REVIEW

Current issues facing the introduction of human papillomavirus vaccine in China and future prospects

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ABSTRACT

The introduction of human papillomavirus (HPV) vaccination in China aims to prevent HPV infection in all women. The issues that China might face include high cost of vaccines made in other countries, shortage in HPV vaccine supply, negative events attributed to vaccination (whether justified or not) that jeopardizes the general public's confidence in the HPV vaccine, cultural and literacy barriers, and sensitivity to receiving a vaccine for a sexually transmitted disease. Ensuring the effective delivery of the HPV vaccine in China, a country with vast economic, geographical, and cultural complexities, will require a commitment of significant resources. In light of the high price of imported vaccines, the availability of locally manufactured HPV vaccines would greatly facilitate the national HPV vaccination program. New evidence supporting the efficacy of a two-dose regime in younger adolescents would also be advantageous in terms of affordability and logistical simplicity of vaccine administration. Furthermore, it would potentially enhance the compliance and uptake, especially for hard to reach women in remote regions.

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1. Introduction

It has been over a decade since the US Food and Drug Administration approved the quadrivalent human papillomavirus (HPV) vaccine in 2006. To date, over 100 countries in the world have licensed one or more HPV vaccines and over 80 countries have established national HPV vaccination programs.¹ China is far behind from many other countries in the world in terms of the introduction and access to the HPV vaccine. GlaxoSmithKline's Cervarix®, a bivalent vaccine (2vHPV), and Merck's Gardasil®, a quadrivalent vaccine (4vHPV), were approved for using in women in China by the Chinese State Food and Drug Administration in July 2016 and April 2017. Merck's Gardasil®9, a 9-valent HPV vaccine (9vHPV), was recently licensed in China in May 2018. Each of the three vaccines is licensed for different age ranges, with 2vHPV recommended for ages of 9–25 (the recommended age was extended to 45 years by the China Food and Drug Administration on July 2018), 4vHPV recommended for ages 20–45, and 9vHPV recommended for ages 16–26.

Cervical cancer ranks as the eighth most frequent cancer among women in China and the second most prevalent cancer in women between 15 and 44 years of age.^{2,3} The crude incidence of cervical cancer in China in 2013 was 15.17/100,000 and the age-standardized incidence rate based on the Chinese standard population was 11.30/100,000.⁴

Moreover, a pooled analysis of data from 1999 to 2008 indicated that the age-standardized prevalence of cervical intraepithelial neoplasia 3+ (CIN3+) was 1.2% and the prevalence of high-risk HPV infection was 16.8%.⁵

The introduction of HPV vaccine, in many countries, has resulted in major decreases in specific HPV infection rates, as well as the incidence of associated disease. Follow-up data from nine high-income countries revealed that in countries with female vaccination coverage of at least 50%, HPV16 and HPV18 infection, and anogenital warts decreased by more than 60% in girls younger than 20 years of age.⁶ Further evidence of vaccine cross protection and herd effects were found, with significant reductions in HPV31, HPV33, and HPV45 infection.⁶ In contrast, in countries with low vaccination coverage, no significant reductions were noted for HPV31, HPV33, and HPV45.⁶ Further, in long-term follow-up studies, ten or more years postvaccination, both 2vHPV and 4vHPV showed continued effectiveness, particularly against HPV-16/18 CIN3+ and CIN2+. ^{7,8} Recent evidence from the first HPV vaccine trial in China showed that 4vHPV demonstrated robust and sustained efficacy against HPV6/11/16/18-related persistent infection and high-grade cervical disease for up to 6.5 years of follow-up among Chinese women.⁹ The vaccine was also well tolerated, with no evidence of vaccine-related serious

adverse events among the Chinese women.⁹ Most importantly, the public should be informed that over a decade of data on hundreds of thousands of boys and girls who received the HPV vaccines indicates that the vaccine is safe and effective.^{10–12} A most recent 12 years of vaccine-vigilance in Southern Italy did not identify new serious or rare unexpected adverse events following HPV immunizations further provided reassuring evidence on safety of the HPV vaccines.¹³ These encouraging findings may enhance the adoption of HPV vaccine among Chinese communities and suggest promising future prospects of HPV vaccination reducing cervical cancer incidence and mortality in China.

This review highlights the current issues faced in HPV vaccine uptake and challenges in reducing cervical cancer incidence in the era of HPV vaccination. The future opportunity of the new 9vHPV to further reduce the HPV-associated cancer burden in China and the potential benefits of the implementation of two- or one-dose regimens in cost reduction and improving compliance and uptake are also discussed. Additionally, this review provides recommendations on several potential avenues for future research.

2. Current obstacles in HPV vaccine uptake

Cervical cancer mortality may only be reduced if HPV vaccine is used routinely in public health programs, resulting in sustained high levels of vaccine uptake and coverage.^{6,14} These challenges include the current high cost of HPV vaccines (which varies across provinces); severe shortage of HPV vaccine supply due to high demand; negative events related to vaccination that jeopardize the general public's confidence in the HPV vaccine; lack of knowledge and awareness of HPV and its link to cervical cancer, especially among underserved women; and cultural, social, and religious sensitivity to accepting a vaccine for a sexually transmitted infection (STI).

2.1 High vaccine cost

The HPV vaccine often is regarded as too expensive for general public uptake in China, costing \$360 USD (¥2397 RMB) for the three doses. At the current price, HPV vaccination is beyond the range of affordability for many women and families in China. In addition, the cost can go as high as \$450 USD (¥2999 RMB) for the three doses after taking into account-added fees for vaccine transport, storage, and administration.¹⁵ The price may be even higher to make the vaccine accessible to underserved women in remote rural areas.

Ultimately, HPV vaccination in China will need to become more cost-effective. A modeling study showed that HPV vaccination becomes cost-effective across all income groups when its cost is less than \$50 USD (¥333 RMB) per vaccinated female.¹⁶ At the current high price of \$360 USD (¥2397 RMB), HPV vaccination does not appear to be cost-effective. Therefore, it will be essential to find ways to reduce the cost of vaccination. Studies suggest that nearly 60% of patients with cervical cancer in China are from rural areas, where access to cervical cancer screening is limited.^{15,17} Thus, reductions in

cost would be particularly helpful to these hard-to-reach women.

2.2 Shortage in HPV vaccine supply

When HPV vaccine entered the Chinese market, the media reported that the newly approved vaccine was in great demand. Additionally, China's large population also contributed to tremendously high total demand for HPV vaccines. It has also been widely reported in the Chinese mass media that high demand for the HPV vaccine has resulted in a shortage in the Chinese market. This great demand has resulted in many scheduled appointments for HPV vaccination for which women could not receive the vaccine, and many women were long waitlisted for it as a consequence of this shortage.¹⁸ The shortage has also led thousands of women who were unwilling to wait to seek HPV vaccination in neighboring countries.¹⁹ Because of the large female population in China, it has been impossible to meet the high demand immediately upon the approval of the HPV vaccine in the Chinese market.¹⁸ To date, there are at least 41 million girls of age 9–14 years in need of HPV vaccination in China.²⁰ It is of utmost importance for young women in China to get protection by getting vaccinated as soon as possible. It is fortunate that the country's locally made HPV vaccines are already on the horizon. With increased demand and urgent needs for cervical cancer prevention, the soon available locally manufactured HPV vaccines may be less expensive and help to counteract vaccine shortages. For the time being, the current pharmaceutical manufacturers should increase the supply of HPV vaccines to China.

2.3 Negative events related to vaccination and HPV vaccine confidence

Issues with fake or contaminated vaccines have led to widespread concerns among the general public in China over the safety of vaccine administration. The biggest vaccine scandal in 2016 revealed that various medical companies illegally sold 25 vaccines to children and adults across the country.²¹ This incident worsened the perspective on vaccination for the general public in China.²¹ It is critical to rebuild public trust toward vaccination because such an event plays a significant role in shaping the general public's health-care decisions. Recently, another vaccine scandal involving rabies and diphtheria, pertussis, and tetanus vaccines occurred in July 2018 that resulted in even higher widespread panic and distrust in vaccination in China.²² This was an unfortunate event as it occurred around the same that the much-awaited HPV vaccination was introduced in the country. Although such influence is transient, these occasional negative events related to vaccination may cause public resistance to vaccination. It is of the utmost importance to restore and sustain the public's confidence in vaccines that are currently available in China by reforming the country's vaccine regulatory system to avoid recurrence of vaccine-related tragedies.²⁰ The Chinese government has taken corrective legal action, including a record-setting corporate fine.²⁰ The high demand for HPV vaccines suggests that the negative events related to vaccines

may not yet have dampened enthusiasm for HPV vaccination. In order to guard against future unwarranted fears about HPV vaccines, and in the event where the locally manufactured HPV vaccines will soon be available, it may be important to launch a large-scale campaign to build and maintain public confidence in HPV vaccines.

2.4 General lack of knowledge of HPV and its link to cervical cancer

Studies often showed that knowledge about HPV, HPV infection, and its association with cervical cancer among the general population was generally poor, especially prior to the introduction of HPV vaccination^{23,24} and within the first few years after its introduction.^{25,26} Study conducted outside of China reported that one of the main barriers to HPV vaccination is lack of HPV awareness.²⁷ Various other countries have also reported that women with intention to receive HPV vaccination and those who received HPV vaccination were often found to be more highly educated.^{28,29} Similarly, a recently conducted study on Chinese parents' HPV vaccination intent found parents with higher knowledge and awareness expressed higher vaccination intention, signifying the importance of HPV vaccine-focused health education interventions for parents.³⁰ To date, despite the fact that the HPV vaccine has been licensed for over a decade in the United States, a study showed that only near 30% women had heard of HPV only slightly, over half knew about the link of HPV infection with cervical cancer.³¹ A recent study that was conducted in the Yunnan province in 2016 reported that approximately 40% of women knew about the role of HPV in cervical cancer development³² versus 26.5% in a 2015 study that was conducted in the same province.³³

Since the HPV vaccine is now available in the country, more research will need to be conducted to assess the knowledge and understanding of the general public about the HPV vaccine, especially among marginalized groups. Such research can provide the most up-to-date insights into HPV knowledge gaps so that the educational needs can be identified and met. An important issue that has not been addressed in the previous studies in China is women's concerns on the HPV vaccine, such as potential side effect, safety, and efficacy of the vaccine. These concerns were critical to the decision-making process of both Western and Asian women on receiving HPV vaccination.^{34,35}

Health-care professionals play a key role in the recommendation and the acceptance of HPV vaccination. Thus, it is very important to ensure that health-care providers are well informed about cervical cancer, HPV infection, and vaccination so that they are able to provide complete and accurate information to women. As a final note, it will be important for educational programs to address the role of men in HPV transmission and disease. Although HPV vaccines in China are not licensed for males, it is essential that the public understand that HPV is not just an issue for women.³⁶ Several countries, including the United States and Australia, include males in their national HPV

immunization programs and it is possible that China may eventually consider gender neutral HPV vaccination as part of its HPV vaccine programming.

2.5 Sociocultural barriers to HPV vaccination

In light of the fact that HPV is sexual transmitted, contextual factors relating to the social and cultural norms of people in China might have implications for the acceptance of HPV vaccination, an issue also faced by several low- and middle-income countries.³⁷ Persons who live in modern urban centers tend to be more open-minded about accepting a vaccine for HPV than those who live in rural areas, who often embrace strict social and religious norms. While cervical cancer mortality has declined considerably in urban parts of China in the recent years, this has not been the case in rural areas and among ethnic minorities.³⁸ The Muslim majority in Hotan of the Xinjiang province is reported to be one of the high-risk populations for cervical cancer in China.³⁸ Among Uyghur women, residing in Xinjiang, the incidence and mortality rates of cervical cancer are 459–590 per 100,000 and 17.78 per 100,000, respectively. These numbers are higher relative to other ethnic groups in China.³⁹ Despite the greater cervical cancer burden, cultural beliefs, social norms and religious practices and teachings might negatively influence the acceptability of HPV vaccination in these communities. HPV vaccination might be viewed as unnecessary by religious denominations that believe in abstaining from sex until marriage and in prohibiting extra-marital sex. In India, just seeking HPV vaccine is stigmatized by the community and viewed as tarnishing a family's prestige, and there were rumors that HPV vaccine itself might cause infection in children.⁴⁰ In Mongolia, allegations that HPV vaccination is unsafe and may cause infertility significantly and negatively impacted HPV vaccine introduction by the Ministry of Health.⁴¹ A multicountry cross-sectional study in India, Peru, Uganda, and Vietnam demonstrated increased rates of HPV vaccine acceptance and uptake, following communication about vaccine benefits and knowledge enhancement during their HPV vaccine introduction campaigns.⁴² Thus, it is important to provide evidence that there is no increase in sexual activity for girls who have received HPV vaccine, compared with unvaccinated girls.⁴³ Therefore, prior to introducing HPV vaccine to these communities, it is important to understand how religion, social, and cultural norms shape health-seeking behaviors and decisions on HPV vaccination in these communities.

3. Challenges in reducing cervical cancer incidence in the era of HPV vaccination and way forward

There are several critical issues that need to be addressed to facilitate the introduction of HPV vaccination in China for reducing cervical cancer burden. Specifically, these challenges include the high cost incurred in the implementation of a national immunization program that reaches the populations that would benefit most from vaccination and the reduction of socioeconomic disparity in HPV infection and cervical cancer mortality.

3.1 Establishment of a national HPV immunization program

The introduction of national HPV vaccination programs in high income countries has resulted in dramatic decreases in the incidence of HPV infection and associated cervical diseases.⁴⁴ In China, the delay in the introduction of HPV vaccines has resulted in ongoing high HPV-related morbidity and mortality, which could have been prevented if HPV vaccine was introduced earlier. If a national HPV vaccination program was available between 2006 and 2012 for girls between 9 and 15 years of age, it could have prevented an estimated 1444,000 high-grade squamous intraepithelial lesions and about 381,000 new cases of cervical cancer.⁴⁵ The implementation of a national immunization program is complex, and careful planning and education for the general public and health service staff are essential.⁴⁶ If a national HPV vaccination program is established or the HPV vaccine is included in China's national immunization plan, a program that is structured to deliver the HPV vaccine to people on the basis of economic background might be required due to the country's geographical and demographic diversity. Ideally, a free national vaccination program should be established for priority populations in remote rural areas that have the highest cervical cancer incidence and mortality, but limited access to cervical cancer screening. Second, school-based HPV vaccine delivery will be greatly advantageous to reach vulnerable girls who may have little access to health and screening services. Social mobilization activities would also be needed to reach out-of-school girls.

Cost is the main barrier that needs to be overcome to establish a national immunization program for HPV. This barrier is considerable, especially if imported HPV vaccines are used in China's national immunization program. It is only at \$9–13 USD per dose that HPV vaccination in China would be cost-effective compared to screening programs.⁴⁷ It is a well-established fact that the HPV vaccination in China needs to be more cost-effective.¹⁵ Thus, it would be necessary to negotiate for a lower price for imported HPV vaccines to enable national HPV immunization programs in China.⁴⁵ National HPV immunization programs will be close to reality if the price of the soon available locally manufactured HPV vaccines falls below the cost-effectiveness threshold.

Overall, a nationwide HPV vaccination program would reduce China's reliance on cervical cancer screening as the main method of cervical cancer prevention thereby reducing the burden that the screening program has on the country's health-care system.⁴⁵ Even when widespread HPV vaccination is introduced in China, cervical cancer screening would continue to be needed in the future, to ensure adequate cervical cancer control among unvaccinated women and for cervical disease caused by non-vaccine-type infections.⁴⁵ The reasons for its continued need are the possibility of incomplete vaccine coverage of the Chinese population, the inclusion of only some high-risk HPV types in current vaccines (although a 9vHPV vaccine is now available), and the large number of women who are already infected with HPV.⁴⁵

3.2 Reduction in the socioeconomic disparity of HPV infection and cervical cancer

Health disparities in China resulting from an increasing income inequality in the population have been a major concern in the country.⁴⁸ The accessibility of the HPV vaccine among the urban and affluent is a classic example of the disparity in access to cervical cancer prevention in China that results in worsening inequality in cervical cancer mortality. The higher level of access and utilization of cervical cancer screening services, cancer treatment, and now access to HPV vaccination among women in urban cities poses a great challenge in current efforts to reduce cervical cancer disparities in China. Without a comprehensive national distribution program, it is predicted by many public health experts that the introduction of the HPV vaccine would aggravate the socioeconomic and regional disparities in HPV infection and cervical cancer incidence rates.¹⁵ As of today, it is a challenge to deliver HPV vaccines to millions of medically underserved rural women who lack access of routine cervical cancer screening and require vaccination the most as they are the major contributing population to cervical cancer burden in China.

Aside from women living in geographically remote rural areas of China, women who have migrated to urban cities from rural regions also require special attention in terms of socioeconomic disparity in HPV infection and cervical cancer incidence, as they represent the lowest wealth quintile. Rapid economic development in urban China has led to mass migration of rural residents into urban areas for better employment opportunities. These migrants have a higher risk of STIs, including HPV, relative to the general Chinese population.^{49–51} Despite living in urban areas that offer opportunities for HPV vaccination, rural migrants might still be deprived of HPV vaccination due to their lack of knowledge and the vaccine's cost. Migrant workers should be a high priority in HPV vaccination programs in order to minimize the spread of HPV infections in urban populations. Therefore, rapid rollout of the HPV vaccine to these groups of women might be a feasible way to narrow present inequalities in cervical cancer burden and prevention.

4. The promising prospects of HPV vaccines and future direction

Mounting evidence suggests that the prophylactic HPV vaccine is very promising for cervical cancer prevention in China, especially now that the 9vHPV is available, the country will see further to reduce the incidence of HPV infections and HPV-related cancers in near future. Further, some promising results in terms of the immunogenicity and efficacy of single-dose HPV vaccination may provide potential future directions for recommendation of fewer than three doses of HPV vaccine.

4.1 The 9vHPV vaccine

The 9vHPV, which provides added protection against additional high-risk HPV types, became available in China in

May 2018. This vaccine, protects against HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58, has the potential to prevent up to 90% of HPV-related cervical cancer.⁵² While HPV types 16 and 18 are responsible for 70% of global cervical cancer cases, types 31, 33, 45, 52, and 58 cause approximately 20% of additional cervical cancer cases.⁵³ Substituting 9vHPV for 4vHPV has been found to be highly cost-effective in reducing the burden associated with cervical cancer and HPV-related diseases⁵⁴ if the additional cost/dose of 9vHPV is less than \$13 USD.⁵⁵ However, the impact of 9vHPV on reducing the burden of cervical cancer and HPV-related diseases in China will largely depend on affordability. The three-dose vaccination series costs up to ¥5800 RMB.⁵⁶

Although at the current price the 9vHPV vaccine may not be cost-effective, nonetheless, evidence points to the potential benefit of the 9vHPV vaccine for certain female populations in China, particularly among those with high prevalence of the additional HPV genotypes in cervical intraepithelial neoplasia and invasive cancers. It has been estimated that the addition of five high-risk HPV types (31/33/45/52/58) in the 9vHPV vaccine could increase the invasive cervical cancer preventable fraction by 11.9% (95% CI 7.5–17.2), and the combination of all nine HPV types in the 9vHPV vaccine could account for 97.3% (95% CI 93.9–99.1) of cervical cancers in China.⁵⁷ Several studies on prevalence of HPV genotypes protected by the 9vHPV vaccine in invasive cervical cancers and cervical intraepithelial neoplasia cases in China^{58–60} provide insights into the benefit of the 9vHPV vaccine. A recent meta-analysis of the distribution of HPV genotypes in cervical cancer in Chinese women confirmed the additional clinical benefit of the 9vHPV. The meta-analysis findings showed that HPV 58 was the second most common type in invasive cervical cancers (12.6%) and HPV 52 was the second most common type in cervicitis/CIN1/CIN2 (16.3–22.0%). HPV 33, 31, 59, 45, and 39 were responsible for 2.1–5.5% of invasive cervical cancers.⁶¹ The meta-analysis also reported that HPV 16 and 18 were responsible for 78.2% of invasive cervical cancers.

Although strong evidence shows the benefit of the 9vHPV vaccine, currently it is recommended for women 16–26 years of age in China, which is older than the typical age recommendations, which range from 9 to 12 years of age. Furthermore, with the recommendation of 2vHPV in China for women ages 9–25 years and the 4vHPV recommended for ages 20–45 years, the varying age range recommendations across HPV vaccines may lead to confusion and uncertainty in vaccine decision making. To help women make informed choices, there is a pressing need for public education about the availability of different types of HPV vaccines, the protection against oncogenic types of HPV and the respective recommended ages for HPV vaccination. There is further need for the provision of information that women still need to undergo Pap smear screening, even after vaccination, because the vaccines are not protective against all types of HPV. Health-care providers should also be trained to accurately convey comprehensive information about the different recommended ages of the 2vHPV, 4vHPV, and 9vHPV vaccines, along with the potential benefits and limitations of protection against HPV genotypes of each of the vaccines

based on best available scientific evidence to support women in reaching informed decision about the choice of the HPV vaccines.

It is also important to note that despite the superiority of the additional five HPV types protected by the 9vHPV and its estimated 11.9% reduction the incidence of invasive cervical cancer,⁵⁷ findings from the recent meta-analysis,⁶¹ noted above, indicate that vaccination with 2vHPV may protect against as many as 78.2% of cervical cancers in China. Therefore, the impending availability of locally produced 2vHPV, which may be less expensive, may be more feasible for widespread use (i.e., likely to be introduced into the national HPV vaccination program) and would be more effective on the population level for cervical cancer prevention.

4.2 Great opportunity of fewer than three doses of HPV vaccine

The high cost and infrastructure complexities have driven research investigating the immunogenicity, efficacy, and effectiveness of fewer than three doses of HPV vaccine. The immune response to two-dose HPV vaccine for girls 9–14 years old was non-inferior than the response to three doses in adult women, when the two doses are at least 6 months apart.⁶² This finding resulted in the recommendation by the WHO in 2014 of a two-dose HPV vaccine schedule using either 2vHPV or 4vHPV vaccines for girls under 15 years.⁶³ A three-dose regime is still in place for older youth and young adults, between the ages of 15 and 26. However, very recent evidence points to the effectiveness of a two-dose regime for girls 15–18 years of age.⁶⁴

There have been some promising findings related to the immunogenicity and efficacy of single dose HPV vaccination. Incident and persistent infections are reduced after one dose of 4vHPV or 2vHPV.^{65–68} Two more recent studies provide an optimistic projection of the long-term efficacy of one dose HPV vaccine. In these studies, a single dose of 4vHPV and 2vHPV was found to continue to protect against HPV 16 and 18, for up to 7 years-equivalent to the two- and three-dose vaccine regimes.^{69,70} Further, one dose of HPV vaccine appears to be effective in preventing high-grade precancerous lesions^{71–73} and against anogenital warts.^{74,75} Although the existing evidence suggests that a single dose of HPV vaccine provides good protection against HPV-related diseases, longer follow-up of in the context of larger randomized trials seems warranted before universally recommending a single dose of HPV vaccine.⁷⁶ If two doses of HPV vaccine provide a satisfactory immunological response and show protective effects for adolescent girls between 15 and 18 years of age, as suggested by Bhatla et al. (2018), it will open a greater opportunity to reach more people in China at less cost. Additionally, if evidence from clinical trials eventually supports the efficacy of a one-dose regime, it would further reduce costs and have the added benefit of overcoming many of the significant logistical barriers faced by a country as large and diverse as China.

Two-dose HPV vaccine schedules have not yet been introduced in China. The two-dose HPV vaccine schedule for

adolescent girls aged 9–14 years has been approved and recommended by the WHO and the Global Alliance for Vaccines and Immunization and has become a standard for many other countries in the world,^{63,77} indicating that it should be recommended in China. A regime requiring fewer doses simplifies the logistics of vaccine administration, likely improving compliance and uptake among young adolescents and women in rural areas and remote regions in China.

5. Conclusion

The late introduction of HPV vaccines in China has led many young women to continue to be vulnerable to the development of cervical cancers and precancers. However, the delay in implementation of HPV vaccination provides China with lessons that can be learned from the difficulties and other countries have encountered with establishing a national HPV immunization program. Importantly, useful information could be gained from other countries on how to successfully introduce widespread HPV vaccination in China and implement an effective national HPV immunization program. In all likelihood, widespread dissemination of affordable HPV vaccination in China will take many years. As a result, as vaccination programs are being scaled up, it will be essential to continue to strengthen current screening programs and cervical cancer treatment facilities as a way to curb the country's rising rates of cervical cancer morbidity and mortality. Moreover, screening is complementary to vaccination, and effective screening programs will continue to be needed for older women, unvaccinated women, and to address cervical diseases caused by HPV types not included in the vaccines. At the current projected pace of HPV vaccine uptake, the introduction of multiple HPV vaccines (including the impending approval of a vaccine manufactured in China), and evidence supporting a two-dose schedule, a significant impact of the HPV vaccine introduction on the prevalence of high-risk HPV types and cervical dysplasia, will undoubtedly be seen in less than a decade in China. If China is able to implement a low-cost or no-cost nationwide HPV vaccination program, the positive effects will be even more profound.

Disclosure of potential conflicts of interest

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