanic ethnicity is a limitation. Hispanic women have the highest rates of ICC of all racial/ethnic groups in the United States, and a better understanding of cervical precursors among Hispanic women is important to identify potential areas of intervention, including targeted screening and HPV vaccination efforts.

One additional concern related to the collection of these data is changing diagnosis terminology. In 2012, the American Society for Colposcopy and Cervical Pathology finalized the consensus recommendations of the Lower Anogenital Squamous Terminology

(LAST) Standardization Project for HPV-Associated Lesions.[35] The LAST project's recommended terminology uses a two -tiered system (low-grade and high-grade lesions, or LSIL and HSIL, respectively) compared with the three-tiered system traditionally used for pathology (CIN). Provider practice generally takes time to evolve, and the LAST recommendations state that providers should include both the two-tiered and the traditional three-tiered terminology in reports. However, an audit of data from Los Angeles and Kentucky suggest that as of 2013, providers were largely continuing to use the traditional three-tiered CIN terminology, with some providers also using LAST terminology in combination with the three-tiered terminology.[6, 34] A very small number of providers were using LAST terminology without also including CIN terminology, which could have resulted in some cases being missed. Periodic updates of this audit will be necessary to ensure that current data collection methods are adequate.

Despite its limitations, this is the largest source of population-based surveillance data collected in the United States on CIN III/AIS. While these lesions are generally treatable, women may suffer serious reproductive outcomes, which is particularly concerning given the young median age at diagnosis.[36] Many of these cases potentially could have been avoided through administration of the HPV vaccine prior to sexual debut. As rates of ICC continue to decline,[37] surveillance of CIN III/AIS becomes important for determining the burden of a preventable disease, identifying the effects of vaccination on future diagnoses, and developing targeting programs. This population-based study of CIN III/AIS provides important information on the burden of cervical disease not traditionally captured in CCRs or reflected in official cancer statistics.

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## HIGHLIGHTS

- Four cancer registries collected data on high-grade cervical cancer precursors.
- These data can help identify effects of HPV vaccination and target programs.
- Cervical cancer precursor rates in Michigan declined among young women.
- Observed declines are likely related to screening and HPV vaccination.

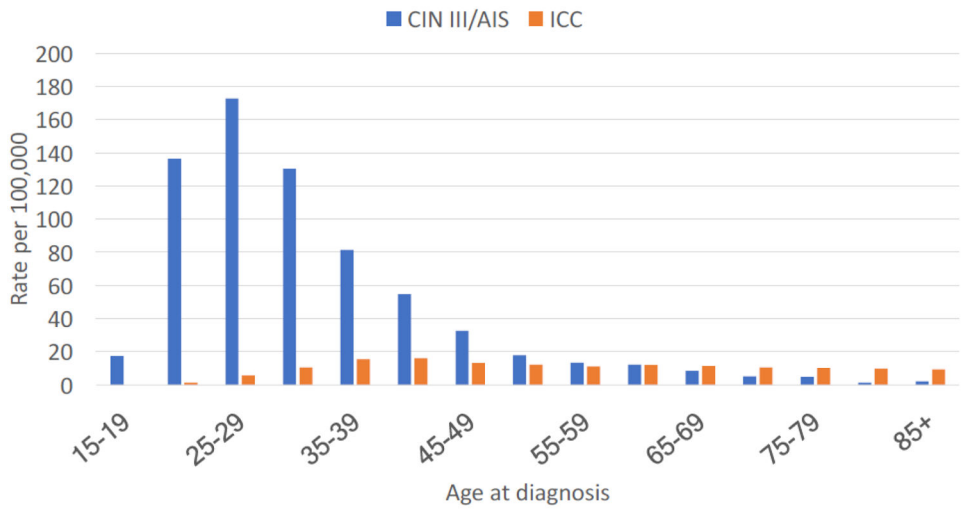


**Figure 1. Rate of High-Grade Cervical Cancer Precursors (CIN III/AIS) by Age, Four US Central Cancer Registries, 2009–2012**

FOOTNOTES:*Cervical adenocarcinoma in situ is included with CIN III.

CIN III/AIS = Cervical intraepithelial neoplasia Grade 3 and adenocarcinoma in situ.

ICC = Invasive cervical cancer.

Data on CIN III/AIS and ICC from Kentucky, Louisiana, and Michigan 2009–2012; Los Angeles 2011–2012. Data analysis was conducted in Atlanta during 2016.

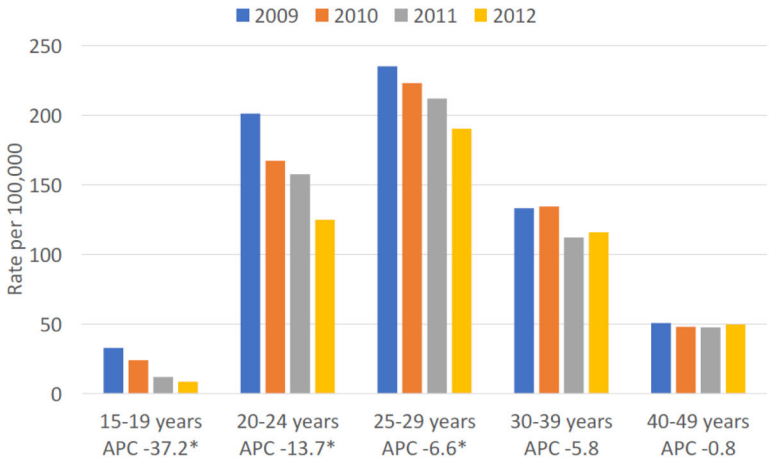


**Figure 2. Short-Term Trends in High-Grade Cervical Cancer Precursors (CIN III/AIS), Michigan Cancer Registry, 2009–2012**

APC = Annual percent change.

*Indicates APC was statistically significant ($p<0.05$).

Data analysis was conducted in Atlanta during 2016.

**Table 1**

Rate of High-Grade Cervical Cancer Precursors (CIN III/AIS), Four US Central Cancer Registries, 2009–2012

| | Los Angeles | | | Kentucky | | | Louisiana | | | Michigan | | | All registries combined | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **N** | **Rate** | **95% C.I.** | **N** | **Rate** | **95% C.I.** | **N** | **Rate** | **95% C.I.** | **N** | **Rate** | **95% C.I.** | **N** | **Rate** | **95% C.I.** |
| **Total** | 1,961 | 19.2 | (18.4, 20.1) | 5,815 | 69.8 | (68.0, 71.7) | 3,874 | 42.3 | (41.0, 43.7) | 10,120 | 55.4 | (54.3, 56.5) | 21,770 | 47.0 | (46.4, 47.7) |
| **Year of Diagnosis** | | | | | | | | | | | | | | | |
| 2009 | *a* | *a* | *a* | 1,640 | 79.3 | (75.5, 83.2) | 1,263 | 55.5 | (52.5, 58.7) | 2,870 | 62.5 | (60.2, 64.8) | 5,773 | 64.6 | (62.9, 66.3) |
| 2010 | *a* | *a* | *a* | 1,371 | 65.6 | (62.2, 69.2) | 834 | 36.9 | (34.4, 39.6) | 2,640 | 58.0 | (55.8, 60.3) | 4,845 | 54.3 | (52.8, 55.9) |
| 2011 | 1,000 | 19.8 | (18.6, 21.0) | 1,389 | 66.8 | (63.3, 70.4) | 933 | 40.5 | (37.9, 43.2) | 2,397 | 52.3 | (50.2, 54.4) | 5,719 | 40.3 | (39.3, 41.4) |
| 2012 | 961 | 18.7 | (17.5, 19.9) | 1,415 | 67.9 | (64.3, 71.5) | 844 | 36.5 | (34.0, 39.1) | 2,213 | 48.8 | (46.8, 50.9) | 5,433 | 38.3 | (37.2, 39.3) |
| **Age in years** | | | | | | | | | | | | | | | |
| 15–19 | *b* | *b* | *b* | 184 | 32.5 | (28.0, 37.5) | 112 | 17.9 | (14.8, 21.6) | 275 | 19.5 | (17.3, 21.9) | 0 | 0 | (0, 0) |
| 20–24 | *b* | *b* | *b* | 1403 | 239.3 | (226.9, 252.2) | 879 | 127.7 | (119.4, 136.4) | 2195 | 161.8 | (155.1, 168.7) | 578 | 17.5 | (16.1, 19) |
| 25–29 | 159 | 20.8 | (17.7, 24.3) | 1503 | 267.4 | (254.1, 281.3) | 1073 | 160.6 | (151.1, 170.5) | 2526 | 215.0 | (206.7, 223.5) | 4636 | 136.5 | (132.6, 140.5) |
| 30–34 | 358 | 47.4 | (42.6, 52.6) | 1080 | 192.6 | (181.3, 204.5) | 679 | 112.6 | (104.3, 121.4) | 1794 | 153.9 | (146.8, 161.1) | 5460 | 172.8 | (168.2, 177.4) |
| 35–39 | 428 | 59.2 | (53.7, 65.1) | 597 | 107.1 | (98.6, 116) | 413 | 74.6 | (67.5, 82.1) | 1142 | 94.9 | (89.4, 100.5) | 3981 | 130.4 | (126.4, 134.5) |
| 40–44 | 302 | 43.3 | (38.6, 48.5) | 429 | 73.0 | (66.3, 80.3) | 279 | 47.7 | (42.2, 53.6) | 814 | 60.9 | (56.8, 65.2) | 2454 | 81.5 | (78.3, 84.7) |
| 45–49 | 242 | 33.4 | (29.4, 37.9) | 248 | 38.6 | (34, 43.8) | 173 | 26.6 | (22.8, 30.9) | 557 | 37.8 | (34.7, 41) | 1764 | 54.6 | (52, 57.2) |
| 50–54 | 157 | 22.3 | (18.9, 26) | 128 | 19.6 | (16.3, 23.3) | 94 | 14.0 | (11.3, 17.1) | 311 | 20.1 | (17.9, 22.4) | 1135 | 32.7 | (30.8, 34.7) |
| 55–59 | 103 | 15.0 | (12.3, 18.2) | 92 | 15.3 | (12.3, 18.8) | 75 | 12.2 | (9.6, 15.3) | 194 | 13.7 | (11.8, 15.7) | 636 | 17.9 | (16.5, 19.3) |
| 60–64 | 77 | 12.6 | (9.9, 15.7) | 76 | 14.4 | (11.3, 18) | 38 | 7.3 | (5.2, 10) | 160 | 13.3 | (11.3, 15.5) | 438 | 13.5 | (12.3, 14.8) |
| 65+ | 63 | 12.3 | (9.5, 15.8) | 75 | 5.6 | (4.4, 7.0) | 59 | 4.5 | (3.4, 5.8) | 152 | 4.9 | (4.2, 5.8) | 337 | 12.2 | (10.9, 13.6) |
| **Race** | | | | | | | | | | | | | | | |
| White | 919 | 12.7 | (11.8, 13.5) | 4,792 | 64.8 | (63, 66.7) | 2,435 | 43.3 | (41.6, 45.1) | 6,397 | 44.6 | (43.5, 45.7) | 14,543 | 41.6 | (40.9, 42.3) |
| Black | 141 | 14.0 | (11.8, 16.6) | 312 | 42.4 | (37.7, 47.4) | 1,212 | 37.9 | (35.7, 40.1) | 1,322 | 43.9 | (41.5, 46.4) | 2,987 | 37.5 | (36.1, 38.9) |
| AI/AN | *b* | *b* | *b* | *b* | *b* | *b* | 23 | 29.5 | (18.6, 44.8) | 26 | 14.9 | (9.7, 22.1) | 53 | 11.1 | (8.3, 14.7) |
| API | 169 | 9.4 | (8.0, 10.9) | 32 | 23.9 | (16.2, 34.6) | 33 | 16.9 | (11.5, 24.3) | 111 | 17.9 | (14.7, 21.6) | 345 | 12.7 | (11.4, 14.2) |

API=Asian/Pacific Islander. AI/AN=American Indian/Alaska Native.

Data on CIN III/AIS from Kentucky, Louisiana, and Michigan 2009–2012; Los Angeles 2010–2012.

[a] Statistic could not be calculated. Los Angeles did not collect data in 2009, and collected only a partial year of data in 2010.

[b] Information based on counts <10 was not presented.

Data analysis was conducted in Atlanta during 2016.

**Table 2**

High-Grade Cervical Cancer Precursors (CIN III/AIS) and ICC Rates by Registry and Histologic Type, 2009–2012

| | Glandular | | | | | Squamous | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Adenocarcinoma in situ (AIS) | | Invasive adenocarcinoma (IA) | | Rate ratio | Cervical intraepithelial neoplasia grade III (CIN III) | | Invasive cervical carcinoma (ICC) | | Rate ratio |
| | N | Rate | N | Rate | AIS:IA | N | Rate | N | Rate | CIN: ICC |
| All registries | 822 | 1.8 | 1,004 | 2.1 | 0.9 | 20,948 | 45.2 | 2,591 | 5.2 | 8.7 |
| Los Angeles | 157 | 1.6 | 252 | 2.5 | 0.6 | 1,804 | 17.6 | 524 | 5.1 | 3.5 |
| Kentucky | 176 | 2.2 | 204 | 2.3 | 1.0 | 5,639 | 67.7 | 546 | 6.0 | 11.3 |
| Louisiana | 67 | 0.8 | 152 | 1.7 | 0.5 | 3,807 | 41.5 | 619 | 6.7 | 6.2 |
| Michigan | 422 | 2.4 | 396 | 2.0 | 1.2 | 9,698 | 53 | 902 | 4.4 | 12.0 |

AIS:IA ratio = The rate of adenocarcinoma in situ diagnosed divided by the rate of invasive adenocarcinoma.

CIN:ICC ratio = The rate of CIN III diagnosed, divided by the rate of invasive cervical carcinoma.

Glandular lesion definitions:

- Glandular cancer precursors (adenocarcinoma in situ) were defined as the following ICD-O-3 histology code: 8140.
- Invasive glandular cancers (adenocarcinomas) were defined as the following ICD-O-3 histology codes: 8015, 8140–8149, 8160–8162, 8190–8221, 8260–8337, 8350–8551, 8560, 8570–8576, 8940–8941 and were microscopically confirmed.

Squamous lesion definitions:

- Squamous intraepithelial lesions were defined as the following ICD-O-3 histology codes: 8010, 8050, 8052, 8070–8072, 8076, 8077.
- Invasive squamous cell carcinomas were defined as the following ICD-O-3 histology codes: 8050–8084, 8120–8131 and were microscopically confirmed.

Data analysis was conducted in Atlanta during 2016.