

Research on the current situation and coping strategies for cervical cancer in China

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Abstract. Cervical cancer caused by human papilloma virus has become one of the most common cancers threatening the life and health of Chinese women. The incidence and mortality of cervical cancer in China has always been high, and cervical cancer has become the sixth most common disease among Chinese women. In this paper, the status quo and existing problems of cervical cancer in China were analyzed, and combined with the actual work of the current immunization program, the vaccination rate of human papilloma virus vaccine was strengthened to help achieve the goal of eliminating cervical cancer.

Keywords: Cervical cancer, The vaccine, Existing problems, Countermeasures and suggestions.

1. Current situation of human papilloma virus in China

Cervical cancer is a malignant tumor disease that endangers women's health. The continuous infection of the virus may cause a series of diseases such as condyloma acuminata, anal cancer, oral cancer, etc. According to the Global Cancer Statistics Report 2020, there were 604,127 new cases of female cervical cancer and 341,831 new worldwide in 2020. The incidence and mortality rate of cervical cancer rank fourth among all female malignant tumors in the world. There are about 11 million cases of cervical cancer in China, an increase of about 3.5% over 2018, ranking sixth among the incidence of female tumors; about 59,000 people died of cervical cancer, an increase of about 23% over 2018, accounting for 5% of the total number of female tumor deaths. All female tumor deaths, cervical cancer are among them. The country ranks seventh, and in recent years, the incidence of cervical cancer has shown a younger trend. China is second only to India in terms of morbidity and mortality, and is the second largest burden of cervical cancer in the world, which seriously affects the quality of life of Chinese women.

More than 200 virus subtypes have been identified in human papilloma virus. According to the benign and malignant lesions induced after infection, HPV subtypes can be divided into high-risk and low-risk types. It is worth noting that both men and women are likely to be infected with HPV. Epidemiological research shows that there are certain regional HPV infections, with higher HPV52/58 infection among northern women and higher HPV18/58 infection among southern women. In addition, there are certain age differences, with two peak infection rates among young women and middle-aged women.

The mortality rate of cervical cancer is relatively high. In developing countries, women account for 88% of global deaths from cervical cancer. In addition to the vaccination of HPV vaccine, HPV screening is also particularly important. In terms of screening, China launched the "Two Cancer Screening" program in 2009 to provide free breast and cervical cancer screening services for rural women aged 35 to 39. The country has since expanded to urban women, and the age has been extended to 64. As of 2021, the number of cervical cancer screenings has exceeded 400 million. In 2020, the penetration rate of cervical cancer screening in China's recommended population was 43%,

which is lower than the 70% screening target set by the World Health Organization. Although China recommends that the number of people under cervical cancer screening increased from 412 million in 2016 to 418 million in 2020, and the penetration rate increased by 7.4%, the gap from the World Health Organization's standards is still large. In terms of cervical cancer detection specifications, on November 26, 2015, CFDA issued the Guidelines for HPV nucleic acid testing and Technical Review of genotyping and reagents, marking the formation of China's own HPV industry testing standards, and HPV testing tends to be more professional, standardized and international.

Because many HPV subtype infections will automatically subside, people are infected unconsciously, unconsciously produce immunity, and disappear by themselves. To some extent, it has led the public to relax its vigilance against cervical cancer. Therefore, regular cervical cancer is very necessary. Epidemiological studies have pointed out that the younger age of first sexual intercourse, irregular sexual partners, low level of HPV screening, and insufficient cognitive ability of Chinese people are all the reasons for the high rate and incidence of HPV infection. This is particularly obvious among developing and backward countries.

2. Problems facing human papilloma virus vaccination

2.1 Shortage of human papilloma virus vaccine

In terms of cervical cancer prevention, HPV vaccine can effectively reduce the incidence of cervical cancer. At present, there are three recognized vaccines around the world, namely, Cervarix, Gardasil and Gardasil 9, which were approved for listing in 2007, 2006 and 2014. Research shows that the Cervarix vaccine can prevent 70% of human papilloma virus; Gardasil vaccine can prevent 70% of human papilloma virus and 90% condyloma acuminata; Gardasil 9 can prevent 90% of human papilloma virus, 85% vaginal cancer and 50% of low-level cervix. Cancer, 90% condyloma acuminata and 95% anal cancer. According to the WHO's recommendation that people aged 9 to 14 are the main vaccination target, at least 41 million women in China need to be vaccinated against human papilloma virus. According to three consecutive doses to complete immunization, China needs at least 123 million doses of human papilloma virus vaccine to complete the vaccination of the main target population. However, from 2017 to 2019, only 18.57 million vaccines of various types of human papilloma virus vaccines in China were approved and issued, and the demand for vaccines far outweighed the supply. The phenomenon of "difficult to find" has lasted for a long time.

2.2 Inadequate knowledge of human papilloma virus vaccine

Cervical cancer is a malignant disease that can be prevented. If detected, diagnosed and treated at an early stage, cervical cancer can be eliminated. Vaccination of HPV vaccine greatly reduces the risk of disease. However, the survey shows that Chinese citizens have low awareness of HPV vaccine-relatedness, with a rate of 57.7%, and their understanding of HPV vaccine mainly comes from the Internet. Women in Hong Kong, China and Taiwan know more about the HPV vaccine than women in mainland China. Most women do not have enough understanding of HPV risk perception, believing that having a normal sex life will not be infected with HPV, ignoring the vaccination of HPV vaccine. If they know that they are infected with HPV, they are more willing to get the HPV vaccine. However, most parents think that their children will not be infected with HPV, so they do not vaccinate their children against HPV. The study found that subjective understanding is related to the willingness to be vaccinated against HPV. If there are medical staff at home, or people around me have been vaccinated against HPV vaccine, I am likely to take the initiative to understand the knowledge of HPV vaccine and get the HPV vaccine.

College students are in a period of sexual activity and are the main group of vaccination. There are also differences in the cognitive status of HPV vaccine among college students in different regions. Vaccines in Hong Kong, Taiwan and other regions of China are on the market earlier than mainland China, and college students in Hong Kong and Taiwan in China have a better understanding of HPV vaccines than mainland China. A survey of four universities in Hong Kong shows that the vaccination

rate of HPV vaccine is 27.6%, the awareness rate of HPV vaccine is 91.4%, women (93.8%) are significantly higher than that of men (86.8), and only 45.8% of respondents know that HPV vaccination is not only applicable to women. Although 86.8% of men have heard of the HPV vaccine, the vaccination rate is only 4.7%, which is far lower than the 22% reported in a survey of men aged 18-22 in the United States .Jiangyi Lai and others surveyed female college students in four colleges and universities in Hangzhou showed that the awareness rate of HPV and HPY vaccine was 25.9%, of which medical and non-medical students were 38.2% and 13.6% respectively, the vaccination rate was 3.6%, and the HPV vaccination willingness rate was 73.2% . It can be seen that the cognitive level of HPV and HPV vaccines among college students in mainland China is lower than that of Hong Kong, Taiwan and other regions of China, and college students of different genders and majors also have different understanding of HPV-related knowledge.

2.3 High cost of human papilloma virus vaccine

Five kinds of human papilloma virus (HPV) vaccines are available in China, including Recombinant, Cecolin, Cervarix, Gardasi, Gardasil 9. The following is specific information on human papilloma virus vaccines.

Table 1. Cervical Cancer Vaccine Information

HPV vaccine types	Recombinant	Cecolin	Cervarix	Gardasi	Gardasil 9
The manufacturer	WALVAX	Wantai biological	GSK	MSD	MSD
Time to market worldwide	2022	2019	2007	2006	2014
Time to Market in China	2022	2020	2016	2017	2018
place of origin	China	China	Belgium	The United States	The United States
The price	957 yuan	1017 yuan	1740 yuan	2340 yuan	3954 yuan

At present, vaccination is mainly based on Cervarix, Gardasi and Gardasil 9. The cost of completing three stitches is 1740, 2340 and 3954 yuan in turn. Obviously, even if the price is relatively low, it costs 1,740 yuan to complete three doses of vaccinations. 1,740 yuan is also a big expenditure for ordinary Chinese families and individuals. Fortunately, with the production and launch of domestic divalent vaccines, it can alleviate the high price of vaccines and increase the vaccination rate of human papilloma virus vaccine to a certain extent.

2.4 Human papilloma virus vaccine targets a small population

According to the approval of HPV vaccine issued by the Central Procuratorate, from the approval of China's first HPV vaccine in 2016 to 2021, a total of 20 million people in China have completed the vaccination of HPV vaccine. In contrast, the number of women aged 9 to 45 in China is about 382 million, and the penetration rate of HPV vaccine is only 7%. In contrast, some European and American countries have introduced a series of vaccination preferential policies. HPV is a type of sexually transmitted virus, mainly through genital contact. Therefore, men are also important transmission vectors and direct victims of HPV. Continued HIV infection in men will cause a series of major diseases such as anal cancer, penile cancer and oropharyngeal cancer. In view of this, the United States encourages men and women under the age of 26 to be vaccinated against HPV. In the United Kingdom, adolescents aged 12 to 13, both men and women, are vaccinated with two free HPV vaccines at six months. In New Zealand, two doses of Gardasil 9 can be vaccinated free for 12-year-old children, men and women aged 9 to 26 can be vaccinated for free HPV vaccine, while people aged 27 to 45 need to be vaccinated at their own expense. In some European and American countries, the age of vaccination has been extended, and the number of people vaccinated has also increased relatively. China's HPV vaccination was introduced late. HPV vaccination is only for women. Compared with some developed countries, there is still a long way to go.

2.5 There are public concerns about the safety of human papilloma virus vaccine

Research shows that human papilloma virus vaccine can reduce the incidence of cervical intraepithelial neoplasia. In the adult population, safety is the most important factor in reducing human papilloma virus vaccination. In April 2019, Hainan Boao Yinfeng Health International Hospital was suspected of illegally vaccinating 38 people with fake HPV vaccines. In May of the same year, Hong Kong's Ta Kung Pao reported that a Hong Kong clinic gave grey-market HPV vaccines to mainland tourists. The operation of the clinic is under the cover of medical beauty. Only mainland tourists are welcome, and the human papilloma virus vaccine can only be booked through an intermediary. The vaccine incident raised public doubts about fake vaccines and questioned the safety of vaccines. Through this incident, we can see that there is a lack of production, circulation and use of human papilloma virus vaccine.

3. Recommendations and strategies for human papilloma virus vaccination

3.1 Accelerate the development and production of human papilloma virus vaccine

Before HPV vaccines are included in the immunization plan, the research and development of domestic high-priced vaccines is particularly important to solve the contradiction between high-priced vaccines and vaccine prices. Therefore, while increasing the vaccination rate of human papilloma virus, we can encourage the research and development of vaccines in biopharmaceutical companies and improve the market supply of vaccines. At present, China's Wantai Biotechnology and WALVAX have successfully developed a divalent human papillomavirus vaccine. Taking Wantai Biotechnology's "Cecolin" as an example, the vaccine has been officially launched in China since May 2020, and the total number of batches issued in the first year has reached 2.46 million. In 2021, its cumulative batch issuance jumped to 10.66 million, and its market share has surpassed GSK. With the expansion of Wantai Biotechnology, Cecolin's production capacity is expected to reach 30 million pieces/year.

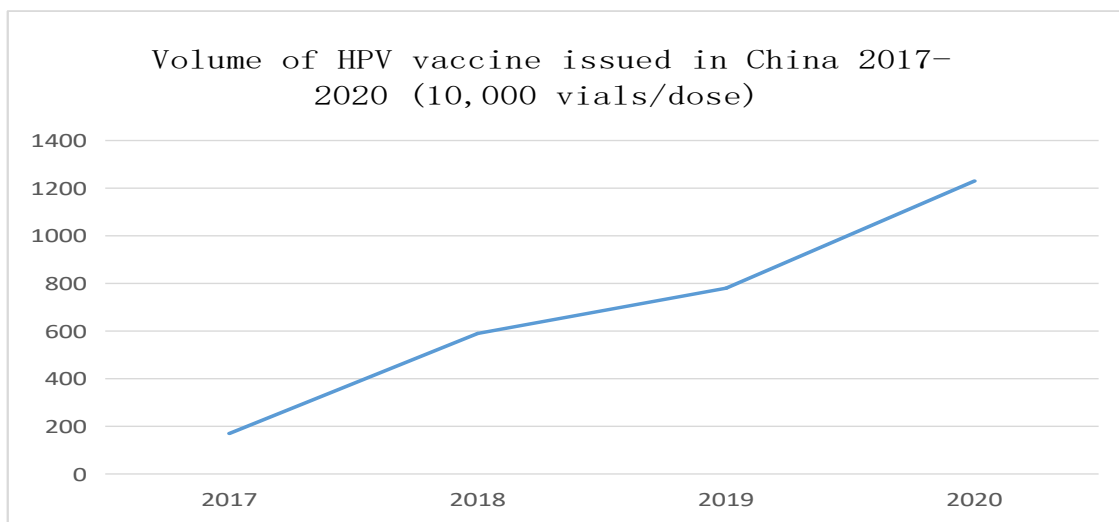


Figure 1. Volume of HPV vaccine issued in China 2017-2020 (10 ,000 vials /dose)

Since 2006, 18 clinical HPV vaccine trials submitted by nine Chinese companies have been approved. Among them, the research and development pipeline of Kangle Guardian includes the trivalent HPV vaccine, which has entered the third phase of clinical trial; the recombinant nine-valent HPV vaccine for women and men has entered the third phase of the clinical trial and the first phase of the clinical trial respectively; the recombinant 15-valent HPV vaccine has entered the preclinical study, and the HPV DNA therapeutic vaccine has entered. Early research.

The Chinese government should continue to support high-priced research and development investment of vaccine enterprises to save costs and create conditions for the inclusion of vaccines in immunization planning. In addition to providing certain financial support, priority should also be given to the approval of HPV vaccines, shorten the approval time of HPV vaccines, simplify the approval process, promote domestic HPV vaccines to enter the market as soon as possible, and make up for the shortage of HPV vaccines in China.

3.2 Accelerate the construction of human papilloma virus vaccine safety

After a strict clinical trial stage, HPV vaccine enters the market to ensure its effectiveness while paying attention to safety. Due to the small number of sample samples from clinical trials and the short duration of clinical trials, there may be adverse vaccination reactions, such as nausea, vomiting, swelling at the injection site, etc. However, what's more serious is that some serious diseases such as premature ovarian failure and autoimmune diseases show a strong correlation with vaccination in statistical analysis.

China's HPV vaccine is on the market late, the vaccination coverage is low, and the data that can be collected is relatively scarce, and it is difficult to deeply analyze the safety of HPV vaccines. China should accelerate the construction and upgrading of the safety supervision system for listed vaccines. First of all, the information reporting model should be improved. The government develops a relevant platform on which the public communicates the vaccination process, feelings, etc. Secondly, strengthen the supervision of HPV vaccines and crack down on vaccine fraud. Finally, communities and hospitals have increased their awareness of the importance and necessity of HPV vaccination to address public safety concerns.

3.3 Increase subsidies for human papilloma virus vaccine

In the past two years, the popularity of HPV vaccine has gradually strengthened, and more and more people have begun to make vaccine appointments. Some people think that the higher the price of human papilloma virus vaccine, the better the effect. Soon after the Gardasil 9 was launched, there was a shortage of vaccines. There is a phenomenon that "one seedling is difficult to find". Therefore, the public is blindly waiting for nine prices. In fact, the human papilloma virus vaccine should be vaccinated as soon as possible. Don't wait.

China can promote pilots first and explore a diversified model of vaccine promotion with a "healthy city pilot". The government should encourage areas in a position to do so to strengthen human papilloma virus vaccination and expand access to HPV vaccines. There are 15 vaccine pilot cities in China. As one of the first pilot cities for healthy China's innovative action model, Chengdu has carried out HPV vaccination for 13- and 14-year-old girls in the city through coordination and cooperation between the government, health, finance and education departments. At the same time, parents of students can choose Cecolin, Cervarix and Gardasil. The government gives a vaccination subsidy of 600 yuan per person. By December 29, 2021, Jinan had vaccinated 34,056 seventh-grade girls with human papilloma virus free of charge, taking the lead in achieving more than 90% of the target coverage in the pilot cities. Looking forward to the future, more and more districts should learn from this model, take government immunization planning as the lead, give HPV vaccination subsidies to the masses, and improve vaccination coverage.

3.4 Strengthening community health services

Building healthy cells is an important part of promoting the construction of healthy China and healthy cities. Primary medical institutions are rooted in the people and have a close relationship with the people. Primary medical institutions not only undertake some basic medical services, such as vaccination, seeing some basic diseases, etc., but also strengthen the health education, health guidance, health consultation and other responsibilities of the residents of the community. Grassroots medical institutions should explain HPV hazards, transmission routes, extreme vulnerability and other knowledge to the residents of the region, answer questions about the health problems of the residents

of the community, and give full play to the role of "gatekeepers" of primary medical institutions in vaccination.

First of all, community primary medical institutions should strengthen the universal access to preventive health care for students and encourage people of the school age to be vaccinated against HPV as soon as possible. Secondly, community grassroots medical institutions should improve the simplicity and efficiency of vaccine appointments, and improve online appointments, school centralized appointments, unit appointments and other services. Finally, community primary medical institutions should ensure the standardized management of vaccines. Cold chain management is an important link to improve the quality of vaccination. The whole process from production to vaccination should ensure the effectiveness of HPV vaccination. Therefore, community grassroots medical institutions should provide solid, pragmatic and high-quality grassroots health services to help prevent cervical cancer diseases, benefit more women, and achieve the goal of eliminating cervical cancer as soon as possible.

4. Conclusion

To sum up, the vaccination rate of papilloma virus in China is low, which is somewhat different from that in Europe and the United States. China is also further strengthening the screening rate of two cancers, which is expected to achieve the World Health Organization's target of 70% screening rate for the target population by 2030. At the same time, unlike other products, vaccine products directly affects the quality of life of the people. Relevant departments should do a good job in the cold chain transportation of vaccines. In view of the low awareness of the public, grassroots communities should do a good job in publicity and hold regular lectures on human papilloma virus to publicize the importance of vaccination against human papilloma virus. In addition, the government should encourage and support vaccine companies to increase the research and development of human papilloma virus vaccine and the training of related talents, provide a solid talent pool for the production of high-quality and inexpensive human papilloma virus vaccines, and further expand the vaccination population to escort the elimination of cervical cancer.

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