Cervical Precancer Among Rhode Island Women, 2018-2019: A Quick Report after the Rhode Island Cancer Surveillance Regulation Change

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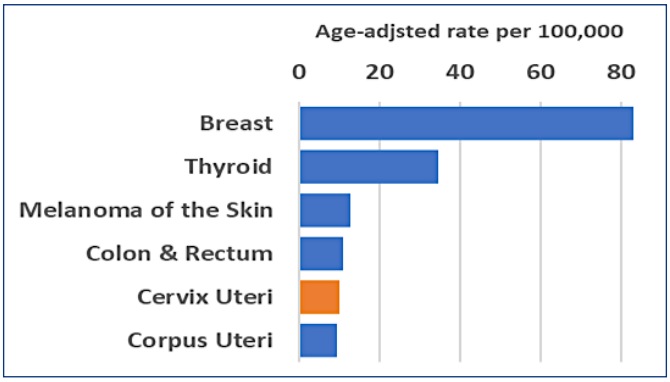
In 2017, the Rhode Island Cancer Registry (RICR) revised the "reportability" definition in its Regulations (Rhode Island Cancer Registry (216-RICR-10-10-2) – Rhode Island Department of State), and reinstituted surveillance of cervical precancer for incident cases diagnosed in 2018 and forward. Cervical precancer reporting was discontinued in most of the U.S. central cancer registries since 1996, due to concerns over data collection and inconsistent disease classification resulting from changes to histopathologic terminology.[1] This report (1) summarizes Rhode Island women's cervical precancerous lesions by age in 2018–2019, compared with invasive cancers, and (2) discusses importance of cervical precancer surveillance.

When women receive regular screening tests (Papanicolaou cytology and Human papillomavirus (HPV) testing) according to age-appropriate and risk-based recommendations, cervical cancer development is largely preventable.[2] Early detections of precancerous changes and carcinogenic HPV infection allow for early intervention, thereby halting the progression of precancerous lesions through effective follow-up and treatment.[2,3]

Since 1995 in Rhode Island, significant declines were observed in *invasive* cervical cancer diagnoses among women, attributed to the effective screening and successful treatment of precancerous lesions.[2] However, cervical cancer is still one of the most commonly diagnosed malignancies among women aged 20–49, and the most common gynecologic cancer (**Figure 1**).

Figure 1. Common Cancer Sites* among Rhode Island Women Ages 20–49 Years, RICR 2015–2019



* These six "common" cancer sites consist of approximately two-thirds of all newly diagnosed cancers, including invasive malignant cancers in all anatomic sites and in-situ urinary bladder cancer; Rate per 100,000 women adjusted to US Standard Population 2000 (19 age groups – Census P25-1130)
Data Source: Rhode Island Cancer Registry (as of December 2021)

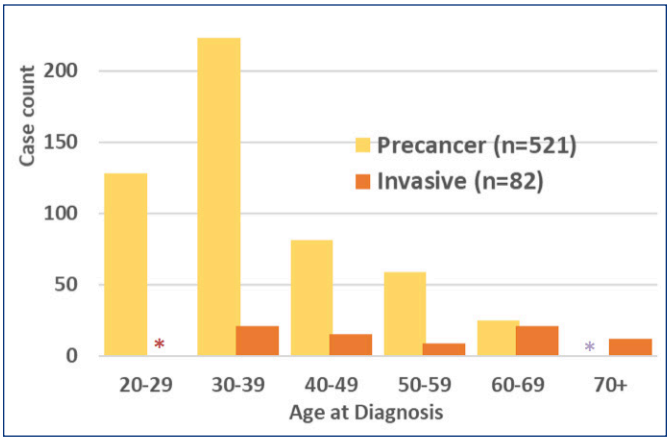
METHODS

Using the RICR data, we obtained records of newly diagnosed precancerous lesions in the cervix – intraepithelial neoplasia grade 3 (CIN3), high-grade squamous epithelial lesion (HSIL), carcinoma in situ (CIS) and adenocarcinoma in situ (AIS) – International Classification of Disease for Oncology, 3rd edition (ICD-O-3) site/behavior/histology codes: C530-C539/2/8010, 8050, 8052, 8070-77, 8140 (WHO Classification of Tumours Online). These lesions are referred to collectively, in this report, as "precancer" or "precursor". Cases diagnosed from January 1, 2018 through December 31, 2019 were limited to women aged 20 years and older, and compared with invasive cases (ICD-O-3 behavior code: 3) that were reported in the same study period. SEER*Stat software v8.4.0 was used to summarize counts and age-adjusted rates (AAR per 100,000 women) to the 2000 US standard population (http://www.seer.cancer.gov/seerstat/index.html), using the RICR records extracted in December 2021. State population estimates for rate denominators were obtained from the National Cancer Institute Surveillance, Epidemiology, and End Results Program (NCI SEER. http://seer.cancer.gov/popdata/download.html).

RESULTS

A total of 521 cervical precancerous lesions were reported in 2018 and 2019 (**Figure 2**). During the same period, 82 invasive cancers were newly diagnosed in Rhode Island women aged 20 and older. Overall incidence of precancerous lesions (by count) was sixfold higher than invasive cervical cancer. Women aged 30–39 had the highest burden of cervical precancers, accounting for 43% of the cases in 2018–2019 (n=223). As women's age increases, precancer cases decrease. Invasive cancer diagnoses peaked in women aged 60–69 years.

Figure 2. Cervical Precancer and Invasive Cancer by Women's Age at Diagnosis (≥20 Years), RICR 2018–2019



* suppressed: statistics are not displayed when count of cases are fewer than 6.
Data Source: Rhode Island Cancer Registry (as of December 2021)

DISCUSSION

This is the *first* reporting of incidence of cervical precancerous lesions among Rhode Island women since revision of the RICR case reporting requirement in 2017. As comparable data was not collected prior to cases diagnosed in 2018, we could not study state-specific incidence changes and trend of cervical precancer over time. However, we could observe (1) a sixfold higher precancer incidence than invasive cancer in Rhode Island women, (2) the highest burden of cervical precancers among women in their age 30s, and (3) a lower precancer incidence in youngest cohort (ages 20–29 years) who were more likely to have received HPV vaccine during their adolescent period than women ages 30–39, given the study timeframe (2018–2019).

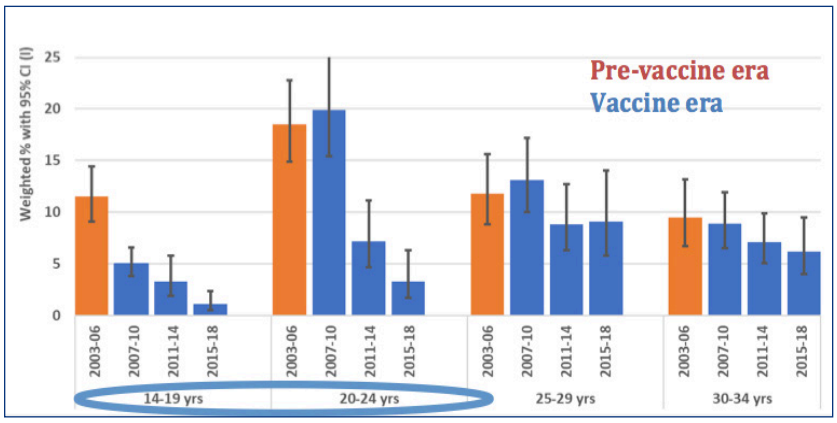
HPV vaccines effectively reduce the causal virus infections that can develop cervical cancer, as well as precancerous lesions.[4] In accordance with the Centers for Disease Control and Prevention (CDC)'s Advisory Committee on Immunization Practices (ACIP)' recommendations,[5,6] the Rhode Island Department of Health requires school children's vaccination against HPV for young females (since 2007), and young males (since 2011) (Immunization Information for Schools & Childcare Providers: Department of Health (ri.gov).

In the pre-vaccine era, HPV infection and precancer diagnosis among women in their 20s was known to be as high as, or even higher, than women in their ages 30s.[7,8] Through multiple population-based monitoring independently conducted in the U.S., early evidence of vaccine efficacy is strong and consistent; significant reductions of vaccine type-specific HPV infections (**Figure 3**), anogenital warts, CIN2+ (grade 2 or higher) diagnoses were reported, particularly among teens and young age women, who likely benefited from vaccine requirements in Rhode Island and nationwide, since 2007.[8-10] Similar results were *not* reported among older cohorts.

In monitoring the HPV vaccine effectiveness, cervical precursor (CIN3/CIS/AIS) surveillance is a practical tool, as it provides a relatively quick and intermediate population-based evidence. It would take decades to find effects on invasive cancer reduction, considering a slow cervical carcinogenic pathway that typically takes 20–30 years. Meanwhile, precancerous lesions can occur only 1–3 years after persistent cervical HPV infection and are much *more common* than invasive cancer, particularly in young women of reproductive ages.[3]

In addition to a lack of women's vaccine history, we were not able to collect the screening method by which precancer and cancer growth were diagnosed. Despite these limitations, population-based cervical precancer surveillance has the potential to provide important information to determine the burden of this preventable disease, to evaluate vaccine impacts on future precancer and invasive cancer diagnoses (intermediate and long-term endpoints), and to assist in the development of other cancer control activities. RICR plans to utilize data from state-based immunization registries and insurance claims to better understand precancer incidence in Rhode Island women associated with HPV vaccination, screening behavior, and risk factors.

Figure 3. Prevalence (%) of 4vHPV Infection* among U.S. Females, NHANES 2013–2018



* 4vHPV: HPV 6,11,16 or 18 (quadrivalent HPV vaccine target strains); collected by cervicovaginal swab
Vaccinated birth cohorts, In circle; CI=confidence interval
Recreated from Table 1. Rosenblum HG, Lewis RM, Gargano JW, Querec TD, Unger ER, Markowitz LE. Declines in Prevalence of Human Papillomavirus Vaccine-Type Infection Among Females after Introduction of Vaccine – United States, 2003–2018. MMWR Morb Mortal Wkly Rep. 2021;70: 415–420.
Data Source: National Health and Nutritional Examination Survey (NHANES)

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Acknowledgment

This article was supported by Cooperative Agreement Number NU58DP006291, funded by the Centers for Disease Control and Prevention. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention or the Department of Health and Human Services.

We thank all dedicated Rhode Island cancer registrars in the central and local hospital registries for their quality cancer surveillance and reporting.

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Disclosure

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