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## COMMENTARY

### The safety of vaginal estrogen in breast cancer survivors

Andrew M. Kaunitz, MD

Currently, more than 3.8 million breast cancer survivors reside in the United States, reflecting high prevalence as well as cure rates for this common malignancy.

When over-the-counter measures including vaginal lubricants and moisturizers are not adequate, vaginal estrogen may be a highly effective treatment for genitourinary syndrome of menopause (GSM), a common condition associated with hypoestrogenism that impairs sexual function and quality of life.

Use of vaginal formulations does not result in systemic levels of estrogen above the normal postmenopausal range. Nonetheless, the U.S. Food and Drug Administration lists a history of breast cancer as a contraindication to the use of all systemic as well as vaginal estrogens.

In premenopausal women, chemotherapy for breast cancer often results in early menopause. Aromatase inhibitors, although effective in preventing recurrent disease in menopausal women, exacerbate GSM. These factors result in a high prevalence of GSM in breast cancer survivors.

Because the safety of vaginal estrogen in the setting of breast cancer is uncertain, investigators at Johns Hopkins conducted a cohort study using claims-based data from more than 200 million U.S. patients that identified women with GSM who had previously been diagnosed

with breast cancer. Among some 42,000 women diagnosed with GSM after breast cancer, 5% had three or more prescriptions and were considered vaginal estrogen users.

No significant differences were noted in recurrence-free survival between the vaginal estrogen group and the no estrogen group. At 5 and 10 years of follow-up, use of vaginal estrogen was not associated with higher all-cause mortality. Among women with estrogen receptor-positive tumors, risk for breast cancer recurrence was similar between estrogen users and nonusers.

## LATEST NEWS

### Older women who get mammograms risk overdiagnosis

M. Alexander Otto, PA, MMS

TOPLINE:

Women who continue breast cancer screening after age 70 face a considerable risk for overdiagnosis.

METHODOLOGY:

- Overdiagnosis – the risk of detecting and treating cancers that would never have caused issues in a person's lifetime – is increasingly recognized as a harm of breast cancer screening; however, the scope of the problem among older women remains uncertain.
- To get an idea, investigators linked Medicare claims data with Surveillance, Epidemiology, and End Results (SEER) data for 54,635 women 70 years or older to compare the incidence of breast cancer and breast cancer-specific death among women who continued

screening mammography with those who did not.

- The women all had undergone recent screening mammograms and had no history of breast cancer at study entry. Those who had a subsequent mammogram within 3 years were classified as undergoing continued screening while those who did not were classified as not undergoing continued screening.
- Overdiagnosis was defined as the difference in cumulative incidence of breast cancer between screened and unscreened women divided by the cumulative incidence among screened women.
- Results were adjusted for potential confounders, including age, race, and ethnicity.

TAKEAWAY:

- Over 80% of women 70-84 years old and more than 60% of women 85 years or older continued screening.
- Among women 70-74 years old, the adjusted cumulative incidence of breast cancer was 6.1 cases per 100 screened women vs. 4.2 cases per 100 unscreened women; for women aged 75-84 years old, the cumulative incidence was 4.9 per 100 screened women vs. 2.6 per 100 unscreened women, and for women 85 years and older, the cumulative incidence was 2.8 vs. 1.3 per 100, respectively.
- Estimates of overdiagnosis ranged from 31% of breast cancer cases among screened women in the 70-74 age group to 54% of cases in the 85 and older group.
- The researchers found no statistically significant reduction in breast cancer-specific death associated with screening in any age or life-expectancy group. Overdiagnosis

appeared to be driven by in situ and localized invasive breast cancer, not advanced breast cancer.

#### IN PRACTICE:

The proportion of older women who continue to receive screening mammograms and may experience breast cancer overdiagnosis is “considerable” and “increases with advancing age and with decreasing life expectancy,” the authors conclude. Given potential benefits and harms of screening in this population, “patient preferences, including risk tolerance, comfort with uncertainty, and willingness to undergo treatment, are important for informing screening decisions.”

**SOURCE:** <https://www.acpjournals.org/doi/10.7326/M23-0133>  
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#### CONFERENCE COVERAGE

### Offering HPV vaccine at age 9 linked to greater series completion

**Tara Haelle**

BALTIMORE—Receiving the first

dose of the human papillomavirus (HPV) vaccine at age 9, rather than bundling it with the Tdap and meningitis vaccines, appears to increase the likelihood that children will complete the HPV vaccine series, according to a retrospective cohort study of commercially insured youth presented at the annual clinical and scientific meeting of the American College of Obstetricians and Gynecologists. The research was published ahead of print in *Human Vaccines and Immunotherapeutics*.

“These findings are novel because they emphasize starting at age 9, and that is different than prior studies that emphasize bundling of these vaccines,” Kevin Ault, MD, professor and chair of the department of obstetrics and gynecology at Western Michigan University Homer Stryker MD School of Medicine and a former member of the CDC’s Advisory Committee on Immunization Practices, said in an interview.

Dr. Ault was not involved in the study but noted that these findings support the AAP’s recommendation to start the HPV vaccine series at age 9. The Centers for Disease Control and

Prevention currently recommends giving the first dose of the HPV vaccine at ages 11-12, at the same time as the Tdap and meningitis vaccines. This recommendation to “bundle” the HPV vaccine with the Tdap and meningitis vaccines aims to facilitate provider-family discussion about the HPV vaccine, ideally reducing parent hesitancy and concerns about the vaccines. Multiple studies have shown improved HPV vaccine uptake when providers offer the HPV vaccine at the same time as the Tdap and meningococcal vaccines.

However, shifts in parents’ attitudes have occurred toward the HPV vaccine since those studies on bundling: Concerns about sexual activity have receded while concerns about safety remain high. The American Academy of Pediatrics and the American Cancer Society both advise starting the HPV vaccine series at age 9, based on evidence showing that more children complete the series when they get the first shot before age 11 compared to getting it at 11 or 12.

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