

The Objective and Subjective Problems of Human Papillomavirus and Optimized Solutions of Solving Human Papillomavirus Vaccines in the Chinese Market

Qingchun Li*

College of Arts and Sciences, University of Miami, Miami, 33146, the United States

*Corresponding author: qxl256@miami.edu

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Abstract: Human Papillomavirus (HPV) can bring about many cervical diseases. In China, people become aware of the seriousness of HPV and start to take HPV vaccines. It is around 20.5% of Chinese have HPV-related diseases. However, the quantity of vaccines is in shortage, and the price of vaccines is also quite high for some people. By using literature analysis and comparative analysis methods, this study identifies three essential and intolerable issues about HPV prevalence in China. First, when did HPV vaccines enter the Chinese market, and the prices of HPV vaccines have changed in recent years? Second, the Chinese show varied attitudes towards HPV vaccines compared to developed countries. At last, this study identifies Chinese are more willing to take 9-valent HPV vaccines and why there are fewer HPV vaccines in the Chinese market. Furthermore, the study mainly discusses some methods to solve the high price of HPV vaccines and increase the number of HPV vaccines. This study will give directions to the Chinese government, releasing the burden of paying for vaccines. Besides, after many Chinese HPV vaccines appear, the Chinese will benefit from them, and other countries will also solve the shortage of HPV vaccines.

1. Introduction

1.1 Research Background

In China, Human Papillomavirus (HPV) has a high prevalence in central China, which takes over 20.5%, and it becomes a serious disease that people would like to take care of. The prevalence of HPV among men sex is also noticeable at 59.9% [1]. As we all know, almost all cases of cervical are caused by HPV. HPV can be highly prevented except by wearing condoms and taking HPV vaccines that work out [2]. Some women in China cannot get vaccination depending on different socioeconomic statuses. Especially, HPV vaccines are not cheap and have three doses. These cost \$271 to \$450 [3]. As a result, making HPV vaccines cost-effective is important for solving high HPV prevalence in China. Based on the prevalence of the disease and the overwhelming death rate, it is essential to do some research and give optimized solutions to change this phenomenon.

1.2 Literature Review

China has the resources to prevent HPV. The World Health Organization (WHO) approved China's first self-developed vaccination against HPV from the latest news. It hoped this vaccination could become cost-effective, proving to other developing countries [4]. In December 2019, HPV 16 and 18 Cocolin, the bivalent vaccine, became available in the mainland. However, safety and efficacy had been judged. Based on some surveys, 62.1% of people lack relevant knowledge about HPV, refusing to take the vaccination. 53.6% of people doubt the safety and efficacy of HPV vaccines. The attitude of people recognizing HPV vaccines is essential. If there are resources, people refuse to take them. It is a waste, and it will lead HPV more server.

Moreover, Price is another reason that people refuse to take vaccines. Some researchers suggested two doses of vaccines that can be considered, which will lower the burden of people at some point [5].

Another study also gave subjective problems that people have conflicts with HPV vaccines. Researchers found the poor regions are more likely to misunderstand HPV vaccines, and only 5% know that there is a connection between HPV and genital warts. After the education, most women are willing to accept the vaccines, 80.3% and 82.2% of women encourage their daughters to be vaccinated. This survey showed the importance of educating people about the benefits of taking HPV vaccines [6]. Another study further indicated the indispensable HPV vaccines that can provide life-lasting protection for people with an immune response.

Moreover, it also mentions that China did not have an HPV vaccination program in August 2020 [7]. This also can be considered why the Chinese could not take control of HPV. The incidence and prevalence of HPV still gradually increase every year.

Another point is the increasing demand for HPV vaccines in the Chinese market; however, the supply cannot meet that huge number of demands. Even 2 million mainland women fly to Hongkong to take the vaccines. Hongkong also has a shortage of vaccines, and they shift their vision to neighboring countries. Surprisingly, two hospitals in Malaysia and one in Singapore also lacked Gardasil [8]. In 2020, the supply of HPV vaccines reached 12.4 million syringes; however, it remains a shortage compared with the demand [9].

1.3 Research Gap

Most studies and researchers focused on investigating the seriousness and prevalence of HPV and the coverage of HPV vaccines. Moreover, many studies compared the difference between rural and urban citizens who have different opinions about HPV and taking HPV vaccines. These are all the facts related to behaviors of facing HPV regardless of subjective and objective aspects. In contrast, studies about solutions to the shortage of HPV vaccines are limited. When people know the importance and necessity, how to solve the problem becomes the most urgent thing. In this study, the main research would be solving the shortage of HPV vaccines and the inequity opportunities to taking the HPV vaccines.

Furthermore, the study will tackle the problems of online appointments to taking HPV vaccines which should be available to everyone. People walked into a hospital and could take vaccines that are the best result of this study. Moreover, the distribution of HPV vaccines is also vital. The poor and prosperous regions should have the same allocation of resources that the Chinese government should involve in the process. Another point is the cost of HPV vaccines. Most studies did not give solutions to this issue, but this study will try to release the burden of making and taking the HPV vaccines.

1.4 Research Framework

At first, the study will indicate the causes of having trouble making inequity when allocating HPV vaccines, whether it depends on government policies or some economic issues. Next, the study will base on these causes of problems giving practical and optimized solutions and, at last, forecasting the best results and drawbacks of these new interventions.

2. Methods

2.1 Literature Research

Literature research is the method of summarizing and synthesizing information about specific areas. It gives a new interpretation of old material or mixes old and new perspectives [10]. In this paper, many aspects depend on this method. For example, researching the number of HPV vaccines in the Chinese market may be collected by some resources or cited by some researchers. Additionally, different regions of China have different levels of income which may bring about high sensitiveness of money, price of HPV vaccines. Moreover, for HPV vaccines themselves, why can they not be allocated equally in China? These issues are possibly found in some old studies and other databases.

2.2 Comparative Analysis

Comparative analysis means comparing two or more objects, phenomena, processes, or documents. This method can largely analyze, clarify, and narrow focus [11]. This paper will use many comparisons to find out the reasons for HPV vaccines shortage in the Chinese market. Using developed countries as comparative targets is a great way to find problems. Why do some other countries not have a shortage of HPV vaccines issues? Is it related to government policy, or is it about population problems? On the other hand, compared to the past and now in the Chinese market, the HPV vaccines suddenly increased. What are the direct and indirect factors between these years? The causes of the soaring rise of the infected HPV population can be identified in this comparison. Besides, though comparing the cost of HPV vaccines between the Chinese market and other countries, it will be clear to know how to release the burden of the high cost of vaccines in China.

3. Results

3.1 HPV Vaccines and HPV in Chinese Market

HPV is mainly transmitted through sexual contact. The effective way to prevent cancers is taking HPV vaccines. The first vaccine, Gardasil, was made by Merck&Co., it became available in June 2006; however, in China, until 2016, the HPV vaccines were allowed to take and approved by China and Drug Administration (CFDA). It is only open to ages from 9 to 25 female. In May 2017, Gardasil, a 4-valent HPV, was available. In April 2018, a 9-valent HPV vaccine entered in Chinese Market, and it allows aged 16 to 26 females to take. In December 2019, the Chinese mainland invented the first HPV vaccine Cecolin, a 2-valent jointly developed by INNOVAX. It can be vaccinated among females who are aged between 9 and 45. In 2020, China already had 354 million women aged 10 to 44, so there is a huge demand for HPV vaccines in the Chinese market [12]. Based on the statistic, in 2017, there were 1.46 million doses of HPV vaccines provided, 7 million issued in 2018, and 8.7 million available in 2019. However, HPV vaccines still face a shortage in China. In 2020, in Shanghai, residents still needed to wait for two to three months at health services centers in communities. Shanghai is one of China's prosperous and developed cities; however, people cannot get vaccinated immediately. In rural areas, most people have no ideas about HPV vaccines.

Furthermore, the cost of vaccines is also needed to pay attention to. The two-valent and four-valent is not that much, respectively 585.5 yuan and 808.5 yuan. The nine-valent could prevent more diseases than the previous two, and it cost much more, 1,300 yuan per dose. People have the second choice to take HPV vaccines in China, for some private clinics provide them, too. The price is sky-high. Three doses of imported two-valent and four-valent HPV vaccines cost 2,788 yuan and 3,888 yuan. The nine-valent costs 5,980 yuan, so generally, it is one's one-half of their monthly salary [13]. Besides, the Chinese government does not cover any HPV vaccine fees in public health services centers among communities or in private clinics. It can be a huge burden to people who want to take HPV vaccines, the long waiting time, and the high spending.

3.2 Problems of HPV Vaccines in China

Chinese have known HPV vaccines very late compared to a developed country. The first HPV vaccines appeared in 2006, and in China, in 2016, the HPV vaccines were available to citizens [12]. Compared with the United States, in 2006, HPV vaccines were already introduced, and people could take them. As a result, Americans have a far ahead opportunity to get access and know about HPV and its vaccines [14]. However, in China, a few aspects of reasons lead to the disparities of getting HPV vaccines compared with the United States. At first, females lack education, live in low-income families, and are without occupation. They tend to ignore the government policy of encouraging screen testing of HPV disease and avoiding taking vaccines.

Furthermore, aged 9 to 14, girls vaccinated only 1% of the population [15]. These groups of people are young, and they depend on their families, teachers, and schools. The 1% of vaccinated rate proved that China lacked health education in schools. Students have not been told what HPV is, why it is

important to take HPV vaccination and its benefits. At last, in recent years, well-educated females and urban females have been eager to take HPV vaccinations; however, quantity demanded is bigger than quantity supply which causes a shortage of HPV vaccines in China. Although many new HPV vaccines have been conducting clinical trials in China, vaccines' cost and efficacy are unknown [16-17].

3.3 Causes of HPV Vaccines problems in China

One of the serious issues is the cost of HPV vaccines. In China, public health services centers in the community always have lack vaccines. However, China has many other channels to take vaccines, many e-commerce platforms, such as Pinduoduo, Taobao, and Juhuasuan, cooperated with Ali Health. These platforms guarantee people will be vaccinated, whereas the cost is extremely expensive compared with normal ones. Taking Pinduoduo as an example, an HPV vaccine million people sold imported 4-valent and 9-valent. For 4-valent costs, 3300 yuan and 9-valent is 5499 yuan. Compared with public hospitals, 4-valent costs 2400 yuan and 9-valent costs 4000. It is clear to see the difference between the price distances. The platforms often cooperated with private hospitals so that the intermediary fee could be high.

Moreover, in China, 2-valent vaccines are not in shortage. People are eager to take the 9-valent vaccine because it can cover 90% protection and prevention. In general, in Guangzhou, China, people need to make an appointment, and choosing different vaccines has varied waiting times. If people choose to take 2-valent, they need to wait for one to two months. If people choose to take 4-Valen or 9-valent, they need to wait longer than take 2-valent. Imported HPV vaccines are limited in China, and the prices cannot be controlled by increasing [17].

The second essential issue of HPV vaccines, low quantities, is related to the overall Chinese vaccine market. There are a few challenges and barriers to vaccines. At first, innovative HPV vaccines need a long period, nearly 10 years, to research and development. It includes considering substantial risks, intensive spending and investments, technological expertise, and human resources. Time-consuming and money spending lead the innovative vaccines that are difficult to make. Conducting Gardasil 9 vaccines cost US\$1.05 to US\$1.21 billion that high entry barriers bring about the lack of market players to join in.

Moreover, the efficacy and preclinical studies need more time. Secondly, vaccine companies need very professional technology platforms' help. Then they could have a competitive advantage in developing vaccines. Thirdly, China has a strict law, the Vaccine Administration Law of the People's Republic of China. Vaccines companies need to meet the demands of Good Manufacturing practices to ensure great quality.

Moreover, they need to have the manufacturing capacity and a developed system to monitor the whole life cycle of vaccines. As a result, human resources and substantial technologies are both required. These harsh regulations burden the vaccines companies in China [18].

4. Discussion

4.1 Price of HPV vaccines

At first, in China, health insurance does not cover the HPV vaccines fee. Could we make it possible which let it be accessible to every citizen? In the United Kingdom, everyone has health insurance, National Health Services, and people get vaccinated when they are in School Year 8. They could be vaccinated for free until their 25th birthday [19]. So why can the UK have well-developed and beneficial health services, and why can China not provide free access to citizens? The NHS funding comes from taxation and National Insurance Contributions.

Interestingly, Chinese public health insurance mainly comes from taxation [20]. China has examples of setting free HPV vaccines. The first example is the Inner Mongolia autonomous region. On August 1st 2020, the news was updated that females aged 13 to 18 can be vaccinated against HPV vaccines [21]. The latest news announced by Guangdong province on October 29th 2021, will provide 600 million yuan to give free vaccinations from 2022 to 2024 to their aged under 14 years old female

[22]. According to these two examples, they show that Chinese provinces have this money to help citizens to get free HPV vaccinations.

Moreover, for domestic HPV vaccines, vaccine companies should also contribute. They could sell their vaccinations to the government, which will give their subsidy. It can slowly provide free vaccines to people, one by one, city by city, province by province. In this way, the government would meet the burden of finance. Meanwhile, companies can have a chance to do research and development.

Another solution to solving the high price of HPV vaccines is decreasing the import vaccines. In the third trial, China has lots of HPV vaccines to appear in the Chinese Market soon [17]. When the number of HPV vaccines increases, the market will naturally lower the price. Additionally, the government could persuade people to take the 2-valent vaccines, and it is the cheapest one. Plus, it also could prevent diseases. It uses social media through different platforms to advertise the efficacy of 2-valent HPV vaccines, such as Pinduoduo, Taobao, Weixing. The new domestic HPV vaccine was made using E.coli bacteria, cheaper than foreign counterparts, and boosted manufacturers' production capacity [23].

4.2 Increasing Supply of HPV Vaccines

At first, China had enough supply of 2-valent HPV vaccines; however, people always wait for 4-valent or 9-valent, which is limited to the imported quantities. There are three kinds of HPV vaccines with nearly the same prevention and protection. Government should encourage people who aged higher than 24 years to take 2-valent. It is the best way to protect themselves because they do not have much time to wait for the 4-valent or 9-valent. If they keep waiting, they will miss the time of getting vaccinated.

Moreover, females aged 30 to 45 will be considered to have a baby. However, the vaccine cannot be injected into pregnant women. Some HPV vaccines may cause warts, and many vaccines need more research about their adverse effects [24]. Secondly, recent news shows that China has many vaccine companies to research and develop. Most of them are going through the third trial. After China has its 9-valent and 4-valent HPV vaccines, the huge demand will not be a problem anymore [17].

Furthermore, the government announced many beneficial policies and laws helping the Chinese vaccines [25]. Another way is to develop the old HPV vaccines. Usually, HPV vaccines need three doses of injection, whereas if companies can change to two doses or one dose, the supply of HPV vaccines will largely increase. At some point, the supply will increase. Imported vaccines and domestic vaccines can both be injected. People will not be afraid of waiting time.

Moreover, when companies have innovative vaccines, people will have more choices. They do not need to make an appointment someday, and they could just walk in get injections. In China, males cannot make an appointment to take HPV vaccines as the lack of supply. If China had different companies producing innovative vaccines, males also could protect themselves. This is the best result that the Chinese government what to see—trying their best to make people healthier.

5. Conclusion

HPV vaccines appear very late in China market because China has a quite strict department to control the entry of medication, CFDA. Chinese are more likely to know the HPV vaccines in 2016. Until now, in this short 6 years, the Chinese have increased the demand for HPV vaccines. The attitudes Chinese face towards vaccines change from resistance to acceptance, taking a long journey. Well-developed cities and provinces have a higher demand for HPV vaccines, for example, Shanghai, Shengzhen.

Moreover, the cost of vaccines also attracts attention. As the quantity of vaccines is low, many online platforms take advantage of intermediary fees by working with private hospitals. As a result, HPV vaccines in private hospitals and these platforms are more expensive. Another main finding is about preference. The Chinese love to wait a long period to get 9-valent or 4-valent vaccines, not 2-valent vaccines. However, China lacks a quantity of 4-valent and 9-valent but a high supply for 2-

valent. Based on many researchers' quotations, these three kinds of HPV vaccines do not have distinct prevention functions. All of them can help people overcome some diseases.

In this study, the shortage of supply and the high price of vaccines is given by optimized solutions of the HPV vaccines issue in China. Aiming to release the burden of paying vaccines fees, the Chinese government could free the charges of injecting HPV vaccines for people at least step by step. Plus, some areas were already provided vaccines for free. On the other hand, increasing the supply of HPV vaccines can be predictable. China has several vaccine companies working on new vaccines and are in two or four trials. Except this, the government could tell people aged nearly 45 years old that 2-valent is also a great choice for preventing diseases. In these ways, vaccines supply will largely increase.

The limitation of this study is the uncertainty of the new vaccines. It cannot predict how many people would accept the new vaccines and maybe still believe the old vaccines. The behavior and attitudes of people towards vaccines are mysterious by now. This puzzle can be solved in the future. People can survey the acceptance of new vaccines that appear in China. If people can largely accept the new vaccines, the shortage of HPV vaccines will be solved.

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