Does HPV vaccination prevent the development of cervical cancer?

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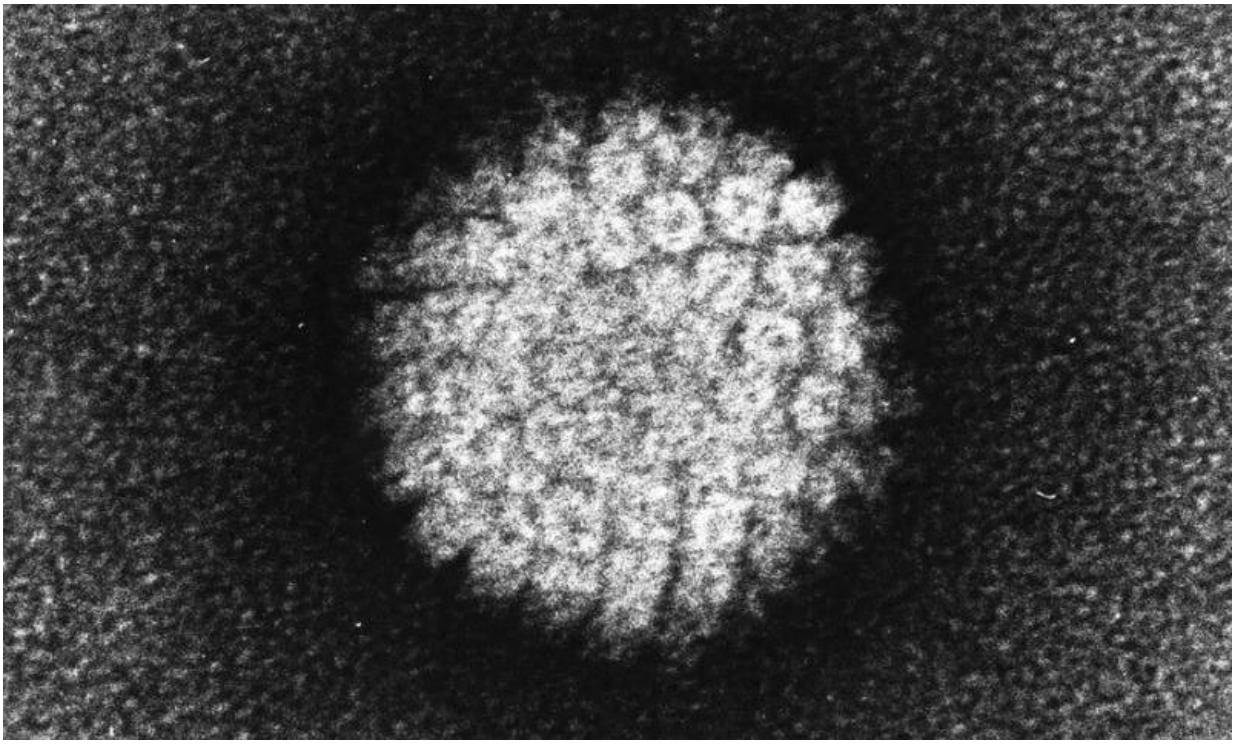

Electron micrograph of a negatively stained human papilloma virus (HPV) which occurs in human warts. Credit: public domain

New evidence published today in the *Cochrane Library* shows that human papilloma virus (HPV) vaccines protect against cervical lesions in young women, particularly in those who are vaccinated between the ages of 15 and 26. It also summarizes findings on harms that have been

assessed in randomized controlled trials.

Most people who have sexual contact at some point in their life will be exposed to the human papilloma virus (HPV). In the majority of women, HPV infection will be cleared by the immune system. When the immune system does not clear the virus, persistent HPV infection can cause abnormal cervical cells. These lesions are known as cervical 'precancer' because over time they can progress to cervical cancer if left untreated.

There are many different types of HPV. Some are associated with the development of cervical lesions that can become cancerous and are considered as high-risk HPV types. Two of these high-risk types (HPV16 and HPV18) account for about 70% all cases of cervical cancer worldwide. Vaccines have been developed that help the immune system to recognize certain HPV types. Because cervical cancer can take several years to develop, regulatory bodies and international health agencies such as the World Health Organization (WHO) regard cervical lesions as the preferred outcome measure for HPV vaccine trials.

A team of Cochrane researchers has summarized results of 26 studies in 73,428 women conducted across all continents over the last eight years. Most women in the studies were under the age of 26 years old, although three trials recruited women between 25 and 45 years. The studies were well-designed, randomizing the women to either HPV vaccine or a placebo. The review evaluates evidence for two vaccines: the bivalent vaccine targeting HPV16 and 18, and the quadrivalent vaccine targeting HPV16/18 and two low-risk HPV types causing genital warts. The newer vaccine that targets nine HPV types was not included in the review since it has not been compared against a placebo in a randomized controlled trial.

The review looked at two groups of people: women who are free of high-risk HPV at the time of vaccination and all women regardless of HPV

status at vaccination. The effects of the vaccine were measured as precancer associated with HPV16/18 and precancer irrespective of HPV type. The review looked at data from ten trials assessing cervical lesion data at between three and a half to eight years after vaccination.

None of the studies have followed up participants for long enough to detect an effect on cervical cancer. The researchers looked at precancer cervical lesions instead. They found that in young women who did not carry HPV, vaccination reduced the risk of developing precancer. About 164 per 10,000 women who got placebo and 2 per 10,000 women who got the vaccine went on to develop cervical precancer.

The researchers also looked at data from all enrolled women regardless whether they were free of high-risk HPV at vaccination or not. Among women aged 15 to 26 years, vaccines reduced the risk of cervical precancer associated with HPV16/18 from 341 to 157 per 10,000. HPV vaccination reduced also the risk for any precancer lesions from 559 to 391 per 10,000.

In older women vaccinated between 25 to 45 years the HPV vaccine does not work as well. This might be because older women are more likely to have been exposed already.

The evidence also shows that the vaccines do not appear to increase the risk of serious side effects which was about 7% in both HPV vaccinated or control groups. The researchers did not find increased risk of miscarriage in women who became pregnant after vaccination. However, they emphasize that more data are required to provide greater certainty about very rare side effects and the effect vaccines have on rates of stillbirth, and babies born with abnormalities in those who became pregnant around the time of vaccination.

Cochrane lead author, Dr. Marc Arbyn, of the unit Cancer

Epidemiology, Belgian Cancer Centre, Sciensano, said: "The findings of this review should be viewed within the context of multiple global surveillance studies, which have been conducted by the Global Advisory Committee on Vaccine Safety from the WHO since the vaccinations were licensed. The committee concluded that the risk-benefit profile of prophylactic HPV vaccines remains favourable and expressed its concerns about unjustified claims of harm that lack biological and epidemiological evidence, and which may affect the confidence of the public. At the same time, the Committee encouraged health authorities to continue surveillance and examination for potential adverse events."

Dr. Jo Morrison, Consultant in Gynaecological Oncology at the Musgrove Park Hospital, Somerset, UK, said: "Vaccination aims to prime the immune system to produce antibodies that can block subsequent natural HPV infection. These data show that immunizing against HPV infection protects against cervical precancer, and it is very likely that this will reduce cervical cancer rates in the future. However, it cannot prevent all cervical cancer and it is still important to have regular screening, even if you have been vaccinated."

She added: "Cervical cancer can take many years to develop following HPV infection and development of precancer lesions, therefore long-term follow-up studies are needed to find out the effects of HPV vaccination on cervical cancer rates."

More information: Arbyn M, Xu L, Simoens C, Martin-Hirsch PPL. Prophylactic vaccination against human papillomaviruses to prevent cervical cancer and its precursors. *Cochrane Database of Systematic Reviews* 2018, Issue 5. Art. No.: CD009069. DOI: 10.1002/14651858.CD009069.pub3