Cervical Cancer Incidence Among Elderly Women in Massachusetts Compared With Younger Women

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Importance: Current cancer screening guidelines recommend cessation of cervical cancer screening at the age of 65 years for most women. To examine residual risk among elderly women, we compared cervical cancer incidence rates (IRs) in Massachusetts from 2004 to 2015 among women younger than 65 years versus 65 years and older.

Materials and Methods: The Massachusetts Cancer Registry was used to identify all women diagnosed with cervical cancer between January 01, 2004, to December 31, 2015. Cancer incidence was calculated based on age of diagnosis (<65 years vs ≥65 years).

Results: In Massachusetts, 2,418 incident cases of cervical cancer were diagnosed from 2004 to 2014, of which 571 (23.6%) were diagnosed among women 65 years and older. When compared with women diagnosed younger than 65 years, women diagnosed at the age of 65 years and older were more likely to be diagnosed with stage II or higher (71.8% vs 43.8%, $p < .001$). Cervical cancer IRs decreased annually for women younger than 65 years from 2004 to 2015. Among women 65 years and older, cancer IRs decreased by 3.9% annually from 2004 to 2013 ($p = .0009$), but 2013 to 2015 showed an increasing trend (annual percent change + 14.1%, $p = .12$).

Conclusions and Relevance: Women 65 years and older account for one quarter of cervical cancer diagnoses in Massachusetts and present with higher-stage disease than younger women. Upcoming planned revisions in screening and prevention guidelines should address the continued risk of cervical cancer for older women.

Key Words: cervical cancer, elderly women, screening guidelines

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Current cervical cancer screening guidelines advise average-risk women to stop screening at the age of 65 years if they have had adequate previous testing with normal results. However, these recommendations were based largely on modeling studies, and more recent data have questioned the appropriateness of current guidelines for screening cessation.[1,2] Recent data show that after controlling for hysterectomy, cervical cancer incidence may not decline until at least the age of 85 years,[3] older women participating in screening are diagnosed at earlier stages than unscreened older women,[4] and profound racial disparities exist in cervical cancer diagnoses older than 65 years.[5] Given concerns about persistent cervical cancer risk in older women, we compared the cervical cancer incidence rate (IR) and stage of cancer presentation among women younger than 65 years compared women 65 years and older in Massachusetts, a state with mandated universal healthcare coverage since 2006.

MATERIALS AND METHODS

Data on cases of invasive cervical cancer (*International Classification of Diseases*, *ICD-O* code C53) from 2004 to 2015 were obtained from the Massachusetts Cancer Registry. The Massachusetts Cancer Registry has been collecting data on incident cancers since 1982 and has been estimated to have more than 95% complete case ascertainment.[6] This analysis was conducted at Massachusetts Department of Public Health under the public health surveillance authority. The population of women with cervical cancer was divided by age (<65 years vs ≥65 years) at diagnosis, and incidence data were examined by race/ethnicity, birth country, region of residence, type of insurance, stage at diagnosis, and histology. We dichotomized at stage II or higher because stage I is both more curable and more likely to be diagnosed by screening, whereas stage II and higher has poorer prognosis and is more likely to be diagnosed based on symptoms. χ^2 tests and Fisher exact tests were calculated for these characteristics. Incidence rates were age-specific rates for each age group per 100,000 female person-years. We used Joinpoint regression to assess trends, to calculate the annual percent change (APC), and to perform hypothesis tests. Multiple APC values are shown when the regression indicated a statistically significant breakpoint. Additional difference-in-differences regression models were run to determine whether observed changes in the APC for women 65 years and older from 2013 to 2015 were significant compared with 2004 to 2012 were significantly different from that for women younger than 65 years.[7]

RESULTS

From 2004 to 2015, 571 (23.6%) of the 2,418 incident cases of cervical cancer diagnosed in Massachusetts occurred among women 65 years and older. The mean ages of women diagnosed at younger than 65 years compared with 65 years and older were 45.3 years old (SD = 10.4) and 75.5 (SD = 7.8), respectively. The age-specific IR was 1.6 times higher among women 65 years and older compared with younger women (8.87 per 100,000 vs 5.40 per 100,000, $p < .05$; see Figure 1). Cancer IRs increased after the age of 35 years and remained stable through the age of 85 years (see Table 1). Older women were more likely to be diagnosed with cancer at stage II or higher than younger women (71.8% vs 43.8%, $p < .0001$; see Table 2). Compared with women diagnosed younger than 65 years, women 65 years and older at diagnosis

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Key points: Cervical cancer rates remained high in women age 65 and older.

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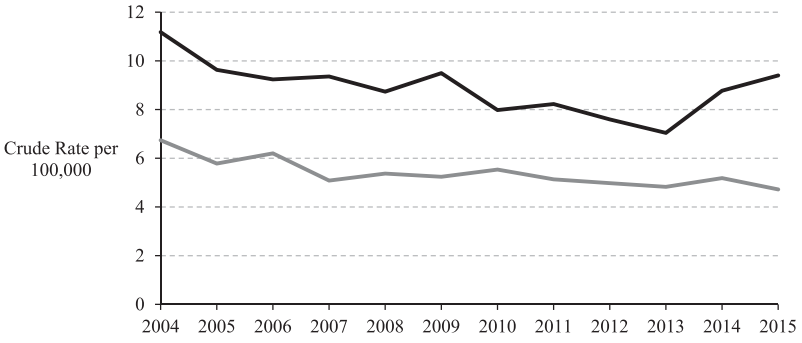

	Rate per 100,000 (95% CI)	APC (95% CI)	p value
Incidence Age <65	5.40 (5.15, 5.64)	-2.46% (-3.58%, -1.34%)	0.0007
Incidence Age 65+	8.87 (8.14, 9.59)	2004-2013: -3.92% (-5.55%, -2.27%)	0.0009
		2013-2015: 14.07% (-4.37%, 36.08%)	0.12

APC = Annual percent change; CI = Confidence Interval; APC is for 2004-2015 unless otherwise specified; multiple APC values are shown when the regression indicated a statistically significant break point; rates are per 100,000 female person-years

FIGURE 1. Trends in the crude incidence and mortality rates per 100,000 of cervical cancer by age group in Massachusetts, 2004–2015.

were more likely to be non-Hispanic black. No differences were noted by country of origin or county of residence within Massachusetts. As expected, older women were more likely to have Medicare insurance.

Over time, IR trends diverged for women younger than 65 years compared with 65 years and older. Cervical cancer IRs decreased consistently among women younger than 65 years by 2.5% each year (95% CI = −3.6% to −1.3%, p = .0007; see Figure 1). From 2004 to 2012, the IR among women 65 years and older, decreased by 3.9% each year (95% CI = −5.5% to −2.3%, p = .0009). However, from 2013 to 2015, the IR among women 65 years and older showed an increasing trend, 14.1% each year (95% CI = −4.4% to 36.1%, p = .12) (see Figure 1). Additional statistical models using difference-in-differences regression analyses supported a nonsignificant relative annual increase from 2013 to 2015 among older women compared with women younger than 65 years (+5.7%, p = .62).

DISCUSSION

Nearly a quarter of cases from cervical cancer in Massachusetts between 2004 and 2015 occurred among women 65 years and older. Older women were more likely to be diagnosed with cancer at stage II or higher than their younger counterparts (≤65 years). These disparities occurred despite mandated universal access to health insurance since 2006 in Massachusetts. Indeed, the Massachusetts' population-wide cervical cancer rates are lower than the US average (5.5 vs 7.4/100,000), which may reflect excellent access to care overall. Current guidelines to exit screening at the age of 65 years, endorsed jointly by American Society of Colposcopy and Cervical Pathology, American Cancer Society, and American Society of Clinical Pathology[8] and separately by American College of Obstetricians and Gynecologists[9] and US Preventive Services Task Force[10] provide the following rationale: "In well-screened women older than the age of 65 in the United States, CIN2+ prevalence is low[11,12] and cervical cancer is rare.[13]" However, according to the Copeland et al[12] reference cited in the guidelines, although the rate of carcinoma in situ decreased with age, the rates of invasive cervical cancer rates rose at the age of 30 years and did not decline through the ages of 80 years and older (Copeland et al,[12] see Figure 4). Interestingly, these data are from 1985 to 2003 in Michigan, yet the IRs are nearly identical to those seen in Massachusetts from 2004 to 2015, indicating that residual cervical cancer risk among elderly women has been persistent for 3 decades and in different US localities despite changes in screening guidelines during this period. We do not currently know what role screening plays in residual cancer risk in women 65 years and older. *Do cancers occur because screening is failing or because women are failing to be screened?*

Based on modeling studies, current guidelines[8] conclude that "for women who have been screened every 3 years prior to age 65 years, the ratio of colposcopies to years of life gained associated with further screening was large (or the years of life gained per colposcopy small) because of the small gains in life expectancy.[1]" However, recent data question this assumption. Population-wide cervical cancer rates are 7 per 100,000 per year among non-Hispanic white women compared with 9.1, 9.5, and 9.7 for American Indian/Alaska Native, African-American, and Hispanic women, respectively,[14] with substantially higher incidence and

TABLE 1. Age-Specific IRs for Cervical Cancer by Age Category, Massachusetts 2004–2015

Incidence				
Age, y	**No. cases**	**IR (95% CI)**	**APC**	***p***
<35	322	1.83 (1.63–2.03)	−4.89	.024
35–44	547	9.75 (8.93–10.57)	−0.97	.44
45–54	546	8.96 (8.21–9.71)	−1.69	.13
55–64	432	8.76 (7.94–9.59)	−3.09	.025
65–74	291	9.48 (8.39–10.57)	−1.41	.28
75–84	188	8.67 (7.43–9.90)	−2.60	.09
≥85	92	7.65 (6.08–9.21)	−2.92	.28

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TABLE 2. Characteristics of Women Diagnosed With Cervical Cancer by Age Group in Massachusetts, 2004–2015

Characteristics of incident cases	Diagnosed age < 65 y (n = 1,847)	Diagnosed age ≥ 65 y (n = 571)	p
Age at diagnosis, mean (SD)	45.3 (10.4)	75.5 (7.8)	<.0001[a]
Race/ethnicity, *n* (%)			.02
Non-Hispanic, white	1,371 (75.2)	420 (74.2)	
Non-Hispanic, black	150 (8.2)	68 (12.0)	
Non-Hispanic, Asian	107 (5.9)	22 (3.9)	
Hispanic	196 (10.8)	56 (9.9)	
Birth Country, *n* (%)			.96
Foreign	353 (31.6)	138 (31.7)	
Native	764 (68.4)	297 (68.3)	
Massachusetts region, *n* (%)			.80
Western	260 (14.1)	79 (13.8)	
Central	203 (11.0)	74 (13.0)	
North Shore	206 (11.2)	64 (11.2)	
Greater Boston	805 (43.6)	233 (40.8)	
South Shore	61 (3.3)	21 (3.7)	
Southeast	159 (8.6)	55 (9.6)	
Cape and Islands	153 (8.3)	45 (7.9)	
Type of insurance, *n* (%)			<.0001
None	77 (4.3)	—[b]	
Private	959 (53.7)	56 (10.4)	
Medicaid	440 (24.6)	72 (13.3)	
Medicare	101 (5.7)	394 (73.0)	
Insurance, NOS	209 (11.7)	16 (3.0)	
Stage at diagnosis, *n* (%)			<.0001
I	1,038 (56.2)	161 (28.2)	
II	583 (31.6)	230 (40.3)	
III	184 (10.0)	127 (22.2)	
IV	42 (2.3)	53 (9.3)	
Histology, *n* (%)			<.0001
Squamous cell carcinoma	1,103 (59.7)	373 (65.3)	
Adenocarcinoma	514 (27.8)	99 (17.3)	
Other carcinomas	184 (10.0)	62 (10.9)	
Other and unspecified neoplasms	46 (2.5)	37 (6.5)	

p values in right column are from χ^2 tests except when denoted by for Fisher's exact tests or [a]for t tests; 28 people had an unknown race/ethnicity, 863 people had missing birth country, 61 people had unknown insurance type; western = Berkshire, Franklin, Hampshire, and Hampden counties, central = Worcester county, north shore = Essex county, greater Boston = Middlesex, Norfolk, and Suffolk counties, south shore = Plymouth county, southeast = Bristol county, cape and islands = Barnstable, Dukes, and Nantucket county; ICD-O-3 codes: squamous cell carcinomas (8050–8078, 8083–8084), adenocarcinomas (8140–8141, 8190–8211, 8230–8231, 8260–8263, 8310, 8380, 8382–8384, 8440–8490, 8570–8574, 8576), other carcinomas (8560, 8010–8035, 8041, 8045, 8082, 8090, 8094, 8098, 8120, 8046, 8144, 8246, 8255, 8323, 8380), and other and unspecified neoplasms (all other codes).

[b]Fewer than 10 women diagnosed with cervical cancer 65 years and older had no insurance.

NOS indicates not otherwise specified.

mortality noted among elderly women of color.[15] Recent data indicate residual cancer rates of 4/100,000 per year for women 65 years and older or a cumulative incidence up to 60/100,000 by the age of 80 years for women exiting screening at the age of 65 years with 3 previous negative cytology tests.[15] Both screening tests and colposcopies are less accurate among postmenopausal women; therefore, the assumptions of modeling studies may overestimate the reassurance provided by negative testing among postmenopausal women.[15] In addition, the current cohort of elderly women came of age during the sexual revolution and has a higher number of sexual partners and probable human papillomavirus exposure than previous cohorts.[16] A recent study in the United Kingdom found that 21.5% of 1,341 women 65 years and older diagnosed with cervical cancer between 2007 and 2012 met the US exiting criteria.[17] Additional research is needed to determine whether elderly women who follow current guidelines for discontinuing screening will be sufficiently protected against cervical cancer.

Furthermore, current guidelines for exiting screening are complex and may lead to unintentional discontinuation of screening among women still at risk. Guidelines state that elderly women should discontinue screening *only if* the clinician can document at least 3 negative Pap tests or 2 negative human papillomavirus tests within 10 years of stopping, with the most recent test within 5 years, and no history of cervical precancer (cervical intraepithelial neoplasia grades 2 or 3) within the past 20 years, no current immunosuppression or HIV infection, and no history of diethylstilbestrol exposure.[8] These guidelines are very difficult to follow in practice because of the need to obtain accurate medical record documentation for a 10- to 20-year period. The burden of extensive medical record review that will often require querying multiple record systems is very difficult for practicing clinicians and raises the likelihood that screening may be discontinued among women still considered to be at risk. Patients may also incorrectly assume that any pelvic examination included cervical cancer screening[18] or fail to understand that the purpose of cytology is to prevent cervical cancer and thus fail to present for screening.[19] Cervical cancer screening rates decline after the age of 40 years, and rates in women 65 years and older are not routinely measured.[8] The extent to which screening cessation guidelines are followed is currently unknown, and our data and others indicate substantial residual risk and late-stage presentation in this age group.[7,20,12] Screening practices in postmenopausal women should be studied to understand the role that inadequate screening may play in cancer development. Simplification of recommendations, as well as improved public education aimed at postmenopausal women and their healthcare providers, could decrease rates of underscreening in this population.

Our study has several limitations. First, because this is a retrospective analysis, we cannot accurately estimate the role of screening guidelines in age-related disparities in cancer incidence, stage, and mortality. We are also unable to adjust for hysterectomy, and based on previous data, reported rates underestimate the true risk of cervical cancer as well as racial disparities in cancer rates among women with a cervix in Massachusetts.[21] In addition, our sample size limits our power to determine the significance of the increase in incidence among older women after 2013. Finally, cervical cancer screening services in Massachusetts may be different from those in other parts of the United States.

CONCLUSIONS

Women 65 years and older represent a growing segment of the population that bears a substantial burden from cervical cancer. Current screening guidelines for screening cessation may be undermining our ability to prevent, detect, and cure cervical cancer among otherwise healthy older women. As national organizations undertake revision of national guidelines, strong consideration must be given to emerging data on the risk of cancer among older women and to changing the guidelines for screening cessation.

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REFERENCES

1. Kulasingam SL, Havrilesky L, Ghebre R, et al. *Screening for cervical cancer: a decision analysis for the U.S. preventive services task force*. Rockville, MD: Agency for Healthcare Research and Quality (US); 2011: Available at: http://www.ncbi.nlm.nih.gov/books/NBK92546/. Accessed July 31, 2018.
2. Gravitt PE, Landy R, Schiffman M. How confident can we be in the current guidelines for exiting cervical screening? *Prev Med* 2018; 114:188–92.
3. White MC, Shoemaker ML, Benard VB. Cervical cancer screening and incidence by age: unmet needs near and after the stopping age for screening. *Am J Prev Med* 2017;53:392–5.
4. Rosenblatt KA, Osterbur EF, Douglas JA. Case-control study of cervical cancer and gynecologic screening: a SEER-Medicare analysis. *Gynecol Oncol* 2016;142:395–400.
5. Beavis AL, Gravitt PE, Rositch AF. Hysterectomy-corrected cervical cancer mortality rates reveal a larger racial disparity in the United States. *Cancer* 2017;123:1044–50.
6. NAACCR. *NAACCR certification year 2017, gold and silver* 2017; Available at: https://www.naaccr.org/certified-registries/. Accessed May 4, 2017.
7. Dimick JB, Ryan AM. Methods for evaluating changes in health care policy: the difference-in-differences approach. *JAMA* 2014;312:2401.
8. Saslow D, Solomon D, Lawson HW, et al. American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology Screening Guidelines for the prevention and early detection of cervical cancer. *Am J Clin Pathol* 2012; 137:516–42.
9. Practice Bulletin No. 157: Cervical Cancer Screening and Prevention. *Obstet Gynecol* 2016;127:e1–20.
10. Moyer VA. Screening for cervical cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med* 2012;156:880.
11. Castle PE, Schiffman M, Wheeler CM, et al. Evidence for frequent regression of cervical intraepithelial neoplasia–grade 2. *Obstet Gynecol* 2009;113:18–25.
12. Copeland G, Datta SD, Spivak G, et al. Total burden and incidence of in situ and invasive cervical carcinoma in Michigan, 1985–2003. *Cancer* 2008; 113:2946–54.
13. Saslow D, Runowicz CD, Solomon D, et al. American Cancer Society guideline for the early detection of cervical neoplasia and cancer. *CA Cancer J Clin* 2002;52:342–62.
14. American Cancer Society. *Cancer Statistics Center* 2018; Available at: https://cancerstatisticscenter.cancer.org/?_ga=2.20975355.1746569515.1533055502-552426982.1496697483#!/cancer-site/Cervix.
15. Yoo W, Kim S, Huh WK, et al. Recent trends in racial and regional disparities in cervical cancer incidence and mortality in United States. *PLoS One* 2017;12:e0172548.
16. Gravitt PE, Rositch AF, Silver MI, et al. A cohort effect of the sexual revolution may be masking an increase in human papillomavirus detection at menopause in the United States. *J Infect Dis* 2013;207:272–80.
17. Castañón A, Landy R, Cuzick J, et al. Cervical screening at age 50–64 years and the risk of cervical cancer at age 65 years and older: population-based case control study. *PLoS Med* 2014;11:e1001585.
18. Howard DL, Hostetter SS, Hunter J, et al. Women's understanding of the term 'Pap smear'. *Matern Child Health J* 2015;19:1455–63.
19. Kasting ML, Wilson S, Zollinger TW, et al. Differences in cervical cancer screening knowledge, practices, and beliefs: an examination of survey responses. *Prev Med Rep* 2017;5:169–74.
20. Diver EJ, Hinchcliff EM, Gockley AA, et al. Assessment of treatment factors and clinical outcomes in cervical cancer in older women compared to women under 65 years old. *J Geriatr Oncol* 2018;9:516–9.
21. Stang A, Hawk H, Knowlton R, et al. Hysterectomy-corrected incidence rates of cervical and uterine cancers in Massachusetts, 1995 to 2010. *Ann Epidemiol* 2014;24:849–54.

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