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The Truth About HPV Vaccination, Part 1: How Safe Is It, Really?

This first installment in a multi-part series about the human papillomavirus, or HPV, vaccine explores peer-reviewed scientific literature that reveals serious safety concerns about a vaccine widely regarded as safe.

By The Epoch Times

By Yuhong Dong

The decline of public trust in COVID-19 vaccines significantly impacts vaccination rates against routine childhood diseases. This multiple-part series explores the international research done over the past two decades on the human papillomavirus (HPV) vaccine — believed to be one of the most effective vaccines developed to date.

Summary of Key Facts

- This multiple-part series offers a thorough analysis of concerns raised about HPV vaccination following the global HPV campaign, which commenced in 2006.
- In the U.S., the HPV vaccine was reported to have a disproportionately higher percentage of adverse events of fainting and blood clots in the veins. The U.S. Food and Drug Administration (FDA) acknowledges that fainting can happen following the HPV vaccine, and recommends sitting or lying down to get the shot, then waiting for 15 minutes afterward.
- International scientists found that the Centers for Disease Control and Prevention's (CDC) Vaccine Adverse Event Reporting System (VAERS) logged a substantial increase in reports of premature ovarian failure from 1.4 per year before 2006 to 22.2 per year after the HPV vaccine approval, yielding a Proportional Reporting Ratio of 46.1.

The HPV vaccine is widely regarded as one of the most effective vaccines developed to date. Nevertheless, safety issues have been raised following its approval, and in response, additional research has been published and litigation has been brought on behalf of those with a vaccine injury.

In this HPV vaccine series, Parts I and II explain how the vaccine works and the evidence suggesting there may be legitimate safety concerns. The remaining parts present questions about real-world vaccine effectiveness and identify specific ingredients which may pose harm.

The information presented here is drawn from peer-reviewed scientific literature from the U.S., Australia, Denmark, Sweden, France and Japan, as well as statistics published by public health agencies in each of these countries.

More than 100 hours of research and internal peer review among scientists with experience in infectious diseases, virology, clinical trials and vaccine epidemiology have been invested in presenting this summary of the evidence.

Large registry-based studies have identified plausible associations between HPV vaccination and autoimmune conditions, including premature ovarian insufficiency or premature ovarian failure, Guillain-Barré syndrome (GBS), postural orthostatic tachycardia syndrome and chronic regional pain syndrome.

While it is easy to be enthusiastic about recent advances in human vaccine technology, we should keep in mind that achieving real and lasting good health is much more than just the absence of a certain virus.

What is HPV?

According to the CDC, HPV is the most common sexually transmitted infection in the U.S.

HPV is a small DNA virus infecting human cutaneous epithelial cells in the mucosa and skin. More than 150 strains of the HPV virus have been identified.

HPV infection is so common that the majority of sexually active people will get it at some point in their lives, even if they have only one or very few sexual partners. It can spread through sexual intercourse and oral sex. It can also pass between people through skin-to-skin contact, even by people who have no symptoms.

HPV infection causes genital warts, some of which can turn into cancer. For the most part, however, HPV infection is benign. More than 90% of HPV infections cause no clinical symptoms and are self-limited, meaning the virus is cleared by the body via natural immunological defenses.

HPV-associated cancers

High-risk HPV types (types 16, 18 and others) can cause cervical cell abnormalities that are precursors to cancers.

Type 16 is associated with approximately 50% of cervical cancers worldwide, and types 16 and 18 together are linked to 66% of cervical cancers.

An additional five high-risk types, 31, 33, 45, 52 and 58, are linked with another 15% of cervical cancers and 11% of all HPV-associated cancers.

Infection with a high-risk HPV type is associated with a higher chance of the development of cervical cancer but, by itself, HPV infection is not the sole risk factor to cause cancer. There are many other reasons, as discussed in this paper.

Given the prevalence of infection, it is unsurprising that globally, cervical cancer is the fourth most common cancer in women. In 2018, an estimated 570,000 women were diagnosed with cervical cancer worldwide and more than 300,000 died of the disease.

In the U.S., nearly 50,000 new HPV-associated cancers occur annually, with women infected at a slightly higher rate than men.

But in 9 out of 10 cases, HPV goes away within two years without causing health problems.

Only persistent HPV infections may lead to cancer. These infections evade the immune system's innate cell-mediated defenses.

The incidence of cervical cancer can be controlled as a result of the implementation of routine testing and screening, including Pap and DNA tests.

HPV vaccines

Three HPV vaccines — bivalent HPV vaccine (Cervarix, 2vHPV), quadrivalent HPV vaccine (Gardasil, 4vHPV or HPV4) and 9-valent HPV vaccine (Gardasil 9, 9vHPV) — have been licensed by the FDA.

The HPV vaccine uses recombinant technology to assemble the shell of the virus — L1 capsid protein. These viral-like particles do not contain the virus genome and are not infectious.

Cervarix, developed by GlaxoSmithKline, is a bivalent vaccine against HPV types 16 and 18, that was pulled from the U.S. market in 2016 due to "very low market demand."

Merck's original Gardasil vaccine was designed to prevent infections from four strains (types 6, 11, 16 and 18).

On June 8, 2006, after the FDA's fast-tracked review, Gardasil was approved for use in females ages 9 to 26 for the prevention of cervical, vulvar and vaginal cancers.

According to the label accompanying the vaccine, the ingredients in Merck's first Gardasil vaccine were proteins of HPV, amorphous aluminum hydroxyphosphate sulfate, yeast protein, sodium chloride, L-histidine, polysorbate 80, sodium borate and water for injection.

On Oct. 16, 2009, the FDA approved Gardasil (HPV4) for use in boys ages 9 through 26 for the prevention of genital warts caused by HPV types 6 and 11, but not for cancer.

In 2010, it approved Gardasil for the prevention of anal cancer in males and females ages 9 to 26.

Four years later, the FDA approved an updated vaccine, Merck's Gardasil 9, for use in girls ages 9 to 26 and boys ages 9 to 15 for the prevention of cervical, vaginal and anal cancers.

Gardasil 9 contains the same ingredients as Gardasil, but offers protection against nine HPV strains, adding five additional types (HPV types 31, 33, 45, 52 and 58).

The current HPV vaccination schedule recommended by the CDC is two doses for both boys and girls aged 11 or 12. However, it is approved for children as young as 9. The second dose is given 6 to 12

months after the first.

For those aged 15 and above, a three-dose schedule is implemented at one- to two-month and six-month intervals, although antibody-level studies suggest that two doses are sufficient.

The vaccine prompts the body to produce neutralizing antibodies against HPV. Antibody responses appear to peak seven months after the first dose (or one month after the third dose). The vaccine-induced antibody levels appear to be 10 to 100 times higher than those after natural infection.

The high vaccine effectiveness (90 to 98%) against the fast-growing, abnormal cells which may cause precancerous lesions in people ages 16 to 26 suggested that the best timing for vaccination was to give it to patients before they became sexually active.

HPV VAERS reports from 2 large countries

U.S. HPV vaccine adverse events

On Aug. 19, 2009, the Journal of the American Medical Association published an article authored by scientists from the FDA and CDC that reviewed the safety data for Gardasil for adverse events reported to VAERS between June 2006 through December 2008.

During that time, there were 12,424 reports of adverse events. Of these, 772 (6.2%) were serious.

VAERS is a passive surveillance system, which is subject to multiple limitations, including underreporting, unconfirmed diagnosis, lack of denominator data and no unbiased comparison groups.

Nevertheless, it is a useful and important tool for detecting postmarket safety issues with vaccines.

A disproportionately high percentage of Gardasil VAERS reports were of syncope (fainting) and venous thromboembolic events (blood clots in the veins) compared with other vaccines. There were 8.2 syncope events per 100,000 HPV doses and 0.2 venous thromboembolic events per 100,000 HPV doses reported, respectively.

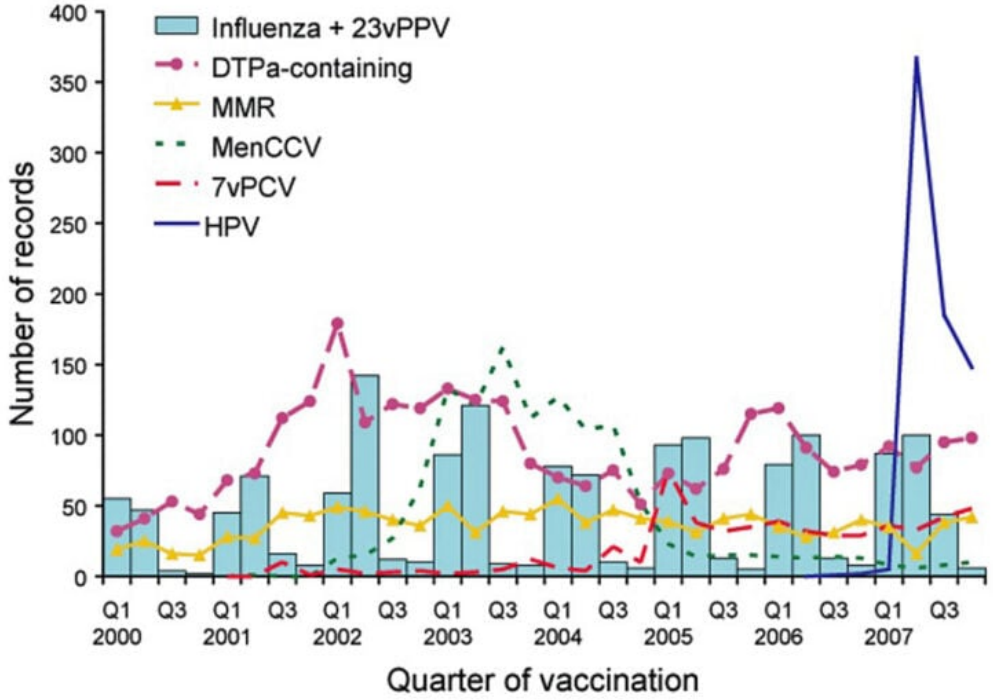
The Gardasil package insert includes a warning about fainting, fever, dizziness, nausea and headaches (page 1) and notes at least the following adverse reactions reported during postmarketing surveillance (section 6.2): Guillain-Barré syndrome, transverse myelitis, motor neuron disease, venous thromboembolic events, pancreatitis and autoimmune disorders.

Australia HPV vaccines adverse events

In 2007, Australia reported an annual adverse drug reaction rate of 7.3/100,000, the highest since 2003, representing an 85% increase from 2006.

Per the analysis of the Adverse Drug Reactions System database by the Australian Department of Health and Aging, this increase was “almost entirely due to” reports following the national rollout of the three-dose HPV vaccination program for young females in April 2007; 705 of the 1,538 adverse drug reactions reported that year were from the Gardasil vaccine.

Figure 2. Frequently suspected vaccines, adverse events following immunisation, ADRS database, 2000 to 2007, by quarter of vaccination



In Australia, the ADR increase in 2007 was almost entirely due to the three-dose HPV vaccination program for females aged 12 to 26 years in April 2007. Credit: Australian Government Department of Health and Aged Care.

Moreover, though people may take different vaccines other than HPV, the HPV vaccine was the only suspected vaccine to cause adverse reactions in 96% of records. Twenty-nine percent had causality ratings of "certain" or "probable" and 6% were defined as "serious."

Table 3. Vaccine types listed as 'suspected' in records of adverse events following immunisation (AEFI), ADRS database, 2007

Suspected vaccine type*	AEFI records	One suspected vaccine or drug only†		'Certain' or 'probable' causality rating‡		'Serious' outcome§		Age group‖			
								<7 years		≥7 years	
	n	n	%¶	n	%¶	n	%¶	n	%¶	n	%¶
HPV**	705	674	96	203	29	43	6	0	–	689	98
DTPa-IPV	288	128	44	113	39	24	8	287	100	1	0
7vPCV	159	7	4	9	6	26	16	158	99	1	1
Influenza	150	111	74	45	30	21	14	30	20	116	77
MMR	131	27	21	16	12	15	11	118	90	13	10
23vPPV	118	87	74	73	62	10	8	4	3	112	95
Hib-Hepatitis B	118	118	100	4	3	14	12	118	100	0	–

In these HPV-induced ADRs, 674 were suspected to be related to HPV vaccines, 203 had causality ratings of "certain" or "probable," and 43 were defined as "serious." Credit: Australian Government Department of Health and Aged Care.

Japan withdraws recommendation, vaccine acceptance plunged

In 2013, the Japanese raised concerns about a variety of widely reported post-vaccination serious adverse events. This led the government to suspend recommending the HPV vaccine for six years. Vaccine acceptance of HPV in Japan plunged significantly after 2013, from 42.9% to 14.3%, or from 65.4% to 3.9%.

Researchers around the world also started to investigate HPV safety. A World Health Organization (WHO) position paper released on July 14, 2017, concluded that the HPV vaccines were "extremely safe."

The same report estimated approximately 1.7 cases of anaphylaxis per million HPV doses, that no association with GBS was found, and that syncope (fainting) was "established as a common anxiety or stress-related reaction to the injection."

In the spring of 2022, Japan announced it was relaunching its HPV vaccination drive. Mainstream news outlets reported that for thousands of women, the cost of caution may have led to preventable HPV-induced cancers and an estimated 5,000 to 5,700 deaths.

However, a true risk-benefit analysis would also consider the number of serious adverse events prevented by putting the program on hold. The question remains: Was Japan's caution warranted, or should their national vaccination program have continued?

Ovarian insufficiency

Concerns that the vaccine may be negatively affecting fertility have been detailed in the scientific literature.

In 2014, a peer-reviewed case series describing premature ovarian failure among Australian women following HPV vaccination was published in the Journal of Investigative Medicine.

This prompted other researchers to systematically examine the VAERS data to see if there was a connection between premature ovarian failure and Gardasil. Their study found a "potential safety signal" and concluded that "further investigations are warranted."

VAERS analysis on ovarian failure

Two recent publications based on VAERS reports (first study, second study) found that events with a probable autoimmune background were significantly more frequent after HPV vaccination compared to other vaccinations.

The team of international scientists that did the second study evaluated reports between 1990 and 2018. They found that among the 228,341 premature ovarian failure reports, 0.1% was considered to be associated with HPV vaccination with a median age of 15 years and the time to onset was 20.5 days following vaccination.

The primary symptoms were amenorrhea (80.4%) and premature menopause (15.3%).

Most strikingly, the mean number of premature ovarian failure cases increased significantly from 1.4 per year prior to 2006 to 22.2 per year after the HPV vaccine was approved, with a proportional reporting ratio of 46.

The investigators noted that the WHO and CDC declared the HPV vaccine safe regardless of lacking adequate research into safety concerns.

For example, the authors note that in a CDC-sponsored VAERS study, 17 cases of premature ovarian failure were identified but 15 were excluded due to insufficient information to confirm the diagnosis. A separate observational study using the Vaccine Safety Datalink found no increased risk.

But this study was too underpowered to detect a signal. In addition, a cross-sectional survey study using National Health and Nutrition Examination Survey data relied on an inaccurate measurement of premature ovarian failure and self-reported HPV vaccination.

In summary, the researchers detected a strong safety signal even after accounting for a potential upswing in reports due to media coverage after the product launch (they refer to this as "notoriety bias").

Because VAERS is a passive reporting system, the data may be incomplete and are often unconfirmed by physicians. Therefore, this study cannot provide a definitive link between HPV vaccination and premature ovarian insufficiency or premature ovarian failure but does generate a hypothetical link.

The authors of the second study conclude by insisting that "this signal warrants well-designed and appropriate epidemiological research." They note that "if the signal is confirmed, the risk is small compared to the lifetime risk of cervical cancer."

However, the benefit-risk profile on an individual level is not uniform.

Given the health impacts of premature ovarian insufficiency and premature ovarian failure — some of which may be irreversible — and the declining mortality rate for cervical cancer even in the prevaccine era, the risk-benefit profile for HPV vaccination remains unclear.

3 case reports on ovarian insufficiency

In the 2014 investigation mentioned above, a general practitioner in Australia noticed that three girls developed premature ovarian insufficiency following HPV4 vaccination.

As a result of vaccination, each of the girls (ages 16, 16 and 18) had been prescribed oral contraception to treat menstrual cycle irregularities. Typically, women present with amenorrhea (no periods) or oligomenorrhea (infrequent periods) as the initial symptom of premature ovarian insufficiency.

One girl had irregular periods following three doses of HPV vaccination. She then became amenorrheic and was diagnosed with premature ovarian insufficiency.

Another girl's periods were "like clockwork" until after the third HPV dose, which she received at age 15. Her first cycle after being vaccinated for the third time started two weeks late, and her next cycle was two months late. The final cycle began nine months later. The patient had no family history of early menopause.

She was diagnosed with premature ovarian failure at 16. Lab work found hormone levels consistent with those of postmenopausal women, but her bone mineral density was normal.

The authors of this case series noted that in preclinical studies of HPV4, the five-week-old rats only conceived one litter and the only available toxicology studies appear to be on the male rodent reproductive system.

However, only two of three doses were administered prior to mating, and the overall fecundity was 95%, slightly lower than the control rats (98%) that received no vaccination prior to mating.

The dose tolerance recommendations were based on an average weight of 50 kilograms for an adolescent girl but failed to take into account that HPV4 is administered to girls ages 9 to 13 years, who range in weight from 28 to 46 kilograms.

Danish retrospective cohort study finds no link

A 2021 study also evaluated premature ovarian insufficiency in a nationwide cohort of nearly 1 million Danish females ages 11 to 34 years.

The researchers used Cox proportional hazard regression to detect an increased risk of premature ovarian insufficiency diagnosis by HPV4 vaccination status during the years 2007-2016. The hazard ratio for premature ovarian insufficiency (vaccinated versus unvaccinated) was 0.96.

One limitation was that data on age at menarche (first menstruation) and oral contraceptive use were not available. Girls who had not yet reached menarche would not be at risk for premature ovarian insufficiency, of course.

The authors excluded girls under age 15 in a sensitivity analysis and still found no signal, concluding that no association was found between HPV4 vaccination and premature ovarian insufficiency.

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