

Assessing the Burden of HPV-Associated Cancers in the United States

Supplement to Cancer

Total Burden and Incidence of In Situ and Invasive Cervical Carcinoma in Michigan, 1985-2003

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BACKGROUND. With the recent licensure of a vaccine that protects against human papillomavirus (HPV) types 16 and 18, US women are expected to experience lower rates of cervical cancer. However, surveillance systems must be in place in the US to measure the real-world effectiveness of vaccination programs. Although population-based registries will provide invasive cervical cancer (ICC) incidence and burden data, the impact of HPV vaccine on cervical cancer will not be measurable for several decades. Cervical carcinoma in situ (CIS), a cervical precancer and the immediate precursor to ICC, is an earlier presentation of HPV-related cervical disease that affects a much larger number of women, and monitoring trends in CIS could provide an earlier measure of HPV vaccine effectiveness. Currently, registries do not collect data on CIS except for the state cancer registry in Michigan, which has been continually collecting CIS data since 1985.

METHODS. All cases of CIS and ICC diagnosed from 1985 through 2003 in the Michigan registry were identified. Available data include age at diagnosis, race, morphologic tumor type, and tumor behavior.

RESULTS. There were 58,144 cases of CIS and ICC, of which 48,272 (83.0%) were CIS and 9872 (17.0%) were ICC. There were 2928 CIS cases and 413 ICC cases diagnosed in Michigan during 2003, compared with 1577 CIS and 516 ICC cases reported in 1985. Age-adjusted CIS rates increased from 1985 (31.7 per 100,000) to 2003 (59.2 per 100,000); rates of CIS were highest among women age <40 years. Age-adjusted rates of ICC have declined since 1990, when the rate was 14 per 100,000 females; the rate is currently down to 7.8 per 100,000 females in 2003.

CONCLUSIONS. The rising rates of CIS in women age <40 years, coupled with declining rates of ICC, suggests the important role of early CIS detection in the prevention of ICC. The CIS trend data, used in conjunction with ICC trend data, help to provide a more thorough picture of cervical disease in the state and also provide baseline data regarding CIS burden in a prevaccine era. The experiences of the Michigan registry can inform the development of CIS surveillance in other registries, an important potential registry role relative to monitoring cervical cancer prevention efforts. *Cancer* 2008;113(10 suppl):2946-54. Published 2008 by the American Cancer Society.*

KEYWORDS: cervical carcinoma, in situ cervical carcinoma, State of Michigan, human papillomavirus.

Although cervical cancer rates in the US have decreased dramatically in the era of cervical screening (approximately 12,000 cases in 2005), US women are expected to experience a further decline in

cervical cancer rates due routine vaccination of 11- and 12-year-old girls with the recently licensed vaccine that protects against human papillomavirus (HPV) types 16 and 18 (the 2 HPV types responsible for approximately 70% of cervical cancers worldwide).^{1,2} Although clinical trial data regarding vaccine efficacy are promising, the real-world effectiveness has yet to be demonstrated, and may prove to be less than expected. Challenges to the real-world effectiveness of the HPV vaccine in the US include 1) affordability of the vaccine to populations at risk (at a cost of \$360 for the 3-dose series), 2) acceptability of a vaccine that prevents a sexually transmitted infection by parents of young girls, and 3) a potential loss of effectiveness of cervical screening programs if immunized women do not continue to appear for routine cervical screening due to a false sense of security conferred by HPV vaccination (they are still at risk for cervical cancer due to oncogenic HPV types other than 16 or 18).

Invasive cervical cancer (ICC) incidence and burden data are routinely collected by population-based registries throughout the US. These include population-based cancer registries participating in the Centers for Disease Control and Prevention's (CDC) National Program of Cancer Registries (NPCR, based on statewide populations) and the National Cancer Institute's (NCI) Surveillance, Epidemiology, and End Results Program (SEER, based on regional populations in states or metropolitan areas); together, these data repositories currently cover 100% of the US population. The NPCR and the SEER programs continuously monitor incident ICC cases as well as ICC-related deaths.^{3,4}

These registries will be the single most important data source on potential reductions in cervical cancer in the vaccine era (just as they have been in the era of screening). However, because the impact of vaccinating 11-year-old and 12-year-old girls will not be measurable until these girls reach late adulthood, the impact of HPV vaccine will not be measurable for several decades. Cervical carcinoma in situ (CIS) is a cervical precancer, and if detected through screening and promptly treated, CIS will not develop into ICC. CIS is the immediate precursor to ICC, is an earlier presentation of HPV-related cervical disease that affects a much larger number of women, and monitoring trends in CIS could provide an earlier measure of HPV vaccine effectiveness. The registries are well positioned to conduct CIS surveillance, because the currently existing infrastructure (especially the expertise of cancer registrars, well-established data streams, and extensive population coverage) could be leveraged to collect these addi-

tional data on CIS cases. A CIS surveillance system that had to be created *de novo* would be considerably more difficult to create and maintain. Currently, trends and demographic factors associated with CIS are largely unknown because NPCR and SEER registries (with 1 exception) do not collect these data because of a joint decision made by CDC, the NCI, and the American College of Surgeons (ACS) to recommend against the collection of cases of CIS after January 1, 1996. The decision was made because of a concern over the loss of comparability in incidence data over time.⁵⁻⁷ A general discussion of this decision and the rationale behind it is presented elsewhere in this supplement.⁸ Despite this decision, the Michigan registry continued to collect data on CIS.

The Michigan Cancer Surveillance Program (MCSP) is a statewide population-based registry in operation since 1981, with legally mandated cancer reporting and statewide population coverage since 1985. It has been funded through the NPCR since 1995. The MCSP also receives data from the Metropolitan Detroit Cancer Surveillance System (MDCSS), part of the national SEER program covering 3 counties in southeastern Michigan. MDCSS provides 42% of the case reports. The MCSP covers a state population of 10.1 million that is 81.3% white, 14.3% black, 2.2% Asian and Pacific Islander, 0.6% American Indian, and approximately 3.8% Hispanic.⁹ From 1985 through 2003, all *in situ* and invasive cancers (other than basal or squamous cell carcinoma of nongenital skin) were reportable to the MCSP, with reportable conditions defined by the Michigan Administrative Code under the authority of Public Act 82 of 1984.

A key consideration behind the MCSP decision to continue CIS data collection was the belief that continued surveillance of CIS within a passive registry and with no active patient follow-up would represent only a modest operating cost to the registry. Furthermore, it was believed that reporting of CIS would inform the efforts of the Michigan Breast and Cervical Cancer Control Program (BCCCCP) and the Cervical Cancer Advisory Committee (CCAC) of the Michigan Cancer Consortium. The early detection of cervical cancer is a key objective of the BCCCCP, making the incidence of cervical carcinoma, including CIS, of particular importance. The CCAC, whose charge is to monitor cervical cancer in Michigan and identify statewide cancer control goals and objectives related to cervical cancer, believed that the CIS data were important to guide statewide cervical screening strategies. The MDCSS also agreed to continue to collect and report CIS diagnosed in facilities within its coverage area, because it was thought that the

added burden of this collection was not significant and the data could provide important estimates of the future ICC burden.

Cervical CIS is collected by MSCP in 1 of 2 diagnostic categories: 1) "carcinoma in situ" or 2) class 3 cervical intraepithelial neoplasia (CIN3) without any qualifier. A diagnosis of "CIN3—severe dysplasia" is not reportable. Since 2000, data on CIS cases have been included in at least 2 ongoing research projects (unpublished data).

The Michigan data currently represent the only source of population-based information on cervical CIS that has been continuously collected since 1985. This article presents what to our knowledge is the first published report on incidence rates and trends of both CIS and ICC reported in Michigan from 1985 through 2003 and examines demographic and disease-related factors associated with these diagnoses.

MATERIALS AND METHODS

All cases of CIS and ICC were identified from data reported to the MCSP and grouped by morphology codes into squamous cell carcinoma, adenocarcinoma, adenosquamous carcinoma, and other and unspecified carcinomas. Cervical tumors other than carcinomas or those not microscopically confirmed were excluded from the analysis. The morphology codes used to create these groupings are described elsewhere in this supplement.¹⁰

All cases among women residing in Michigan at the time of their diagnosis between the years 1985 and 2003 were selected. This dataset was used in the tabulation of incident cases and in the calculation of incidence rates for CIS and ICC by age. Analyses of incidence by race were limited to white and black women, because there were either too few cases or inadequate population data for meaningful analyses of other racial and ethnic groups. Total figures and rates include other and unknown racial data. The 2000 Michigan Census data for females, by race, were used in the calculation of age-adjusted rates of ICC and CIS. All rates are expressed per 100,000 females and are age-adjusted unless otherwise specified.

All analyses were conducted by use of FoxPro, Excel, Joinpoint (version 3.0), and SAS (version 9.1) statistical software. Statistical differences in categorical frequencies were tested by calculating Z scores for differences between proportions, using the normal approximation to the binomial, whereas differences in the ratio of ICC to CIS rates were determined by calculating confidence intervals for the resulting odds ratios to determine whether the value crossed

1. Confidence intervals for age-adjusted rates were calculated for the purpose of testing differences in age-adjusted rates. Joinpoint trend shifts were determined on the basis of the Z score of the regression coefficient for the estimated intercepts. The level of significance was $\alpha = .05$ for all analyses.

RESULTS

For the period 1985 through 2003, there were 58,144 cases of CIS and ICC reported, of which 48,272 (83.0%) were CIS and 9872 (17.0%) were ICC (see Table 1). Of the 974,054 reported in situ and invasive cases of all sites and types in Michigan between 1985 and 2003, ICC represented 1% and CIS represented 5% of all cases.

In Situ Cervical Cancer

Reported cases of CIS increased from 1577 in 1985 to 3090 in 2000, with little variation since that time (Table 1). Age-adjusted rates for CIS increased from 31.7 per 100,000 females in 1985 to 61.9 in 2003, rising from 31.7 per 100,000 females in 1985 to 61.9 in 2000 and dropping slightly to 59.2 in 2003 (Fig. 1). Trend estimation using Joinpoint indicates a rising trend line for rate from 1985 through 1991, with a continued increase in rate from 1991 through 2003, but at only one-third the rate of increase observed before 1991 (data not shown).

Age-adjusted CIS rates were similar for white and black women in 2003 (46.0 and 48.0, respectively) (Table 1). Rates of CIS were significantly higher for black women than white women in the years 1985, 1996, 1997, and 1999. White and black rates have been similar since 2000. The Joinpoint estimated trend line slope for white women follows the same pattern as the overall trend mentioned above, with rate declines since 2000 not found to be statistically significant. The Joinpoint trend lines estimates for black women rose more slowly from 1985 and extending to 1999, followed by a statistically significant declining rate trend during 2000-2003 (Fig. 1).

Invasive Cervical Cancer

Case frequencies for ICC in Michigan increased from 516 cases in 1985 to 658 cases in 1990, then declined to 413 cases reported in 2003 (Table 1). Joinpoint analysis of these data identifies an increasing rate of ICC incidence from 1985 through 1989 and then a sharply declining incidence rate from 1990 through 2003 (data not shown).

Overall, the age-adjusted ICC rates are higher for black women compared with white women in Michi-

TABLE 1
Number and Age-adjusted Rates of In Situ and Invasive Carcinomas of the Cervix Uteri by Year of Diagnosis and Race, Michigan, 1985-2003*

Year of Diagnosis	Total				White				Black			
	In Situ		Invasive		In Situ		Invasive		In Situ		Invasive	
	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate
1985	1577	31.7	516	11.7	1183	28.0	405	10.6	235	38.4 [†]	98	19.1 [†]
1986	1643	32.0	543	12.1	1246	28.9	428	10.9	199	29.8	90	18.4 [†]
1987	1854	36.0	521	11.5	1442	33.2	396	10.2	228	34.0	100	19.8 [†]
1988	1902	36.5	616	13.2	1507	34.5	481	12.0	199	29.2	105	19.6 [†]
1989	2105	40.6	605	13.0	1700	39.0	496	12.5	213	30.2	91	15.9
1990	2494	48.2	658	14.0	1955	45.3	529	13.2	287	39.8	107	18.1 [†]
1991	2730	52.0	584	12.2	2096	48.0	450	11.0	339	45.8	114	20.4 [†]
1992	2507	47.8	559	11.6	1897	43.7	448	10.9	275	36.9	91	15.3 [†]
1993	2612	50.3	537	11.0	1998	46.5	415	10.0	290	38.6	104	16.8 [†]
1994	2557	49.3	508	10.3	1880	44.0	395	9.4	322	42.3	95	15.5 [†]
1995	2766	53.6	484	9.7	2008	47.2	363	8.5	395	52.1	95	15.0 [†]
1996	2946	56.7	520	10.2	2063	48.4	401	9.3	453	58.0 [†]	93	14.5 [†]
1997	2784	53.8	541	10.6	1975	46.6	418	9.7	428	54.8 [†]	106	16.4 [†]
1998	2902	56.4	504	9.8	2072	49.3	388	9.0	424	54.2	96	14.1 [†]
1999	2912	57.2	443	8.5	1989	47.8	343	7.9	478	61.4 [†]	90	13.5 [†]
2000	3090	61.9	460	8.8	2194	54.7	361	8.2	436	55.4	80	12.2 [†]
2001	2949	59.2	453	8.7	2082	52.0	351	8.0	409	52.2	89	13.0 [†]
2002	3014	60.7	407	7.8	1924	48.4	305	7.0	375	47.5	77	11.0 [†]
2003	2928	59.2	413	7.8	1817	46.0	289	6.6	377	48.0	85	11.8 [†]

*Age-adjusted rates are per 100,000 population and are computed by the direct method using the 2000 US standard population. Population data in 19 age groups are from the Michigan Information Center, Michigan Department of Management and Budget.

[†]Significantly different from the proportion for white females at $\alpha = .05$.

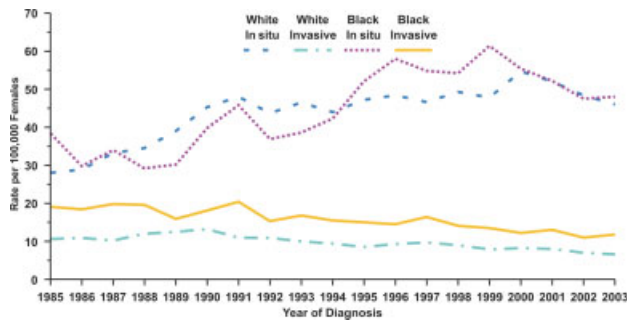


FIGURE 1. Age-adjusted in situ and invasive cervical carcinoma rates by race and year of diagnosis in female Michigan residents, 1985 through 2003.

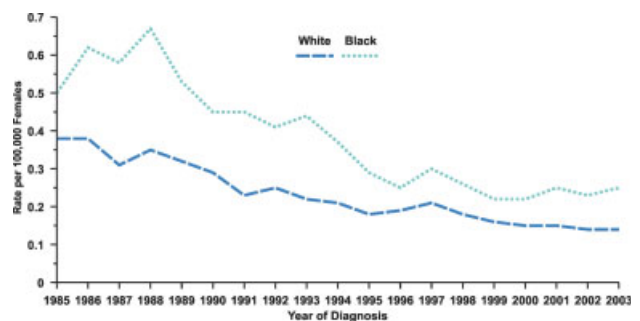


FIGURE 2. Ratio of age-adjusted invasive to in situ cervical carcinoma rates by race and year of diagnosis in female Michigan residents, 1985 through 2003.

gan ($P < .05$) (Table 1). The incidence rate of ICC for blacks averaged 80% above white rates over the time period. In 1985, the rate of ICC among black women, at 19.1, was 80% above the rate of 10.6 observed for white women. By 2003, the ICC rate among black women had declined to 11.8, which was still 80% higher than the rate of 6.6 for white women. Trends in disease rates over time, based upon a Joinpoint analysis, confirm declining ICC incidence rates among black women from 1985 through 2003,

whereas among white women, increasing rates are observed through 1989, with a declining trend since that time. In summary, ICC rates for both white and black women are declining at similar rates, whereas the relative racial disparity in rate has remained unchanged.

Ratio of Invasive to In Situ Cervical Cancers

The ratios of ICC rates to CIS rates for blacks and whites in Michigan are displayed in Figure 2. These

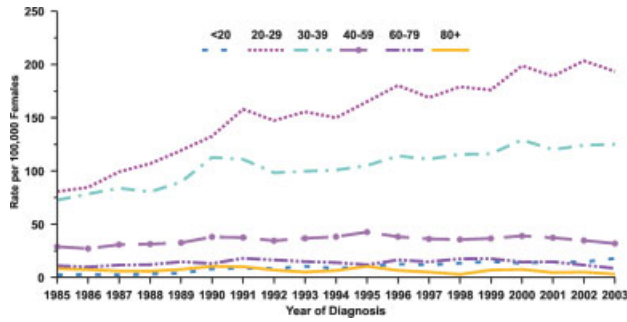


FIGURE 3. Age-specific in situ cervical carcinoma incidence rates by age and year of diagnosis in female Michigan residents, 1985 through 2003.

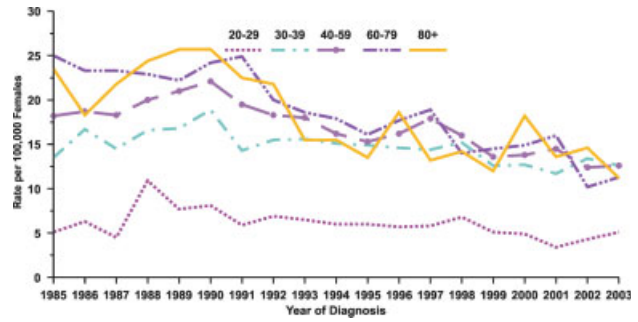


FIGURE 4. Age-specific invasive cervical carcinoma rates by age and year of diagnosis in female Michigan residents, 1985 through 2003.

data indicate a considerable disparity in the ratio between blacks and whites, with ratios for black women noted to be nearly twice that for white women through 1993. The disparity widened during the years 1985 through 1993, began to narrow from 1993 through 1999, and has gradually widened since 2000. Analysis of the trends in this ratio for white and black women corroborates these patterns in disparities. The trend in the ratio of ICC to CIS for whites declined from 1985 through 1996, then continued to decline at a slower rate through 2003. For black women, the trend line increased from 1985 through 1987, and then sharply declined from 1987 through 1996. Since 1996, the trend line slope estimate for black women has been essentially 0. Therefore, despite a considerable decline of the racial disparity in risk during the 1990s, the risk of invasive disease at diagnosis remains much higher for black women, with 1 ICC case for every 4 CIS cases in black women and 1 ICC case for every 7 CIS cases for white women.

Age-specific Rates of In Situ and Invasive Cervical Carcinoma

Observed trends in CIS rates were found to be inversely related to age, with CIS incidence increasing among women aged <40 years and declining among women aged >40 years. The highest incidence rates are noted in women ages 20 to 29 years, whereas the greatest increase in rate was observed in women aged <20 years. The rate observed among women aged <20 years rose from 2.3 in 1985 to 17.8 in 2003 (Fig. 3). Rates for women ages 20 to 29 years increased from 80.7 in 1985 to 193.5 in 2003, whereas rates for women ages 30 to 39 years nearly doubled from 72.6 in 1985 to 125.1 by 2003. Although not apparent from the figure due to scale, the data indicate decreasing rates for women aged ≥40 years. Rates of CIS among women aged ≥40 years have

declined in Michigan since the early 1990s. For women ages 40 to 59 years, the CIS rates rose from 28.8 in 1985 to a peak of 42.6 in 1995, and then declined to 31.8 by 2003. For women aged ≥60 years, a similar pattern of rising then falling rates is observed, with the CIS rate for women ages 60 to 79 years and ≥80 years at 8.5 and 3.0, respectively, in 2003. Joinpoint analysis corroborates that rate trends started statistically significant declines beginning in 1991 for women ages 40 through 59 years and in 1999 for women ages 60 to 79 years. CIS rates for women aged ≥80 years declined throughout the entire period, with a rate of 8.3 in 1985 falling to 3.0 by 2003.

Although rates of CIS declined with age, rates of ICC increased with age (Fig. 4). In 2003, the rate of ICC ranged from 5.1 per 100,000 for women ages 20 to 29 years to 12.6 per 100,000 for women ages 30 to 59 years. Rates of ICC in women aged <20 years could not be calculated because of low case count. For all age groups, the rates of ICC have declined since the early 1990s.

The ratio of ICC rate to CIS rate was found to be strongly associated with advancing age (Fig. 5). Statistically significant declines in the ratios of ICC rate/CIS rate were observed for all age groups <80 years since the early 1990s based upon a Joinpoint analysis, although there were too few ICC cases diagnosed for women aged <20 years to permit ratio calculations. There was no observed trend in this ratio for women aged ≥80 years. In 2003, the ratios ranged from 0.03 ICC cases per CIS case diagnosed (ages 20-29 years) to 3.7 cases of ICC per CIS case diagnosed (women aged ≥80 years).

Histology

The majority (70.3%) of CIS cases diagnosed from 1985 through 2003 were squamous cell type (Table 2). Only 2.1% of CIS cases were adenocarcinoma and

27.5% were reported as other or unspecified carcinoma. The proportion of cases with an unspecified carcinoma was 7.2% among ICC cases ($P < .05$). Among ICC cases, squamous cell cancers remained the most common morphologic type (71.7%), followed by adenocarcinoma (17.2%) (Table 3). Among white women, adenocarcinoma represented 19.3% of all ICC cases, which is more than twice that observed among black women (8.4%, $P < .05$).

DISCUSSION

Between 1985 and 2003, CIS cases outnumbered ICC cases by a ratio of nearly 5:1 (from 3:1 in 1985 to approximately 7:1 in 2003). Trends in the incidence of CIS and ICC demonstrate important changes in these rates from 1985 through 2003. The trends identified vary significantly by age, with CIS being more common in younger women and ICC becoming

increasingly common after 60 years of age. ICC incidence also varies by race, with higher rates of ICC noted in black women throughout the time period.

Although current comparable data on CIS are not readily available from other cancer registries, CIS rates from the California central cancer registry over the years 1988 through 1995 have been published, as have data from SEER (for 1976-1995).^{11,12} Age-adjusted CIS rates identified for Michigan were marginally lower than California rates during 1988 and 1989, but are comparable for 1990 through 1995 for total, white, and black rates. Although California CIS data are not available past 1995, Michigan CIS rates appeared to increase more rapidly than rates in California up to that year. An analysis of CIS using SEER data for the years 1976 through 1995 also identified rising rates of in situ disease.¹² An analysis of SEER data by Sherman et al¹² cited improving cervical sampling devices and methods as contributing to increases in CIS rates through 1995. The increase in CIS rates in the presence of stable survival was associated with declining rates of ICC and cervical cancer mortality. Declines in invasive squamous cell carcinoma and declines in mortality for both squamous cell carcinoma and adenocarcinoma were found.

Increasing CIS rates and decreasing ICC rates during 1985 through 2003 observed in the MCSP data suggest increased success of cervical screening. Two important changes took place on a statewide level in Michigan during this time period. First, in 1991, the National Breast and Cervical Cancer Early Detection Program began funding Michigan's Breast and Cervical Cancer Control Program (BCCCP).¹³ This statewide program provides free or low-cost cer-

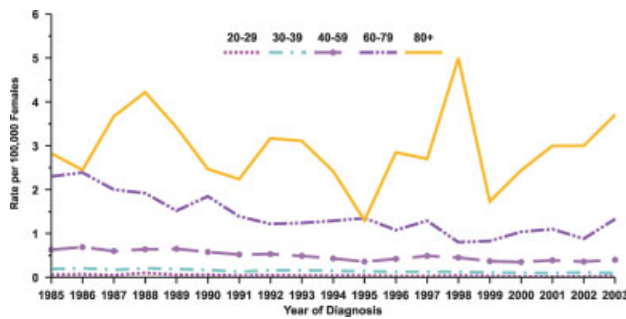


FIGURE 5. Ratio of age-specific invasive to in situ cervical carcinoma rates by age and year of diagnosis in female Michigan residents, 1985 through 2003.

TABLE 2
First Primary In Situ Cervical Carcinoma Cases by Morphologic Type, by Race, and by Age at Diagnosis, Michigan, 1985-2003*

Category	Total		Squamous Cell Carcinoma		Adenocarcinoma		Adenosquamous Carcinoma		Other and Unspecified Carcinoma	
	No.	Percent	No.	Percent	No.	Percent	No.	Percent	No.	Percent
Total	46,461	100.0	32,663	70.3	963	2.1	59	0.1	12,776	27.5
White	35,382	100.0	24,805	70.1	876	2.5	54	0.2	9647	27.3
Black	6389	100.0	4449	69.6	36	0.6	5	0.1	1899	29.7
Age, y										
<20	2443	100.0	1897	77.7	23	0.9	0	0.0	523	21.4
20-29	19947	100.0	14,033	70.4	270	1.4	16	0.1	5628	28.2
30-39	14801	100.0	10,325	69.8	361	2.4	23	0.2	4092	27.6
40-59	7375	100.0	5125	69.5	268	3.6	15	0.2	1967	26.6
60-79	1610	100.0	1100	68.3	34	2.1	5	0.3	471	29.3
≥80	192	100.0	125	65.1	6	3.1	0	0.5	61	31.3
Unknown	93	100.0	58	62.4	1	1.1	0	0.0	34	36.6

*Histology categories are defined in Watson et al 2008.¹⁰

TABLE 3
First Primary Invasive Cervical Carcinoma Cases by Morphologic Type, by Race, and by Age at Diagnosis, Michigan, 1985-2003*

Category	Total		Squamous Cell Carcinoma		Adenocarcinoma		Adenosquamous Carcinoma		Other and Unspecified Carcinoma	
	No.	Percent	No.	Percent	No.	Percent	No.	Percent	No.	Percent
Total	8472	100.0	6075	71.7	1461	17.2	322	3.8	614	7.2
White	6637	100.0	4639	69.9	1283	19.3	270	4.1	445	6.7
Black	1567	100.0	1255	80.1	132	8.4	47	3.0	133	8.5
Age, y										
<20	33	100.0	20	60.6	4	12.1	0	3.0	9	27.3
20-29	731	100.0	517	70.7	93	12.7	19	4.0	102	14.0
30-39	1950	100.0	1395	71.5	314	16.1	95	5.8	146	7.5
40-59	3247	100.0	2362	72.7	569	17.5	131	4.9	185	5.7
60-79	2056	100.0	1501	73.0	370	18.0	65	3.9	120	5.8
≥80	447	100.0	276	61.7	109	24.4	12	3.8	50	11.2
Unknown	8	100.0	4	50.0	2	25.0	0	0.0	2	25.0

*Histology categories are defined in Watson et al 2008.¹⁰

vical cancer screening to women ages 40 to 64 years who are uninsured or underinsured and have incomes <250% of the Federal Poverty Level. Evidence suggests that the majority of ICC cases occur in women who have either never had a Papanicolaou (Pap) test or have not had 1 within the previous 5 years.¹⁴ Based on this finding, the Michigan BCCCP is making a concerted effort to identify and recruit women ages 40 to 64 years who have been “rarely or never-screened” for cervical cancer. Currently, >20% of the women new to the BCCCP are in this group. Second, beginning in 1999, the Michigan BCCCP has worked with the state’s Family Planning program to provide follow-up cervical cancer diagnostic services for younger women served by Family Planning agencies throughout Michigan. Since 2001, all women diagnosed with CIN 2 or higher through the Michigan BCCCP have been eligible to apply for Medicaid to pay for treatment.

The introduction in 1991 of coverage by Medicare for cervical cancer screening has been found to have reduced the ratio of ICC to CIS for women aged >65 years in California.¹¹ Michigan data indicate improved ratios of ICC to CIS for women ages 60 to 79 years; however, the falling trend in this ratio predated the 1991 policy change. There was no observed decrease for women aged >80 years.

According to data from the Michigan Behavioral Risk Factor Surveillance System (BRFSS), the proportion of women who did not receive cervical screening within the last 3 years remained relatively stable (range 12%-17%) during 1992 through 2002.¹⁵ This should not, however, be interpreted as conclusive

evidence that increased screening in at-risk populations did not occur because the BRFSS is a telephone survey and women benefiting from newer Michigan screening initiatives may be underrepresented. In addition, BRFSS data could not be evaluated by age group to further delineate any changes.

The joint decision by CDC, NCI, and ACS to recommend against the collection of cases of CIS after January 1, 1996, was made due to a concern over the loss of comparability in incidence data over time, especially with the increasing implementation of the Bethesda classification system. As can be seen by the data presented in our report, there is no evidence of any sudden shift in incidence during the early and mid-1990s, when the Bethesda protocol was introduced.^{16,17} This suggests any increase in CIS is not due to changes in diagnostic classifications. During the time period for which CIS data were collected, efforts in Michigan have emphasized distinguishing dysplastic disease from CIS by reporting facilities, in an attempt to separate CIS cases from non-CIS cases with severe dysplasia. It is not clear, however, whether or to what extent this distinction is actually being made by the diagnosing pathologist.

An extensive analysis of the Michigan data to accurately measure the degree to which the Bethesda protocol has caused dysplastic conditions (ie, “not CIS”) to be reported as CIS should be conducted. A review of the frequency of coding cases to ICD-0 third edition code 8077 of 2 (squamous intraepithelial neoplasia, grade 3 or CIN 3) does indicate an increase in the use of this code over the time period. In 1992, when the 8077 code was first introduced

into the morphology coding scheme, 46.3% of Michigan's CIS cases were coded to 8077 of 2. By 2003, this percentage had risen to 72.6%.

The findings presented in this report indicate the usefulness of CIS incidence data for estimating disease burden, incidence, and trends. They also provide baseline data for CIS burden in a prevaccine era. The CIS trends, used in conjunction with ICC trends, provide a more complete picture of the effectiveness of cervical cancer prevention programs. As such, these data can be used to guide future cervical screening strategies, especially in addressing health disparities across different racial groups. In addition, the younger mean age of women diagnosed with CIS provides an earlier measure of the impact of cervical cancer prevention programs including screening and vaccination than does measuring ICC alone. The surveillance data may also provide evidence for the success of HPV vaccination if decreased rates of ICC are seen in conjunction with decreasing CIS rates.

There are several limitations to these data. The analysis was limited to examining rates and trends for white and black women only. The lack of adequate numbers of Hispanic, American Indian, and Asian/Pacific Islander women in Michigan limits the usefulness of the data for these populations; there were a high percentage of women with unknown race in the dataset, particularly those with CIS. In addition, because of the small number of nonsquamous cell cancers, we could not evaluate trends by morphology type. Finally, MCSP is a passive surveillance registry and although the accuracy and completeness of invasive cancer data meet NAACCR standards, this has not been evaluated for CIS. However, the MCSP does receive approximately 42% of its reports from the MDCSS, which obtains records through active surveillance, and an additional 43% are received from hospitals with cancer registries, suggesting that data completeness and quality may be similarly high.

Michigan has found that the collection of CIS cases can be accomplished efficiently while limiting the burden to reporting facilities. Our experience has been that CIS data are obtainable and useful; data collection was conducted without the use of additional funds. The resulting data provide insight into the prevalence of cervical disease in the statewide population. Possible future uses of these data include estimating the healthcare costs of CIS and assessing the burden of CIS surveillance on registry function. Michigan is currently participating in a feasibility study of ongoing population-based CIN 3 surveillance to continue and expand surveillance of precancerous cervical lesions in Michigan.

Conclusions

Michigan cancer registry data demonstrate an increasing CIS trend accompanied by a decreasing ICC trend over the same time period, suggesting success of cervical screening in preventing ICC. The increasing rate of precancerous cervical lesions underscores the importance of regular cervical cancer screening to prevent invasive disease and suggests the impact of an effective HPV vaccine on women's health will be considerable.

CIS data have provided useful baseline (prevaccine) data as well as adjunctive data on cervical cancer in Michigan. CIS data collection in Michigan has proven to be feasible. Increased costs related to CIS reporting were not an issue because this registry is not a follow-up registry. Conducting case surveillance alone for CIS is not costly. Another concern that led to the discontinuation of CIS data collection through NPCR and SEER, that changing diagnostics would erode the comparability of CIS trend data, does not appear to have been warranted, given the quality of the Michigan CIS data. However, additional work needs to be done to determine the accuracy of incidence data for this diagnosis. We hope that the experience of CIS data collection in the MSCP can inform the development of cervical CIS surveillance activities in other registries. This type of expanded registry function can play an important role in monitoring future progress in cervical cancer prevention.

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