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Trends in cervical cancer incidence rates by age, race/ethnicity, histological subtype, and stage at diagnosis in the United States

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ABSTRACT

Recent trends of cervical cancer incidence by histology and age in the United States (U.S.) have not been reported. We examined contemporary trends in cervical squamous cell carcinoma (SCC) and adenocarcinoma (AC) incidence rates in the U.S. by age group, race/ethnicity, and stage at diagnosis after accounting for hysterectomy. Incidence data (1999–2015) were obtained from the U.S. Cancer Statistics Incidence Analytic Database. Hysterectomy prevalence was estimated using National Health Interview Survey data (2000–2015). Overall SCC incidence rates continued to decrease in all racial/ethnic groups except among non-Hispanic whites in whom rates stabilized in the 2010s, largely driven by stable trends in ages < 50 years and a slower pace of decrease in ages 50–59 years. After a stable trend between 1999 and 2002, AC incidence rates among non-Hispanic whites rose during 2002–2015 (1.3% per year), mostly due to increases in ages 40–49 (4.4% annually since 2004) and 50–59 years (5.5% annually since 2011). Overall AC incidence rates during 1999–2015 decreased in blacks and Hispanics but were stable in Asian/Pacific Islanders; in all these race/ethnicities, rates were generally stable in ages < 50 years but decreasing in older ages. Rates of distant stage cervical SCC and AC among non-Hispanic whites increased in several age groups but were generally stable in non-whites. Increasing or stabilized incidence trends for AC and attenuation of earlier declines for SCC in several subpopulations underscore the importance of intensifying efforts to reverse the increasing trends and further reduce the burden of cervical cancer in the U.S.

1. Introduction

Although overall cervical cancer incidence rates in the United States have declined steadily since the mid-20th century (Jemal et al., 2013; Smith et al., 2018; Van Dyne et al., 2018), previous studies reported an increase in cervical adenocarcinoma incidence rates since the late 1970s, particularly among younger women (Wang et al., 2004; Zheng et al., 1996; Zhu et al., 2015). However, those studies did not account for hysterectomy prevalence, which is considerable in the U.S. (e.g., 25% in ages 50–54 years) and varies by age group and race/ethnicity (Beavis et al., 2017). Thus, without correction for hysterectomy prevalence, comparisons of endometrial and cervical cancer incidence rates across age and racial/ethnic groups would be biased (Siegel et al., 2013). In addition, earlier studies of incidence trends by histological subtype were based on data from the Surveillance, Epidemiology, and End Results (SEER) Program covering only 10%–12% of the U.S. population, which may not be representative of the entire population, especially when examining differences in trends according to race and ethnicity. Further, the most recent study examined the trends by age and histology through 2010 (Zhu et al., 2015), and thus it is unclear whether the reported increase for cervical adenocarcinoma is continuing.

Herein, we extend previous studies by examining contemporary trends in cervical cancer incidence rates in the U.S. by age, race/ethnicity, major histological subtypes, and stage at diagnosis using up-to-date nationwide data after accounting for hysterectomy prevalence.

2. Methods

The number of incident cases of malignant cervical cancer during 1999–2015 by age group, race/ethnicity, histology, histological confirmation status, and stage at diagnosis were obtained from the U.S. Cancer Statistics Incidence Analytic Database as reported by the Centers for Disease Control and Prevention's National Program of Cancer Registries and the National Cancer Institute's SEER Program, which collectively approached complete coverage of the U.S. population (CDC/NCI, 2017). Cervical cancers were defined as topography code C53 according to the International Classification of Diseases for Oncology, third edition (ICD−O−3), with histology codes 8000-9992 for all histologies combined, 8050-8084 for squamous cell carcinoma

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(SCC), 8140-8550/8570-8576 for adenocarcinoma, 8560-8563 for adenosquamous carcinoma, and 8000-8022 for cervical cancers with unknown histology or unspecified carcinomas. Due to sparse data, other histologic subtypes were not examined separately. We used data on stage of diagnosis from 2001 to 2015, for which records based on the SEER Summary Stage 2000 were available; stages were coded as localized, regional, distant, and unstaged. Race/ethnicity was coded as non-Hispanic white (white), non-Hispanic black (black), non-Hispanic Asian/Pacific Islander (Asian/PI), and Hispanic. Age groups were defined as < 20, 30–39, 40–49, 50–59, 60–69, and ≥70 years. We do not show results for ages < 20 years due to sparse data, but this age group is included in results for all ages combined throughout this article.

The total number of cervical cancer cases during 1999–2015 was 218,244; the total number by histological subtype was 145,545 (66.7%) for SCC, 46,540 (21.3%) for adenocarcinoma, 7278 (3.3%) for adenosquamous carcinoma, and 13,707 (6.3%) for cervical cancers with unknown histology or unspecified carcinomas. The number of cases with a histologically confirmed diagnosis was 210,238 (96.3%) for all cervical cancers, 143,566 (98.6%) for SCC, 45,951 (98.7%) for adenocarcinoma, and 7245 (99.5%) for adenosquamous cell carcinoma. The proportion of histologically confirmed cancers with information on stage at diagnosis during 2001–2015 was 94.6% for all cervical cancers, 94.5% for SCC, and 96.0% for adenocarcinoma. Data on hysterectomy during the study period (1999–2015) by age group and race/ethnicity were obtained from the 2000, 2005, 2010, 2013, and 2015 National Health Interview Surveys (Appendix Table 1), as women were only queried about hysterectomy in those years (National Center for Health Statistics, 2018).

2.1. Statistical methods

Hysterectomy prevalence was calculated using SAS-Callable SUDAAN (version 9.4) after accounting for sample size (weighted) and complex survey design of the National Health Interview Survey. To impute annual hysterectomy prevalence, we assumed a linear trend in hysterectomy prevalence between each two consecutive survey years with available data; for 1999, however, hysterectomy prevalence was estimated based on backward extension of the trend between 2000 and 2005. The number of women at risk for cervical cancer in each year, age group, and race/ethnicity was estimated based on the proportion of women with hysterectomy (P_{hyst}) and number of women in the general population (N_{pop}) in the corresponding stratum: $N_{at\text{-}risk} = N_{pop} - (P_{hyst} \times N_{pop})$. Then, we calculated hysterectomy-corrected age-standardized cervical cancer incidence rates (2000 U.S. standard population) in each year (1999–2015) by age and race/ethnicity using Stata software (version 13.1).

We examined trends in the age-standardized incidence rates during 1999–2015 by age group, race/ethnicity, histological subtype, and stage at diagnosis using Joinpoint Regression Program (version 4.6.0.0). We specified a logarithmic transformation of age-standardized rates and a maximum number of two joinpoints to avoid capturing unstable trends due to relatively small numbers of cases in some age and racial/ethnic groups. We repeated this analysis by stage at diagnosis (2001–2015) for all cervical cancers combined, SCC, and adenocarcinoma by age group among whites and all U.S. women, and for all age groups combined among other race/ethnicities. To provide information on contemporary incidence patterns, we also examined incidence trends in the last 5 years of the study period (2011–2015). We present hysterectomy-corrected incidence trends for histologically confirmed cervical cancer by stage at diagnosis. In supplementary analyses, we similarly examined trends in age-standardized incidence rates without correction for hysterectomy, as well as trends with inclusion of cancer cases without a histologically confirmed diagnosis.

3. Results

3.1. Cervical cancer (all histologies combined)

Among whites, the overall incidence rate of histologically confirmed cervical cancer decreased by 4.1% per year from 1999 to 2003 and by 1.1% per year from 2003 to 2013; rates stabilized afterwards (from 2013 to 2015) (Appendix Table 2). The stabilization of the rates during the most recent period largely reflects increases in rates in ages 40–49 years since 2004 and in ages 30–39 years since 2012 and the stabilization of rates in ages 50–59 years since 2011. Among blacks and Asian/PIs, overall cervical cancer incidence rates continuously decreased in almost all age groups throughout 1999–2015. Similar patterns occurred among Hispanics, except for ages 40–59 years, among whom the pace of declines slowed or rates stabilized in more recent years.

3.2. Cervical SCC

Overall incidence rates of histologically confirmed cervical SCC decreased during 1999–2015 in all race/ethnicities and all age groups, except Asian/PIs aged 20–29, among whom rates were stable and the number of cancer cases per 100,000 was < 1 (Table 1). Among whites, however, overall cervical SCC incidence rate was stable during the most recent years (2011–2015) largely driven by stable trends in ages < 50 years. In contrast, rates continued to decrease in older ages during 2011–2015, although the decrease substantially attenuated in ages 50–59 years (Table 1, Fig. 1). Among Hispanics, although overall cervical SCC rate continued to decline during 2011–2015, in some age groups rates stabilized (30–39 years) or the pace of declines slowed (50–69 years). Among blacks and Asian/PIs, cervical SCC incidence rates continued to decrease in almost every age group during 2011–2015.

3.3. Cervical adenocarcinoma

Among white women, the overall incidence rate of histologically confirmed cervical adenocarcinoma increased during 2002–2015 (1.3% annually), after a stable trend in 1999–2002 (Table 2). This increase was largely confined to ages 40–49 years (4.4% per year during 2004–2015) and 50–59 years (5.5% per year during 2011–2015) (Fig. 1). In contrast, rates were stable in ages 60–69 years and declined in ages 20–29 and ≥ 70 years throughout 1999–2015. In ages 30–39 years, rates increased between 1999 and 2009 but stabilized afterwards.

Among black women, although overall cervical adenocarcinoma rates showed a decline during 1999–2015 (1.9% annually), rates stabilized in more recent years. Overall rates continued to decrease in Hispanics (0.9% annually) and remained stable in Asian/PIs throughout 1999–2015. By age group, except for an increase in incidence rates of histologically confirmed cervical adenocarcinoma among blacks aged 30–39 years, trends were stable in ages < 50 years and generally declined in older age groups among black, Hispanics, and Asian/PIs throughout 1999–2015.

3.4. Trends by stage at diagnosis

Among whites, age-standardized rates of localized and regional stage cervical cancer, SCC, and adenocarcinoma were stable or decreased between 2001 and 2015 in all age groups except for women aged 40–49, among whom rates of localized and regional stage adenocarcinoma increased (Fig. 2, Appendix Table 3). In other race/ethnicities, incidence rates of localized and regional stage cervical cancer and SCC decreased from 2001 to 2015, but for cervical adenocarcinoma, they remained stable, except for a decrease in regional stage adenocarcinoma among blacks (Fig. 3).

Table 1
Incidence rates (2011–2015) and trends (1999–2015) for histologically confirmed cervical squamous cell carcinoma by age and race/ethnicity after accounting for hysterectomy, United States.

Cancer by age and race/ethnicity	Trends 1995–2015						AAPC 1999–2015	AAPC 2011–2015	Average rate and *N* 2011–2015	
	Trend 1		Trend 2		Trend 3					
	Years	APC	Years	APC	Years	APC			Annual *N*	Rate
Non-Hispanic white										
20–29 years	1999–2004	−9.1[a]	2004–2015	−0.5			−3.3[a]	−0.5	249	2.0
30–39	1999–2013	−2.2[a]	2013–2015	5.9			−1.2[a]	1.8	851	7.6
40–49	1999–2011	−1.8[a]	2011–2015	2.1			−0.8	2.1	1106	9.9
50–59	1999–2002	−8.6[a]	2002–2006	−2.5	2006–2015	−0.8[a]	−2.7[a]	−0.8[a]	1113	9.5
60–69	1999–2015	−3.9[a]					−3.9[a]	−3.9[a]	769	9.2
≥70	1999–2015	−3.0[a]					−3.0[a]	−3.0[a]	575	7.6
All ages	1999–2003	−4.9[a]	2003–2013	−1.9[a]	2013–2015	2.2	−2.1[a]	0.1	4665	5.4
Non-Hispanic black										
20–29 years	1999–2015	−2.9[a]					−2.9[a]	−2.9[a]	69	2.1
30–39	1999–2015	−2.5[a]					−2.5[a]	−2.5[a]	226	8.2
40–49	1999–2015	−2.4[a]					−2.4[a]	-2.4[a]	332	14.1
50–59	1999–2005	−7.2[a]	2005–2015	−1.5			−3.7[a]	−1.5	347	18.2
60–69	1999–2015	−5.4[a]					−5.4[a]	−5.4[a]	210	18.3
≥70	1999–2015	−3.0[a]					−3.0[a]	−3.0[a]	187	20.6
All ages	1999–2006	−4.7[a]	2006–2009	0.8	2009–2015	−4.8[a]	−3.7[a]	−4.8[a]	1372	9.0
Hispanic										
20–29 years	1999–2015	−2.8[a]					−2.8[a]	−2.8[a]	94	2.2
30–39	1999–2011	−4.1[a]	2011–2015	0.0			−3.1[a]	0.0	330	8.4
40–49	1999–2015	−4.8[a]					−4.8[a]	−4.8[a]	365	11.7
50–59	1999–2005	−7.0[a]	2005–2015	−3.9[a]			−5.0[a]	−3.9[a]	275	14.1
60–69	1999–2006	−3.6[a]	2006–2011	−9.1[a]	2011–2015	−2.7	−5.1[a]	−2.7	168	15.4
≥70	1999–2015	−3.8[a]					−3.8[a]	−3.8[a]	139	16.7
All ages	1999–2015	−4.5[a]					−4.5[a]	−4.5[a]	1372	7.6
Asian/PI										
20–29 years	1999–2015	0.6					0.6	0.6	9	0.7
30–39	1999–2015	−1.7[a]					−1.7[a]	−1.7[a]	55	3.5
40–49	1999–2015	−2.8[a]					−2.8[a]	−2.8[a]	86	6.4
50–59	1999–2015	−3.6[a]					−3.6[a]	−3.6[a]	96	9.5
60–69	1999–2015	−3.3[a]					−3.3[a]	−3.3[a]	70	11.0
≥70	1999–2015	−4.9[a]					−4.9[a]	−4.9[a]	60	11.1
All ages	1999–2015	−3.5[a]					−3.5[a]	−3.5[a]	376	4.5
All U.S.										
20–29 years	1999–2004	−6.7[a]	2004–2015	−1.4[a]			−3.1[a]	−1.4[a]	436	2.0
30–39	1999–2013	−2.5[a]	2013–2015	3.6			−1.7[a]	0.5	1502	7.6
40–49	1999–2013	−2.1[a]	2013–2015	2.8			−1.5[a]	0.3	1930	10.6
50–59	1999–2004	−6.4[a]	2004–2015	−1.3[a]			−3.0[a]	−1.3[a]	1858	11.1
60–69	1999–2015	−4.3[a]					−4.3[a]	−4.3[a]	1237	10.9
≥70	1999–2015	−2.8[a]					−2.8[a]	−2.8[a]	976	9.9
All ages	1999–2003	−4.5[a]	2003–2013	−2.4[a]	2013–2015	0.5	−2.6[a]	−1.0	7940	6.0

AAPC, average annual percent change; PI, Pacific Islander.
Average incidence rates are age-adjusted to the 2000 U.S. standard population and are per 100,000 women. 'All U.S.' also includes other racial-ethnic groups not listed in this table. Results for ages < 20 years are not shown because of sparse data. Due to rounding of average annual number of cases during 2011–2015 and inclusion of cancer cases aged < 20 years, numbers may not add up to the totals.
[a] The annual percent change (APC) is significantly different from 0.0 ($P < 0.05$).

In contrast, age-standardized rates of distant stage cervical cancer, SCC, and adenocarcinoma among whites increased in several age groups and remained stable in others. In other race/ethnicities, incidence rates of distant stage cervical cancer, SCC, and adenocarcinoma remained stable, except for an increase in distant stage cervical cancer rates among Hispanics and a decrease in rates of distant stage adenocarcinoma among Asian/PIs. In general, incidence rates of unstaged cancers continuously decreased in all race/ethnicities. However, absolute decreases in rates of unstaged cervical SCC or adenocarcinoma were much smaller than increases in rates of other stages in some age groups among white women, notably in ages 40–49 years (Fig. 2).

3.5. Other results

Due to relatively small number of reported cervical cancers without a histologically confirmed diagnosis, trends after inclusion of these cancers were generally similar to those described above (Appendix Table 4). An exception was that the increasing trend of histologically confirmed cervical adenocarcinoma in ages 30–39 years among blacks turned to a stable trend when all cervical cancers were included.

Incidence rates of cervical adenosquamous carcinoma and cervical cancers with unknown histology or unspecified carcinomas decreased in most age groups in all race/ethnicities during 1999–2015 (Appendix Tables 2 and 4). However, incidence rates and absolute changes in rates over time for these subtypes generally were much smaller than those for cervical adenocarcinoma among younger white women with increasing adenocarcinoma rates (Fig. 1). As expected, incidence rates for cervical cancer and its subtypes without accounting for hysterectomy were generally lower than rates presented above, particularly in older ages, but incidence trends were mostly comparable, although often with relatively smaller annual percent of changes in rates (Appendix Table 5).

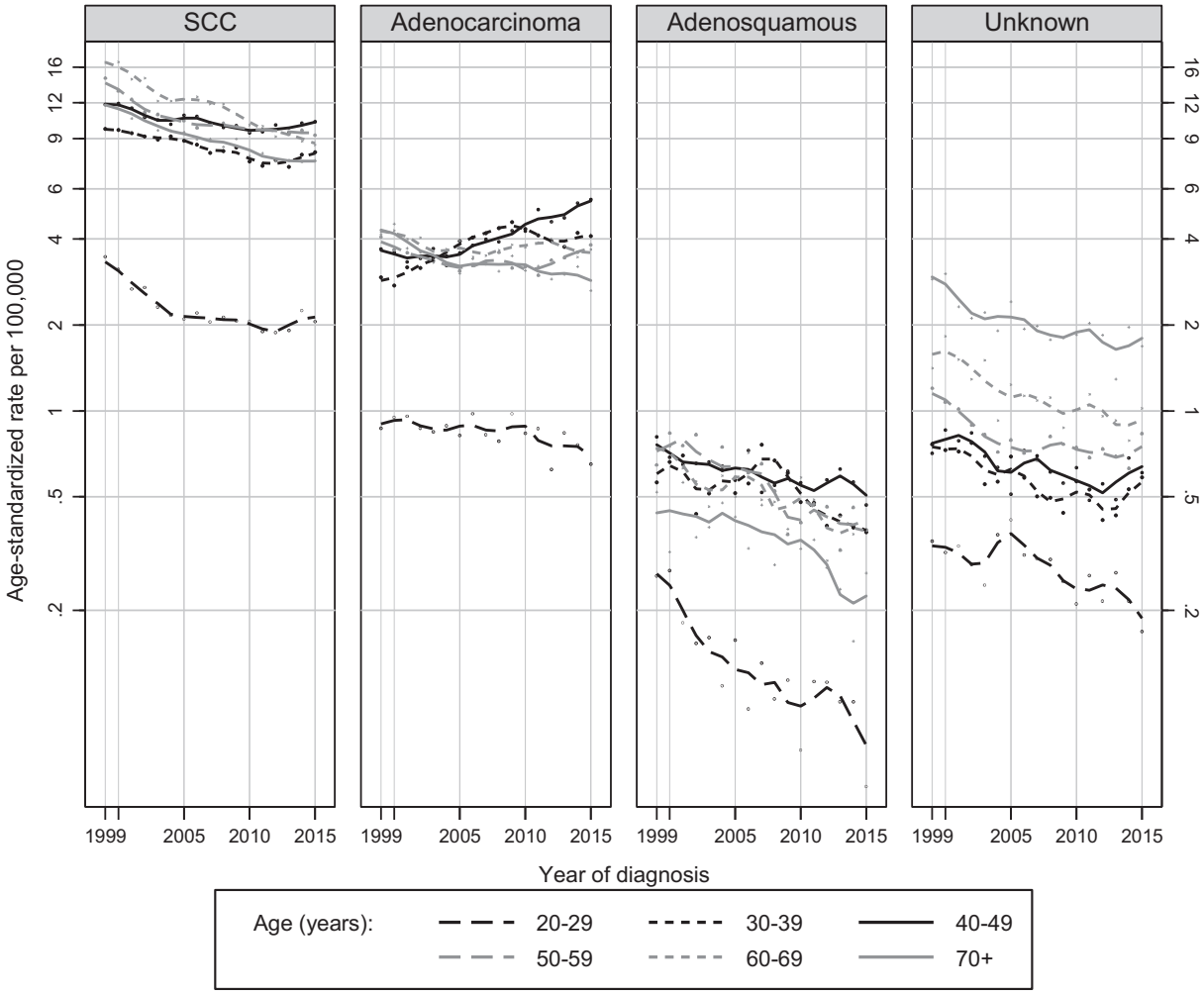

Fig. 1. Trends in cervical cancer incidence rates (1999–2015) among non-Hispanic white women by age and histology after accounting for hysterectomy, United States.

Rates are for histologically confirmed cancers except for the 'Unknown' group and are standardized to the U.S. 2000 standard population. The 'Unknown' group in this figure includes malignant cervical cancers with unknown histology and unspecified cervical carcinomas, including those without a histological confirmed diagnosis. Results for ages < 20 years are not shown because of sparse data. The dots show observed values, whereas the lines represent smoothed values, which were calculated by fitting locally weighted regression (LOWESS) curves, with applying 30% of the data in the smoothing, using Stata software (version 13.1).

4. Discussion

In this nationwide study of trends in cervical cancer incidence in the U.S., we found that during the most recent period (2011–2015) adenocarcinoma incidence rates increased and the pace of declines in SCC incidence slowed in several subpopulations. A decrease in incidence rates of cervical cancers with unknown histology or unspecified carcinoma did not appear to explain the increase in cervical adenocarcinoma incidence rates. Further, incidence rates of distant stage cervical SCC and adenocarcinoma increased in several age groups among whites. These findings underscore the importance of intensifying efforts to reverse the increasing adenocarcinoma incidence rates and further reduce the burden of cervical cancer in the U.S.

Our results show that previously reported increases in adenocarcinoma incidence rates in the U.S. are continuing. An increase in adenocarcinoma incidence rates has also been observed in several countries in Western Europe (Baldur-Felskov et al., 2015; Bray et al., 2005; Orumaa et al., 2019). These increasing trends are thought to in part reflect changing sexual behaviors (Bray et al., 2005; Ryser et al., 2017). However, overall cervical cancer incidence rates in the U.S. have substantially decreased since the 1960s following wide dissemination of the Papanicolaou (Pap) test (Jemal et al., 2013). The overall patterns are driven by declines in SCC (Wang et al., 2004), which is the most common type of cervical cancer, and the sensitivity of Pap testing is better for SCC and its precursors compared to adenocarcinoma (Castle et al., 2017; Katki et al., 2011). Had screening not been widely available or disseminated, rates of SCC may have increased in line with adenocarcinomas (Lonnberg et al., 2015). A modest decline in screening prevalence rates (defined as past 3-year Pap testing in ages 21–65 years) in recent years has been reported in the U.S. (Watson et al., 2017; White et al., 2017), which might have contributed to attenuation of declining trends in cervical SCC rates. However, it should be noted that examination of changes in screening prevalence over time could be challenging because of changes in cervical cancer screening guidelines. The contribution of Pap testing to adenocarcinoma rates is not as clear as less is known about the natural history of adenocarcinoma (Gradissimo and Burk, 2017). Indeed, chronological trends in rising cervical adenocarcinoma incidence rates in SEER data somewhat resemble those of other HPV-related cancers with no routine screening in the U.S., such as oropharyngeal and anal SCC (Ryser et al., 2017).

Earlier cervical cancer screening guidelines in the U.S. were solely based on Pap testing (Saslow et al., 2002; Smith et al., 2001). As human papillomavirus (HPV) is the main etiologic factor for cervical cancer (Crosbie et al., 2013), high-risk HPV DNA testing (hereafter, HPV DNA

Table 2
Incidence rates (2011–2015) and trends (1999–2015) for histologically confirmed cervical adenocarcinoma by age and race/ethnicity after accounting for hysterectomy, United States.

Cancer by age and race/ethnicity	Trends 1995–2015						AAPC 1999–2015	AAPC 2011–2015	Average rate and *N* 2011–2015	
	Trend 1		Trend 2		Trend 3					
	Years	APC	Years	APC	Years	APC			Annual *N*	Rate
Non-Hispanic white										
20–29 years	1999–2015	−1.4[a]					−1.4[a]	−1.4[a]	93	0.7
30–39	1999–2009	5.0[a]	2009–2013	−4.7	2013–2015	5.3	2.5[a]	0.2	451	4.0
40–49	1999–2004	−1.1	2004–2015	4.4[a]			2.6[a]	4.4[a]	565	5.0
50–59	1999–2011	−1.5[a]	2011–2015	5.5[a]			0.2	5.5[a]	403	3.4
60–69	1999–2015	−0.5					−0.5	−0.5	313	3.7
≥70	1999–2015	−2.2[a]					−2.2[a]	−2.2[a]	226	3.0
All ages	1999–2002	−2.3	2002–2015	1.3[a]			0.6	1.3[a]	2054	2.4
Non-Hispanic black										
20–29 years	1999–2015	2.7					2.7	2.7	7	0.2
30–39	1999–2015	1.9[a]					1.9[a]	1.9[a]	38	1.4
40–49	1999–2015	0.6					0.6	0.6	57	2.4
50–59	1999–2015	−1.7[a]					−1.7[a]	−1.7[a]	52	2.7
60–69	1999–2015	−2.6[a]					−2.6[a]	−2.6[a]	61	5.3
≥70	1999–2015	−2.9[a]					−2.9[a]	−2.9[a]	49	5.4
All ages	1999–2002	−7.6	2002–2015	−0.5			−1.9[a]	−0.5	265	1.8
Hispanic										
20–29 years	1999–2015	0.4					0.4	0.4	25	0.6
30–39	1999–2015	0.4					0.4	0.4	119	3.0
40–49	1999–2015	0.3					0.3	0.3	158	5.0
50–59	1999–2015	−1.7[a]					−1.7[a]	−1.7[a]	85	4.3
60-69	1999–2015	−0.9					−0.9	−0.9	52	4.8
≥70	1999–2015	−3.8[a]					−3.8[a]	−3.8[a]	30	3.6
All ages	1999–2015	−0.9[a]					−0.9[a]	−0.9[a]	470	2.5
Asian/PI										
20–29 years	Sparse data	–					–	–	5	0.4
30–39	1999–2015	1.9					1.9	1.9	28	1.8
40–49	1999–2015	0.3					0.3	0.3	47	3.5
50–59	1999–2015	−2.6[a]					−2.6[a]	−2.6[a]	32	3.2
60–69	1999–2015	−2.3					−2.3	−2.3	19	3.0
≥70	1999–2015	−1.4					−1.4	−1.4	13	2.5
All ages	1999–2015	−0.5					−0.5	−0.5	145	1.7
All U.S.										
20–29 years	1999–2015	−0.9					−0.9	−0.9	135	0.6
30–39	1999–2008	3.9[a]	2008–2015	−1.3			1.6[a]	−1.3	652	3.3
40–49	1999–2004	−1.3	2004–2015	3.4[a]			1.9[a]	3.4[a]	844	4.6
50–59	1999–2005	−3.6[a]	2005-2015	0.7			−1.0[a]	0.7	584	3.5
60–69	1999–2003	−6.6[a]	2003–2011	1.3[a]	2011–2015	−3.3[a]	−1.9[a]	−3.3[a]	451	4.0
≥70	1999–2015	−2.4[a]					−2.4[a]	−2.4[a]	322	3.3
All ages	1999–2004	−2.5[a]	2004–2007	3.2	2007–2015	0.3	−0.1	0.3	2990	2.3

AAPC, average annual percent change; PI, Pacific Islander.
Average incidence rates are age-adjusted to the 2000 U.S. standard population and are per 100,000 women. 'All U.S.' also includes other racial-ethnic groups not listed in this table. Results for ages < 20 years are not shown because of sparse data. Due to rounding of average annual number of cases during 2011–2015 and inclusion of cancer cases aged < 20 years, numbers may not add up to the totals.
[a] The annual percent change (APC) is significantly different from 0.0 ($P < 0.05$).

testing) has been included in more recent guidelines—i.e., Pap/HPV DNA co-testing since 2012 and primary testing since 2018 (U.S. Preventive Services Task Force et al., 2018), after clinical trials showed that it detects more cervical cancers and reduces the risk of invasive cancers compared to Pap testing alone, notably for cervical adenocarcinoma (Melnikow et al., 2018; Ronco et al., 2014; Zhao et al., 2017). However, although nationally representative information on HPV DNA testing prevalence in the U.S. is based on self-reports, with a considerable proportion (17% in 2015) of women not knowing having HPV DNA testing at their most recent screening, HPV DNA testing utilization in eligible ages appears to be low: prevalence of Pap/HPV DNA co-testing within 3 years in 2015 was 41% in ages 30–39 years, 30% in 40–49 years, and 20% in 50–65 years (Watson et al., 2017). Nevertheless, more information is needed on the uptake of HPV DNA testing in the U.S. and its correlation with cervical cancer incidence trends by histological subtype.

To further reduce the burden of cervical cancer among adult women in the U.S., more efforts are needed to increase screening utilization according to guidelines and appropriate follow-up of positive results (Doubeni et al., 2018; Watson et al., 2017). Additionally, current strategies/practices should be improved to reduce overuse of screening beyond the recommendations (Alber et al., 2018). HPV DNA testing increases the sensitivity of cervical cancer screening, but it is associated with more false-positive results and higher colposcopy rates compared to Pap testing alone (Melnikow et al., 2018). Thus, an increase in HPV DNA testing uptake in the U.S. is likely to reduce cervical cancer incidence rates, but it may also result in an increase in overdiagnosis, and consequently, overtreatment. As such, more research on natural history of cervical cancer, HPV carcinogenicity, and relevant biomarkers is required to improve screening strategies (Gradissimo and Burk, 2017; Joste et al., 2015; Luttmer et al., 2016; Mirabello et al., 2016); for example, further research on associations between HPV and histological subtypes of cervical cancer according to HPV variant lineages (Mirabello et al., 2016).

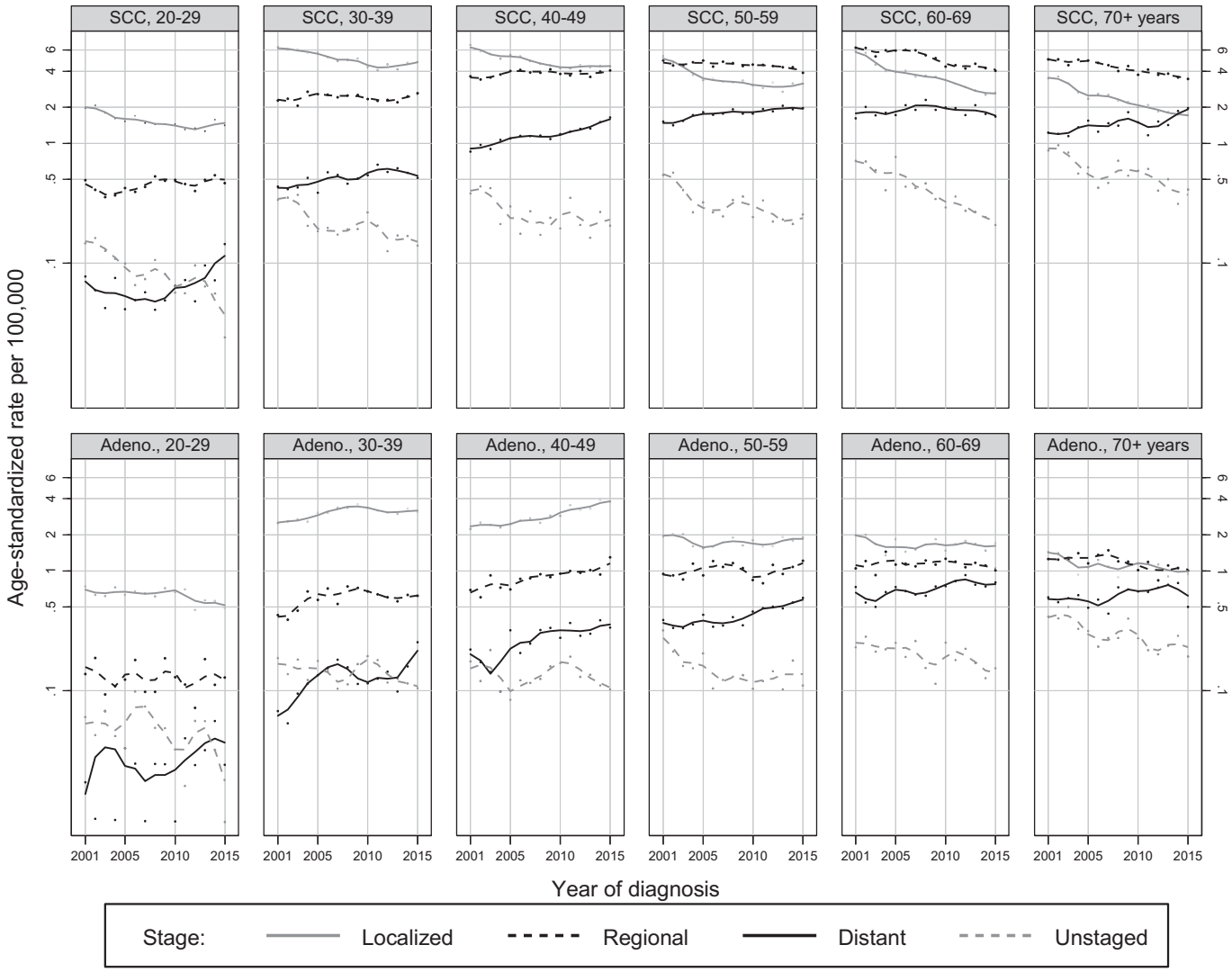

Fig. 2. Trends in cervical SCC and adenocarcinoma incidence rates (2001–2015) among non-Hispanic white women by age and stage at diagnosis after accounting for hysterectomy, United States.

Adeno., adenocarcinoma; SCC, squamous cell carcinoma.

Rates are for histologically confirmed cancers and are standardized to the U.S. 2000 standard population. The dots show observed values, whereas the lines represent smoothed values, which were calculated by fitting locally weighted regression (LOWESS) curves, with applying 30% of the data in the smoothing, using Stata software (version 13.1).

As virtually all cervical cancers are caused by HPV infection, HPV vaccination is an effective tool to prevent this cancer (Guo et al., 2018; Saslow et al., 2007). HPV vaccination was recommended by the Advisory Committee on Immunization Practices in the U.S. in mid-2006, primarily for females aged 11 or 12 years, and through ages 26 years if not previously vaccinated (Markowitz et al., 2016). However, although prevalence of carcinogenic HPV types covered by quadrivalent vaccine (HPV-6, -11, -16, and -18) significantly declined in teens and women in their early 20s in recent years (Markowitz et al., 2016), it is too early for HPV vaccination to affect the overall cervical cancer incidence rates (Guo et al., 2018), given substantially higher incidence rates of cervical cancer in older age groups. In order to fully realize the promise of HPV vaccination in reducing cervical cancer burden, concerted efforts are needed to increase its coverage, as HPV vaccination uptake remains suboptimal; only 53% of girls aged 13–17 years were up-to-date with the vaccination nationally in 2017 (Walker et al., 2018).

Limitations of our study include lack of information on molecular characteristics of cervical tumors, such as HPV typing. Information was also missing on histology and stage at diagnosis for some cancer cases, but it is unlikely to substantially affect our results because the proportion of those with missing information was modest. We also relied on self-reported hysterectomy data, which is subject to recall bias, though the sensitivity exceeds 90% compared to medical records (Phipps and Buist, 2009). Due to lack of data, we were not able to examine some other factors that might have influenced cervical cancer incidence trends. For example, the sensitivity of cervical cancer screening may be lower in obese women (Clarke et al., 2018), and prevalence of obesity among women is increasing in the U.S. (Hales et al., 2018). However, a lower screening sensitivity among obese women is unlikely to explain the differential increases in adenocarcinoma rates. Strengths of our study include examination of hysterectomy-corrected nationwide cervical cancer incidence data to describe contemporary incidence trend by histology, age group, race/ethnicity, and stage at diagnosis.

5. Conclusions

We found increasing or stable incidence trends for cervical adenocarcinoma and attenuation of earlier declines in SCC rates, with increases in incidence rates of distant stage cancers, in several

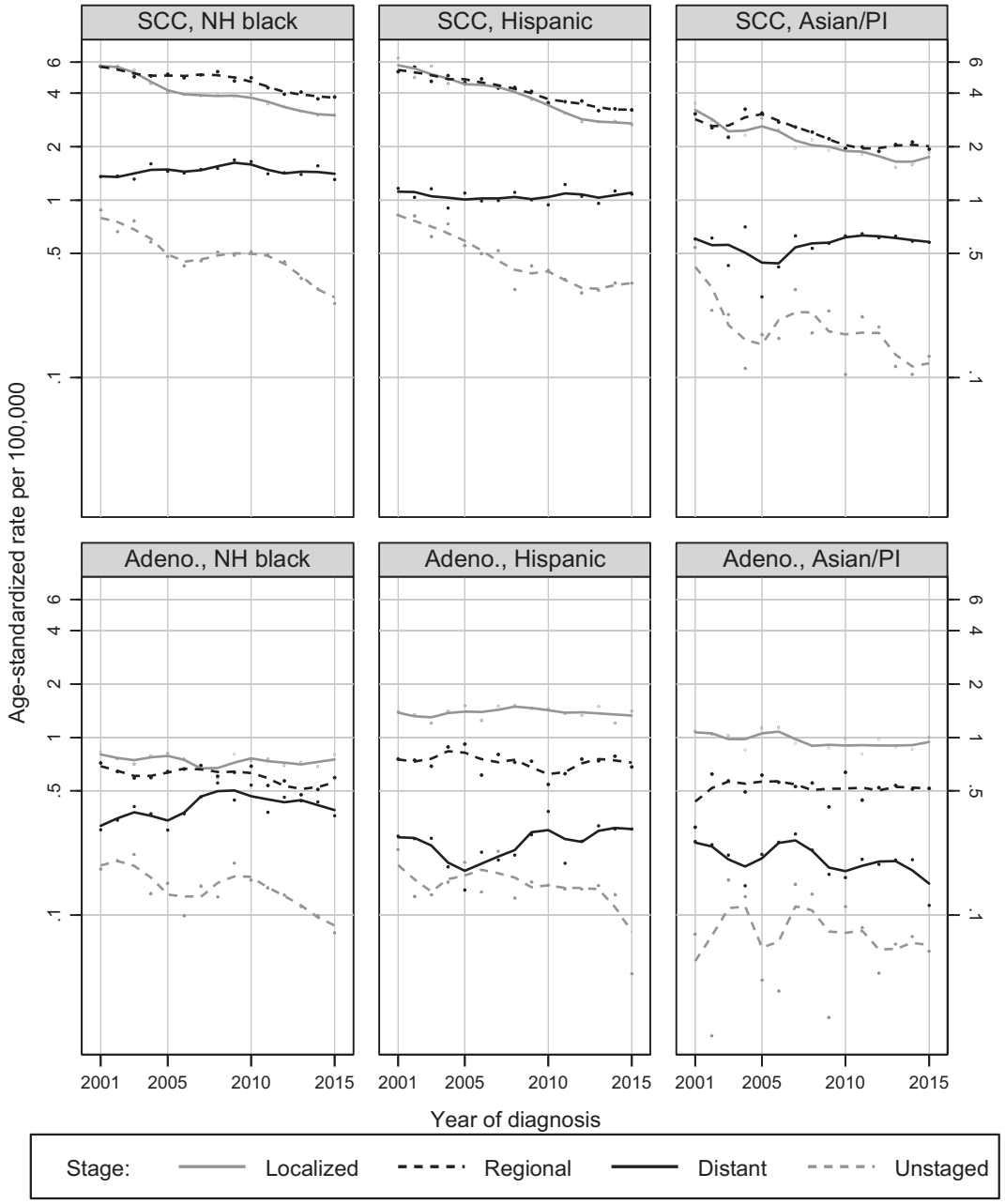

Fig. 3. Trends in cervical SCC and adenocarcinoma incidence rates (2001–2015) among non-Hispanic black, Hispanic, and Asian/PI women by stage at diagnosis after accounting for hysterectomy, United States.
Adeno., adenocarcinoma; NH, non-Hispanic; PI, Pacific Islander; SCC, squamous cell carcinoma.
Rates are for histologically confirmed cancers and are standardized to the U.S. 2000 standard population. The dots show observed values, whereas the lines represent smoothed values, which were calculated by fitting locally weighted regression (LOWESS) curves, with applying 30% of the data in the smoothing, using Stata software (version 13.1).

subpopulations in the U.S. Our findings have significant public health implications in view of the opportunity to reduce premature morbidity and mortality and societal cost associated with the disease in young women when they are in the workforce and supporting their families. Increasing uptake of screening and HPV vaccination could help halt and reverse the increasing adenocarcinoma trend and accelerate the declining SCC trend in the country.

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Conflict of interest disclosures

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Author contributions

Dr. Islami had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data

analysis. Study concept and design: all authors; acquisition of data: Islami, Fedewa; analysis and interpretation of data: all authors; drafting of the manuscript: Islami; critical revision of the manuscript for important intellectual content: all authors; statistical analysis: Islami, Fedewa; study supervision: Jemal.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ypmed.2019.04.010.

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