MEDPAGE TODAY®

Evidence Grows for One-Dose HPV Vaccination

— Another study suggests the number of doses matters less than the age of initiation

by Kristin Jenkins, Contributing Writer, MedPage Today
February 11, 2020

Even a single dose of the quadrivalent human papillomavirus (4vHPV) vaccine was associated with lower incidence of pre-invasive cervical disease compared with no vaccination in adolescent women, according to researchers.

In a large retrospective matched cohort study involving women age 15-19, risk of histologically confirmed cervical intraepithelial neoplasia II/III (CIN-II/III) was equivalent with one, two, or three doses of 4vHPV vaccine. The adjusted hazard ratios (HRs) were 0.64, 0.72, and 0.66, respectively, all with statistical significance.

"This supports the use of any HPV vaccination in reducing the burden of the disease," Ana M. Rodriguez, MD, MPH, University of Texas Medical Branch at Galveston, and colleagues reported online in *Cancer*. "HPV-related disease remains a significant source of morbidity and mortality in both developed and developing countries, and this underscores the need to increase vaccination coverage to effectively reduce HPV infection and disease."

One key caveat in the study, however, was the relatively short follow-up -- only about 2 years on average.

Current evidence "clearly indicates" that the HPV vaccine is more efficacious and the immune response more robust in younger, HPV-naive cohorts, Rodriguez and colleagues pointed out, noting that the average age of first sexual intercourse for U.S. women is 16 to

18.

These findings parallel those from a recent analysis reported by *MedPage Today*. It showed that a single-dose HPV vaccination regimen had similar efficacy against HPV infection in women age 18-26 compared with the recommended two- or three-dose series. The researchers on that study cautioned that more research is needed.

In an editorial accompanying the current study, Julia M.L. Brotherton, BMed(Hons), MPH(Hons), PhD, of the VCS Foundation, Melbourne, Australia, and Karin Sundström, MD, PhD, of the Karolinska Institute in Stockholm, said these data "add to emerging population-based studies supporting one-dose effectiveness against cervical pre-cancer."

In spite of the many different study settings and approaches, "the consistency of this finding gives the one-dose effectiveness hypothesis further credibility," they added.

Although recent studies from Denmark, Sweden, and Australia have reported similar observations, the current study included a comparatively higher proportion of women who received a single dose of HPV vaccine (20.5% vs <5%). In addition, the data were adjusted for sexually transmitted infection and pregnancy, the editorialists pointed out.

"Most population-based data sets have no or limited data elements that can be used as a proxy for sexual behavior, and this study thus contributes valuable knowledge," they said, predicting it could now be possible to analyze cervical outcomes in women "vaccinated predominantly before their sexual debut." At a time when HPV vaccine shortages threaten cancer prevention policy worldwide, one-dose HPV vaccination could potentially expand the reach of the existing supply, reducing overall cost, Brotherton and Sundström suggested.

Study details

In the study, 133,082 females ages 9-26 who received one or more quadrivalent HPV vaccine doses (January 2006 to June 2015) or no HPV vaccination (January 2006 to December 2016) were identified using the claims database of a large private U.S. insurance company.

After stratification by the number of HPV vaccine doses (0, 1, 2, and ≥3 doses) and the age at vaccination initiation (<15, 15-19 years, and >20), 66,541 vaccinated women were matched 1:1 with 66,541 unvaccinated women based on region, age, and history of sexually transmitted disease and pregnancy. Mean follow-up was 26.1 months in the vaccinated groups and 22.7 months in the unvaccinated group.

The vast majority of vaccinated women (91.2%) received their first dose of HPV vaccine when they were age 15 or older, with 41.7% receiving one or two doses. Women vaccinated with a single dose tended to be older than those in the two and three-dose

groups, the analysis confirmed.

The study showed that women age 15-19 who received three doses of the vaccine had a lower risk for high-grade cytology results on screening compared with unvaccinated peers. "High-grade cytology includes either an HSIL [high-grade squamous intraepithelial lesion] or atypical squamous cells, which cannot exclude a high-grade squamous intraepithelial lesion," the researchers noted.

Compared to unvaccinated women, however, there was no significant difference in high-grade cytology seen in women age 20 and older receiving the vaccine compared with unvaccinated women. "This may be due to exposure to high-risk HPV before vaccination," the investigators concluded. "No inference on vaccine dose effectiveness is possible."

Through 5 years of follow-up (reached by roughly 10% of participants), significant differences were observed in the unadjusted event rates among women age 15-19 across all four vaccination groups. In the unvaccinated group, the unadjusted event rate was 2.65% compared with 1.62%, 1.99%, and 1.86% for the one-, two-, and three-dose groups, respectively.

Although 35.3% of the 4,971 women in the two-dose vaccination group received vaccinations more than six months apart, there was no significant difference in the risk of pre-invasive cervical disease compared with those who received their second dose less than six months after the first.

Women who have undergone HPV vaccination may not realize the need for continued screening and testing, the study authors pointed out. "Regardless of the number of doses needed and the age of vaccine initiation, cervical screening is still recommended."

In women who are vaccinated when they are age 18 or older, "more long-term followup data are needed to draw definitive conclusions about the need for beginning and continuing cervical cancer screening," they suggested. "Future studies are needed to examine screening behaviors among those vaccinated at later ages."

In women younger than age 25, however, the effectiveness of cervical cancer screening remains questionable, Rodriguez and colleagues said. Compared with older women, they have a lower incidence of cervical cancer but a higher incidence of false-positive screening results and of spontaneous resolution of pre-cancerous lesions.

An increasing number of studies demonstrate that regression rates for HSILs can range from about 50% to 70% in young women, the researchers noted. Results from the COMPASS trial, for instance, has led to advocacy for a more conservative management approach in these patients, they said.

The study had no commercial funding. Study authors reported no relevant financial interests. Both editorialists reported past participation in research funded by vaccine manufacturers but did not personally receive financial benefits.

Primary Source
Cancer
Source Reference: *Rodriguez AM, et al "Comparison of the Long-Term Impact and Clinical Outcomes of Fewer Doses and Standard Doses of Human Papillomavirus Vaccine in the United States: A Database Study" Cancer 2020; DOI: 10.1002/cncr.32700.*

Secondary Source
Cancer
Source Reference: *Brotherton JML, Sundström K "More Evidence Suggesting That 1-Dose Human Papillomavirus Vaccination May Be Effective" Cancer 2020; DOI: 10.1002/cncr.32696.*