Catch-up HPV vaccine effective for women aged up to 20 years, US study suggests

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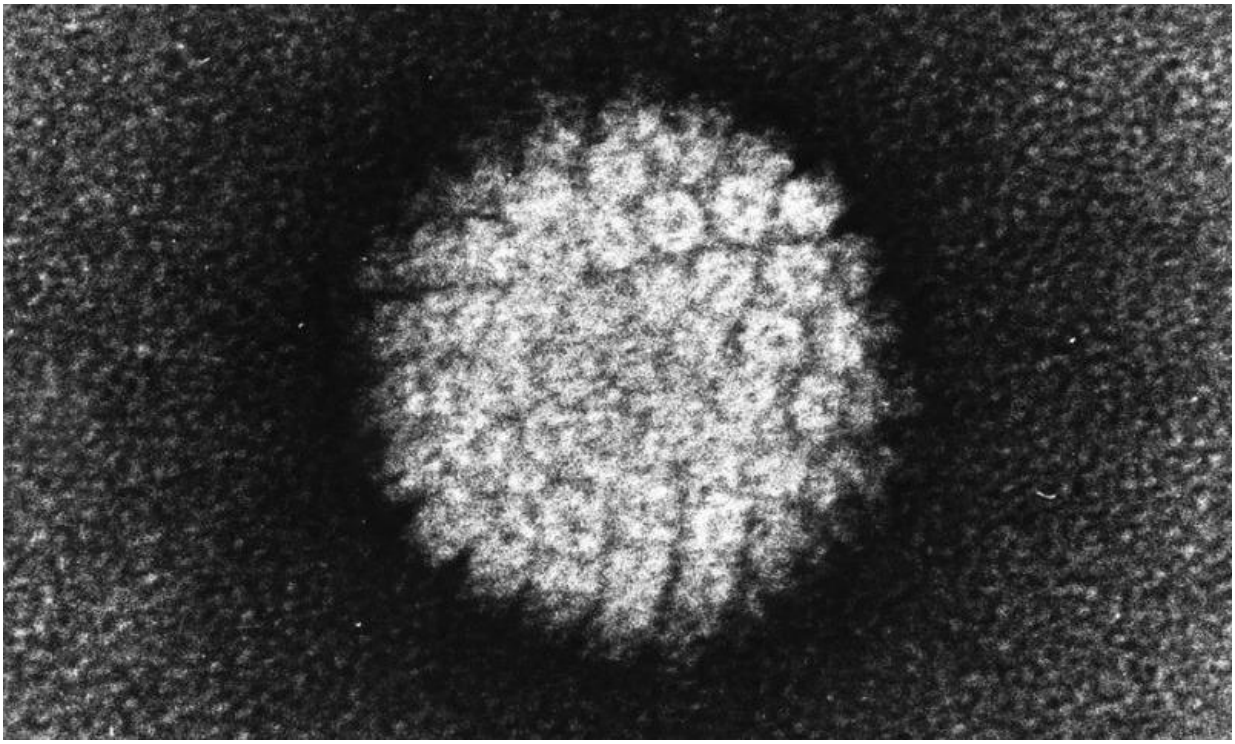

Electron micrograph of a negatively stained human papilloma virus (HPV) which occurs in human warts. Credit: public domain

US study confirms effectiveness of quadrivalent human papillomavirus (HPV) vaccine in women aged up to 20 years who receive all three doses, but more research is needed in women aged 21-26 years.

For women aged 14-20 years, catch-up HPV vaccination—offered if American women miss the recommended vaccination series at 11-12 years—is effective against the risk of important cervical precancers if women receive all three doses, according to a population case-control study of over 25000 people published in *The Lancet Child & Adolescent Health* journal.

The study analysed cases of CIN2+ or CIN3+ (cervical intraepithelial neoplasia—abnormal growth of cells on the surface of the cervix that could potentially lead to cervical cancer) in a population of women and girls in California (USA).

In the USA, HPV vaccination is recommended for girls aged 11-12. For those who did not receive the vaccine at this age, catch-up vaccination is recommended for girls and women aged 13-26 years. The vaccine is approved as a three-dose series, and the US Centers for Disease Control and Prevention also allows for a two-dose series for girls aged 9-14.

However, rates of adolescent HPV vaccination are relatively low in the USA, with less than half of girls aged 13-17 years up to date with the HPV vaccine series.

The findings of the new study suggest catch-up with the full three-dose series for girls and women who receive the first dose at age 14-20 years will offer significant protection. However, they find that more research is needed to confirm the effectiveness of catch-up vaccination in older women aged 21-26 years.

Importantly, the study looked at the effectiveness of the quadrivalent HPV vaccine, and not of the more recently introduced nonavalent HPV vaccine, which is anticipated to prevent more CIN2+ cases than the quadrivalent HPV vaccine. Therefore, further research, including in women aged over 21 years, will be important as new vaccines become

more widely used.

The study included 4357 women with CIN2+ or CIN3+ who were aged 26 or younger when the quadrivalent HPV vaccine was introduced in 2006. For each case, five age-matched controls without CIN2+ or CIN3+ were randomly selected (21773). All women were enrolled at Kaiser Permanente North California. A total of 2837 women enrolled in the study had received at least one dose of the vaccine between 2006 and 2014.

The strongest protection against CIN2+ and CIN3+ was identified for women who had received at least three vaccine doses and had received their first dose aged 14-17 years, or aged 18-20 years. No significant protection was found in women who received their first dose aged 21 years or older, or who received fewer than the full three dose in the series.

"In comparison to other countries, HPV vaccine uptake in the US has been relatively low. Our findings show that girls and women who did not receive the full vaccine series at age 11-12 can still benefit from significant protection if they receive the full three doses of vaccine by the age of 20. The evidence suggests that protection is strongest the earlier the vaccine is initiated, and after the age of 21, the evidence of effectiveness is unclear. Further research in other settings, and using the recently introduced nonavalent vaccine, will now be needed to assess the effectiveness of vaccinating women aged 21-26 years," says lead author Michael J. Silverberg, a research scientist with Kaiser Permanente Northern California's Division of Research, Oakland (USA).

The authors note that only 23 women were diagnosed with cervical cancer in the study, of which only 3 had had prior HPV vaccination. All three women had received at least three doses, and all were 21 or older at the age of the first dose. However, the small numbers limit the

researchers' ability to quantify the effect of the HPV vaccine on cervical cancer incidence, rather than the composite outcomes of CIN2+ and CIN3+, which includes both cancer and precancerous lesions.

Additionally, the authors note that the study was conducted in a single health-care setting, meaning that it may only be generalizable to other integrated health care settings and insured women in the area, which may not represent the most at-risk populations. The study did not look at the effect of the HPV vaccine on other clinically important outcomes such as low-grade dysplasia (i.e., CIN1), persistent HPV infection, or genital warts.

Writing in a linked Comment, Sarah Dilley and Warner Huh, Division of Gynecologic Oncology, University of Alabama, Birmingham (USA) advise caution before abandoning the practice of catch-up vaccination in women aged over 21 years: "The results of this study confirm existing research which showed that the HPV vaccine is most effective when given at younger ages, but no benefit was found in patients older than 21 years. Efforts towards increasing HPV vaccine uptake should be focused on younger adolescents—with a priority on vaccinating children aged 11-12 years—and providing catch-up dosing for older adolescents. However, in the setting of low rates of HPV vaccination in the USA, the importance of catch-up dosing in young women should not be ignored. Given that prospective efficacy studies have shown benefits for catch-up vaccination up to at least age 26 years, more data is needed before abandoning this practice."

More information: *The Lancet Child & Adolescent Health*, www.thelancet.com/journals/lan … (18)30220-7/fulltext

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