



Hepatitis E vaccine in China: Public health professional perspectives on vaccine promotion and strategies for control



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ABSTRACT

Background: A hepatitis E (HepE) vaccine was developed and released in China in 2011. Uptake is currently very limited. The aims of this study were to characterize what public health professionals thought about promoting the HepE vaccine in Shanghai, China, and to develop realistic goals for the HepE vaccine based on this information.

Methods: Public health professionals from Shanghai and other jurisdictions of China were contacted to participate in in-depth qualitative interviews between October 2017 and August 2018. Participants were asked about their perception of the HepE vaccine roll-out. Codes were initially based on the structure of the questionnaire. Subsequently, similar ideas were further developed into themes based on what was present in the transcript data.

Results: Thirty-five individuals participated. Major topics of discussion included (1) clarifying the roles and responsibilities of private and public institutions in promoting and marketing the HepE vaccine, (2) identifying what methods of promotion were most efficient, and, (3) endeavoring to formulate a reasonable and realistic goal, if any, for HepE prevention and control in China. Participants emphasized that public sector sources can be trusted sources of information (although the private vaccination company can also be useful in disseminating information) and social media such as WeChat can be good ways to disseminate articles (although netizens may be worried about the spread of fake news). Vaccine promotion is restrained given limited levels of knowledge in the government, hospitals, and public health vaccination centers.

Conclusion: Successful promotion and use of this vaccine in China, even in limited settings (for instance, certain workplaces, or certain groups) could provide additional information on long-term safety and could promote its adoption in other regions of the world where HepE has high morbidity among pregnant women and other populations.

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1. Introduction

Hepatitis E (HepE) is a common cause of acute hepatitis in Africa, South Asia, and China [1], and has been recognized as an emerging

infectious disease by the U.S. National Institutes of Health's National Institute of Allergy and Infectious Disease in 2014 [2]. The HepE virus was first identified in 1983 [3,4], and belongs to its own family *Hepeviridae*, although it shows some amino acid similarity to viruses in the *Togaviridae* family like rubella virus [5]. HepE has a similar disease presentation as hepatitis A (HepA), and they are both enteric pathogens spread through the oral-fecal route [3]. HepE is also waterborne [1]. Within China, HepE virus is often spread through uncooked pork products [6], and swine workers have higher HepE seroprevalence than other groups [7].

Globally, there were over 19.4 million cases of acute hepatitis attributable to this virus in 2017 [8], and an estimated 50 thousand deaths in 2013 [9], yet HepE is not well known in medical and pub-

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lic health communities. In China, which routinely immunizes for HepA, HepE has become the leading cause of acute viral hepatitis: China reported 76,102 cases of HepA and 15,397 cases of HepE in 2005, but only 26,704 cases of HepA and 27,943 cases of HepE in 2014 [10]. There are four genotypes of HepE [5], and infection with genotypes 1 or 2 (which are common in South Asia [11]) during pregnancy has been associated with substantial maternal mortality, ranging from 20% to 70%, but typically around 30% [6,12]. There is thought to be only one serotype of HepE virus, indicating that immunity gained through natural infection or vaccination from one strain should protect against others [3].

Development of the HepE vaccine progressed with phase I clinical trials in the 1990s [11]. US pharmaceutical companies have since stopped further development of the vaccine [13]. Another HepE vaccine was later developed by a Chinese company, and, after successfully passing through clinical trials [14] and receiving regulatory approval, it was released onto the private market in China in 2011 [15]. Results from the clinical trial show that, after 4.5 years, vaccine efficacy was 87% (95% confidence interval (CI): 71–94%), and the rate of adverse events was not significantly different between those who were vaccinated and those who were not [16]. Longer-term efficacy data are not yet available, but may be important to consider given that little is known about long-term persistence of antibodies following vaccination or natural infection [17].

The vaccine is currently optional and only recommended for use in individuals ≥ 16 years with a cost of 170 RMB (\$25) per dose and 3 doses in the full series. The vaccine is considered to be a category 2 vaccine, meaning it is not publicly subsidized, in contrast to category 1 vaccines (like the HepA vaccine) which are provided for free by the Chinese government to citizens. The China Experts Advisory Committee on Immunization Program recommends vaccines to be included as category 1 vaccines based on characteristics related to the target disease (associated morbidity, mortality, and socioeconomic distribution) and target vaccine (biological characteristics as well as supply and availability) [18].

Currently China is the only country globally where HepE vaccine is commercially available. Thus far, its limited use in China (with only a couple hundred vaccinees in Shanghai, for example) may limit momentum for introduction and uptake in other countries [19]. Exporting the vaccine to select countries for use in young adult women and other high risk groups could prevent excess morbidity and mortality. HepE has also been shown to cause chronic hepatitis among immunocompromised individuals, including people living with HIV [20] and those with organ transplants [21], and so HepE vaccination programs could benefit these groups as well.

Little is known about how HepE vaccine was introduced in China. The HepE vaccine is among the first of a generation of vaccines which has been developed outside of a high income country with intended primary use in low resource settings. More information about how HepE was introduced could inform future vaccine introductions in a low- or middle-income country especially for those which are indigenously developed and produced without guidance from the World Health Organization, the Gavi Alliance, or high-income countries.

This qualitative study was conducted in China and aims to characterize what public health professionals thought about promoting the HepE vaccine in Shanghai, China, and to develop realistic goals for the HepE vaccine based on this information.

2. Methods

2.1. Study population

Public health professionals, predominantly from Shanghai, but also from other provinces – Fujian, Guangdong, Sichuan, and Tian-

jin, were contacted to participate in in-depth qualitative interviews. Participants were selected as key informants with special expertise in HepE, specifically in disease surveillance, disease control, vaccination development, or vaccination promotion. Initial interviews were conducted with individuals responsible for HepE control at provincial-level Centers for Disease Control and Prevention (CDCs), and these respondents provided contact information for others who also had responsibility over HepE. Most interviews were in person, although interviews with participants outside of the municipality were conducted over the phone. The professionals worked within the field of public health, at different levels of CDCs, in the Ministry of Health, in academia, or in industry. There was no pre-determined sample size. In accordance with standard practice for qualitative questionnaires, we stopped obtaining new interviews after we had reached saturation, i.e., we did not obtain substantively new information in the last three interviews. Questionnaires were conducted between October 2017 and August 2018.

2.2. Questionnaire

The questions asked were based on previous research [22], and on guidelines for conducting stakeholder analyses [23]. Broadly speaking, participants were asked about their knowledge of HepE and the HepE vaccine, about what attributes of the disease and vaccine were most important for vaccine promotion, and about their perception of the HepE vaccine roll-out in China. The full questionnaire is available online at figshare: <https://figshare.com/s/b5ec02d8cc48649fa5cf>.

2.3. Analysis

The interviews were conducted in Mandarin Chinese and were transcribed by a native Mandarin speaker. The interviews were coded by two native Mandarin speakers, using a thematic analysis approach [24], whereby codes were initially based on the structure of the questionnaire. Subsequently, similar ideas were further developed into themes based on what was present in the transcript data. NVivo 10 (QSR International, Melbourne, Australia) was used to analyze the transcripts. These themes are described in the Results section, along with representative quotes, which have been translated into English.

2.4. Ethical approval

This protocol for this study was examined by the University of Michigan Health Sciences and Behavioral Sciences Institutional Review Board (HUM00134336) and the Fudan University ethics review committee (2018-01-0658). All participants were given an informed consent form, and verbally gave consent prior to any data collection.

3. Results

In total we contacted 35 persons to participate in an interview, and all agreed to participate: 3 individuals working in a province-level CDC, 10 individuals at municipal-level CDCs, 1 from a prefecture-level CDC, 5 from district-level CDCs, 6 vaccination providers, 1 from the Ministry of Health, 4 from a public university, and 2 from vaccine companies.

Major topics of discussion from the interviews included the following: (1) clarifying the roles and responsibilities of private (pharmaceutical firms) and public (governmental) institutions in promoting and marketing the HepE vaccine, (2) identifying what methods of promotion were most efficient at disseminating infor-

mation, and, (3) endeavoring to formulate a reasonable and realistic goal, if any, for HepE prevention and control in China.

3.1. Roles played by different institutions in promoting HepE vaccines

3.1.1. Private vs government sector responsibilities and roles

Participants expressed varying opinions on the respective roles of private companies (like the vaccine manufacturer) versus governmental agencies, including vaccination providers at community health centers. These concerns centered around what each stakeholder should do to promote the HepE vaccine. For example, one individual indicated that problems with promotion are due primarily to the private company rather than the government.

“First of all, in regards to promotion, [vaccine] companies themselves have responsibility. If the vaccine has been promoted badly, [vaccine] companies themselves have responsibility. They didn’t promote this vaccine.” (R01)

Similarly, some believed that the government should have no role in promoting category 2 vaccines, particularly due to limited resources and the need to devote limited resources towards promoting category 1 vaccines.

“Community health centers won’t help with this [promoting HepE vaccines]. There is no possibility; [community health centers] don’t deal with assessing HepE vaccines.” (R15)

“From the government’s perspective, the government will not help its promotion process because the HepE vaccine is a category 2 vaccine. Category 2 vaccines only have the manufacturer lead the government to promote the vaccines. For category 1 vaccines, the government will lead vaccine companies to promote the vaccine.” (R01)

However, many cautioned against relying too much on commercials for public health promotion. The government may even regulate certain types of public health or medical advertisements, limiting the ability of vaccine manufacturers to promote or advertise the vaccine in certain settings:

“There are several problems that exist when companies promote the vaccine right now. Vaccination providers are not allowed to commercially advertise any category 2 vaccine, they are only allowed to do wide-range public promotions.” (R04)

“There are not many things that can be done to promote the vaccine because the government has set up some restrictions. For example, promoters from pharmaceutical companies are not allowed to enter hospitals. There may also be some similar restrictions for vaccine companies. As a result, companies want to promote via education, especially education for high-risk population.” (R09)

These restrictions limit the ability of vaccine manufacturers to promote the vaccine. The government would face no such restrictions. And, in contrast to some participants mentioning that the government did not have the resources to promote the vaccine, at least one participant mentioned that the government may wish to promote the vaccine because the vaccine is indigenously produced and is an example of the progression of Chinese science.

“I think the government will vigorously promote one of our independently researched products.” (R09)

The participants mentioned benefits of using the government, rather than private companies, as a source of health information. For one, using the government was thought to be an important way to give information to the general population or high risk

groups because Chinese people trusted the government. In contrast, patient-consumers would be less trusting of companies which had a commercial interest in the product.

“First of all, the main promoter should be authoritative and trustworthy. It is inappropriate if the company is the main driver of the promotion because it feels like they are selling health products.” (R11)

The government did not have such a commercial interest, and it follows that individuals would therefore be more likely to get vaccinated if the source of that information came from the government:

“If the information is official, it’s trustworthy because Chinese believe in our government. Official sources are definitely reliable.” (R09)

3.1.2. Use of hospitals and health care providers for vaccine promotion

Vaccination providers (known also as community health doctors) and infectious disease or other clinical doctors were also mentioned as other sources of vaccine promotion. Because community health doctors focus primarily on infants and the elderly, vaccinating younger adults would not be seen as a priority and there is little knowledge on the part of community health workers for these types of vaccines. On the other hand, because individuals do occasionally go to a hospital, health messaging at the hospital or from clinical doctors could be efficient at promoting the vaccine, especially among adults, who do not regularly visit community health centers, where most pediatric vaccinations are offered.

“Because it’s hard for people to avoid illness during their lifetime, if you do some promotion in the hospital, or use doctors to tell them to get this vaccine, I believe that the power of the vaccine promotion may be stronger.” (R01)

“[Doctors] should also know that there is a HepE vaccine, especially doctors who treat hepatitis, because there are many hepatitis patients that are repeatedly infected, for example, infected with both hepatitis C and HepE. Doctors can talk about vaccines to prevent hepatitis when treating patients to increase patients’ awareness.” (R10)

However, participants mentioned limits to using doctors. Many clinical doctors lack knowledge of HepE:

“Many hospitals do not even conduct indirect diagnosis of HepE at all. For example, patients with hepatitis are tested for HepA, HepB, and HepC in the past. If doctors do not have enough knowledge, the general population still listen to doctors’ advice, and doctors do not diagnose HepE, and the general population will not know what kind of disease HepE is. As a result, there will be no way to treat the disease [as HepE]. In regards to the education they receive, doctors are not updating their knowledge so quickly, and HepE is considered to be a disease with many new development. Most doctors weren’t educated about HepE, and there is not much related knowledge in their minds. [...] The doctors in the hospital, including the staff of the disease control system, don’t quite understand HepE.” (R11)

3.1.3. Other units that could promote vaccines

Colleges, border control, and marriage licensing units were other institutions that could promote vaccines. Even if college-aged individuals were not a high risk group for HepE, they could be targets of vaccination programming, given the infrastructure in place and that they are a captive audience:

“Young people are not the main high-risk group, but I think that there is one benefit in providing HepE vaccination on university

campuses. The students are graduating soon, they may get married and give birth to kids. Because pregnant women are one of the high-risk groups with a relatively high mortality rate, I think the university campus is also one focus.” (R09)

3.2. Efficiency of different types of methods promoting the HepE vaccine

3.2.1. Use of traditional and social media in vaccine promotion

Participants struggled with how best to promote the vaccine. New forms of social media were thought by many to be superior to print media/newspapers or television because they were more efficient. Efficiency was construed as the potential for dissemination of information to a wide audience. WeChat is a Chinese social media site similar to Facebook, where individuals can message friends in “WeChat groups” and post updates or their own articles they find online in a section called “Moments.”

“TV media is more authoritative while social media can reach more people. For example, for well-done social media accounts, just simply forward a WeChat article. and if the article is good, it will spread very widely.” (R11)

“WeChat is used more frequently in China right now. Almost everyone, except the very old, will have WeChat groups if they have a mobile phone. [...] There are a lot of people in the [WeChat] group. If somebody introduces this thing, and also shares information with each other in Moments, everyone may pay attention to it - if this person is interested in this.” (R05)

Many participants described how public accounts on WeChat or Weibo (similar to Twitter) could be used to disseminate news:

“Nowadays, every hospital has its official WeChat and Weibo public account, and they often pushes some articles. As long as you are following these accounts, they will push articles. Don’t underestimate WeChat. It’s often that after an article is pushed and immediately forwarded to Moments, that millions of people will know about it within a day.” (R08)

Some participants were concerned about fake information being spread through social media, but believed that public accounts could counter this misinformation:

“Now through modern news media, professional organizations are still very important, like the city CDC and the health promotion center, and city professional institutions are still very important. They can disseminate information through WeChat, Weibo, or their own government websites. [...] They can also correct some shortcomings about disease awareness from social media.”

3.2.2. Other sources of vaccine promotions

Integrated marketing strategies were another venue for promotion, such as using certain days (public health day, hepatitis day) to promote the vaccine in tandem with television appearances.

“We have publicity day every year, and we will use some traditional ways to promote, for example, some posters or some promotional materials.” (R10)

Participants brought up how lecture series could introduce certain groups in the population to HepE, in order to increase awareness of the disease and vaccine.

“We carry out a lot of research related to the health of elders here. [...] There are various community promotion activities, and our activities are actually integrated with their activities,

such as providing many volunteer lectures to elderly individuals. There are series of lectures. In the past, these have mostly focused on chronic diseases, such as diabetes, high blood pressure etc.. We can also cover some other health topics, such as viral hepatitis, infectious disease.” (R11)

3.3. Goals for HepE control

3.3.1. Public health strategies for prevention and control

Participants disagreed on what long-term public health goal was most appropriate for HepE. One basic distinction was whether the focus should be on elimination, as it is for some vaccine-preventable diseases, like measles, or whether something less than complete prevention should be the goal (such as preventing outbreaks, or reducing transmission below endemic levels)

As one participant posits, the availability of a vaccine suggests that elimination is reasonable:

“Since there is this vaccine, and the vaccine is highly efficient, it would be the best to be able to completely control it to the level of elimination.” (R07)

Whereas another participant indicates that controlling incidence of disease is a more reasonable first step:

“In fact, it is difficult to eliminate a disease. But if the incidence are controlled to a very low level, it is still ok to maintain a low incidence first.” (R08)

When considering a shorter term goal, many participants agreed that realistically focusing on promoting awareness of HepE and its vaccines was more reasonable than trying to attain a certain vaccination coverage:

“Because it’s difficult to regulate category 2 vaccines’ vaccination rates, for now, for the HepE vaccine, we hope that people’s awareness of HepE and its vaccine can be promoted.” (R09)

“Only category 1 vaccines have vaccination rate requirements, but we have to consider various factors, for example, what the cost-benefit is. I think what we can do now is to focus on a promotion targeted towards high-risk populations to promote their awareness of vaccination.” (R10)

Many participants believed that HepE control goals should focus on high risk individuals instead of on the general population. However, there was confusion in what constituted a high risk group. Commonly mentioned groups include pregnant women, food preparers, and individuals working in slaughterhouses. Pregnant women were often mentioned as an example for explaining to others the importance of the vaccine:

“For example, we should let everyone know that if pregnant women get HepE, the outcome will be more serious. In my opinion, the promotion can target high-risk population.” (R07)

3.3.2. Goals for HepE compared with goals for other hepatitides

Strategies for addressing other hepatitides, notably HepB and HepA, were used as guides or paradigms for HepE prevention and control, especially since the WHO has formalized guidelines for eliminating HepB and HepC by 2030.

“The goal right now is eliminating hepatitides by 2030, and a general plan is going to be set up.” (R03)

“Of course the goal is eliminating hepatitides by 2030, according to WHO” (R09)

“As for the level of control, I think [HepE] should be at a level similar to hepatitis A, at a relatively low level. I believe this has a lot to do with our lifestyle. [...] The control of infectious

diseases is not only through vaccinations, but also through improvements in lifestyle improvements.” (R16)

3.3.3. Limits to goal-making

Stakeholders mentioned that there were several impediments to the control of HepE. One is that it is a zoonotic disease, with humans not the only reservoir:

“If the effect of the vaccine is reliable, eliminating the disease is still a process, and it’s possible. But animals can also get infected.” (R05)

Several participants also suggested that more longer term findings on safety and effectiveness would be necessary for decision-makers.

“[Studies] should include a larger sample size and monitor the data for a longer period of time to illustrate the protective and effective time of the vaccine. The information I have learned so far is from data from a five-year trial from Xiamen Wantai [the vaccine development company]. I think the sample size and the length of follow-up are not sufficient to prove the effectiveness of this vaccine.” (R03)

The lack of a clear goal for the control of HepE could also be tied to the fact that many medical doctors or individuals in positions of authority in the government just do not know about the disease.

“Tell the government because the leaders of the governmental departments do not know how serious the disease is. But if you show data from disease monitoring, or the big burden caused by the disease to the government and relevant authorities, they may pay attention to HepE and its vaccine.” (R01)

“On the other hand, this is a vicious circle. The hospital can’t diagnose it, so the diagnostic report can’t show it. Then people don’t know about the cases. As a result, people think that HepE is rare in China. In fact, in areas where HepE is better diagnosed, the incidence of the disease increase significantly. I think that the medical staff’s own knowledge update is a relatively important thing.” (R11)

Overall, the lack of knowledge about this vaccine limited the number of individuals requesting it, which in turn limited the number of health clinics which were willing to stock the vaccine.

“Since last year, with category 2 vaccines, including HepE vaccine, vaccine procurement has been in the district CDCs. They procure based on whether there is a demand from the public. If there is not a public demand, then they will not bring on this vaccine, they will not procure this vaccine, so it is a vicious circle. Because the general population is not vaccinating, the district CDCs do not procure, so that individuals who want to get vaccinated cannot.” (R13)

Regardless of the difficulties in promoting the vaccine in the current circumstances, the potential for HepE disease to increase in incidence in the future, and the availability of a vaccine, would seem to necessitate a goal being made.

“In the past few years, HepE incidence has increased, and it is difficult to predict to what level it will increase in the future. But I have always thought that vaccination is the best way to prevent disease. Even if there is a vaccine, if you don’t get vaccinated, it is a pity.” (R14)

4. Discussion

Although causing far fewer deaths or cases of illness than parenteral hepatitis (HepB or HepC), HepE has emerged as an

important cause of acute viral hepatitis – surpassing HepA in incidence in China, and it is a substantial cause of maternal mortality in South Asia. A recently developed vaccine is only available in China, but it has had extremely low uptake (with only a couple hundred vaccines administered in Shanghai, for example), and it is unclear how the vaccine should be promoted within the country. Moreover, misinformation about HepE vaccine initiated in China could spread to other countries and the lack of an successful roll-out of a vaccine could limit other country’s enthusiasm for adopting it.

This study involving qualitative interviews with public health professionals in Shanghai and other parts of China to identify who should promote the vaccine and how it should be promoted. Overall, participants mentioned how there is little knowledge of HepE as a form of hepatitis, even among clinicians, and even less knowledge about its vaccine. In general, participants emphasized that public sector sources can be trusted sources of information (although the private vaccination company can also be useful in increasing awareness) and social media such as WeChat can be good ways to disseminate articles (although netizens may be worried about the spread of fake news). Attempts to increase vaccination have been very restrained given limited levels of knowledge in the public sector – among the government, hospitals, and public health vaccination centers. The best short-term goals could focus on educating scientists and public health professionals and tying HepE into goals to control other hepatitides.

4.1. Institutions and types of promotions

Public sector sources were thought to be the most important and trusted sources of information among the stakeholders consulted. Trust in public institutions does vary between different groups; one study found this trust higher in recent rural-to-urban migrants, than long-standing urban and rural dwellers [25]. And limited trust can have real impacts on vaccination; for example parents with less trust in a government-run measles vaccination campaign were less likely to get their children vaccinated in Beijing in 2010 [26].

In one study from the United States, parents trusted information from doctor’s websites more than websites run by the government, vaccine manufacturers, or anti-vaccine groups [27]. This potentially speaks to the importance of doctors developing personalized messaging surrounding vaccines, instead of copying and pasting information from official sources. In general, using memorable, personal stories to elicit emotion from potential vaccinees can be one way to increase positive feelings towards vaccination and uptake itself [28].

However, using health care providers to promote a vaccine which requires payment could call into question whether they had competing financial interests. Conflicts of interests became more of a concern in China in the 1990s and 2000s as liberalization of the economy led more doctors to rely on prescribing pharmaceutical products as an important source of income [29]. In result, many patient-consumers have reduced trust in the medical system or even committed violence against medical providers [30].

The use of social media holds great promise in increasing awareness and knowledge of this vaccine, although there are perils to the use of social media as well. Social media also offers the ability to target special groups – for instance individuals living in certain areas, certain types of workers, and some high-risk individuals may have pre-formed certain friend groups, and information spread in these groups could be highly targeted and highly beneficial. The importance of WeChat in spreading public health information and the potential for this to become viral is perhaps epitomized by one WeChat user’s post about the quality of a routine vaccine (diphtheria-tetanus-pertussis) which rapidly spread

through the country and which the country's president eventually responded to [31].

4.2. Goals

Developing a clear goal can help clarify what institutions should be involved in promoting HepE control, and how they should promote it. Participants had differing ideas about what should be a goal related to HepE. Their thoughts about whether a zoonotic disease can be eliminated, or to what extent vaccinations should be used, echo previous disagreements on how best to deal with malaria or smallpox [32]. A pertinent question is how much resources are available to be devoted to a disease; with increased control of a disease, costs per preventing each additional case of disease rise substantially [33]. Additionally, many criteria have been established for determining the eliminability of an infectious disease, with three indicators being of primary importance: (1) an effective intervention, like vaccination, to prevent transmission, (2) sensitive and specific diagnostic tools, and (3) humans being essential for the life-cycle of the agent [34]. Obviously HepE fulfills criterion 1, but, although a test for HepE is available, the potentially low sensitivity of the surveillance system in its current form would indicate that elimination is currently not possible. In addition, the genotypes of HepE that circulate in animal reservoirs, as genotype 4 dose in pigs in China, would seem to limit its eliminability currently.

Overall, it is largely conjectural to compare HepE vaccination to the roll-out of vaccines in other countries, because the HepE vaccine is currently only available in China. Other vaccines, such as enterovirus 71, are also developed by China and only available there. Nonetheless, the initial rollout period of a vaccine within a given country or region represents a transient window during which a sustained impression on the public may be made and impact how the vaccine is perceived for years to come. The introduction of human papillomavirus (HPV) vaccine and the HepB vaccine in the US offer instructive examples of difficulties that may unexpectedly arise during the roll-out. The HPV vaccine in the US continues to be characterized by relatively low coverage more than a decade after its introduction [35], because of the initial marketing and framing with its introduction there, which focused on the relationship between vaccination and sexual intercourse [36,37]. The introduction of the HepB vaccine differed in that it was initially promoted to just high-risk groups, including men who have sex with men, health care workers, and illicit drug users. Because high-risk individuals are often difficult to reach and more prone to infection prior to vaccination, the HepB vaccination program was distinctly unsuccessful at decreasing the incidence of disease in specific areas until the subsequent recommendation for vaccination of the general population was implemented [38]. The lessons from the HPV and HepB vaccines for the roll-out of HepE and other new vaccines is that careful and well-informed messaging about the vaccine prior to and during introduction is essential for successful adoption and uptake. Additionally, any cost-effectiveness analysis comparing universal and targeted vaccination programs should be cognizant about difficulties in identifying high risk groups.

4.3. Public health recommendations

It is difficult to place HepE in terms of its public health importance. As many participants mentioned in this study, clinicians may lack knowledge of the disease. Therefore, although HepE is a notifiable disease in China, it may be underreported. HepE is a large source of concern among some populations, and the availability of a vaccine in China is an opportunity to develop best prac-

tices for promoting the vaccine. We believe the following recommendations can be starting points:

1. Increase awareness of HepE and HepE vaccine among health care providers (including clinicians) and among the general population. Clarify what information should be provided by the public vs private sector.
2. List high risk groups to target for vaccination.
3. Increase evidence about the use of vaccination, including (1) its use in certain populations, such as children or chronic carriers of other hepatitides, and (2) the duration of protection.
4. Evaluate the current disease surveillance system in terms of its sensitivity for HepE cases and infection status.
5. Identify an acceptable price point for the HepE vaccine and increase adult vaccination service quality. An intriguing possibility would be to develop a hepatitis combination vaccine (with HepA, HepB, and HepC antigens), which could be included in government procurement and management.
6. Tie HepE control into HepB and HepC elimination procedures. Developing a standardized algorithm for testing and diagnosing the different hepatitides, by incorporating tests from all four pathogens depending on certain symptoms, could be one start.

Global promotion of the vaccine could also be kick started with WHO prequalification [1], or if Gavi included HepE as a priority infection [39].

4.4. Strengths and limitations

As a qualitative study, this analysis has several limitations. We are unable to assess how generalizable our findings are to the whole population given our sampling scheme. Our participants had greater knowledge and awareness of HepE than members of the general population. Because the participants were notified about the topic during screening and prior to interview, it is possible they could have sought out information about HepE in the interim period. We have a limited view of the breadth of attitudes and opinions about HepE. Future research can examine vaccine decision-making and uptake in the general population and high-risk groups in quantitative surveys. A strength of the study was the use of professionals across different levels of CDCs and from different regions of China.

4.5. Conclusions

The HepE vaccine is a pharmaceutical achievement, in that it represents one of the first vaccines this generation to be produced outside of the United States and Europe, for a disease that affects individuals mostly in LMICs. Successful promotion and use of this vaccine in China, even in limited settings (for instance, certain high risk groups) could provide additional information on long-term safety. If the vaccine is proven safe and effective in other regions of the world, its use could help prevent significant related morbidity among pregnant women and other populations.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Author contributions

All authors attest they meet the ICMJE criteria for authorship.

XXC participated in acquisition of data, interpretation of data, and revised manuscript critically for important intellectual content. ALW conceived of the study, contributed to data acquisition and analysis, and drafted the article. JYX contributed to data analysis and interpretation, and revised manuscript critically for important intellectual content. XBZ and MLB contributed to interpretation of data, and revised manuscript critically for important intellectual content. YHL and HR conceived of study design, contributed to interpretation of data, and revised manuscript for important intellectual content. All authors gave final approval of the manuscript to be published and agreed to act as guarantors of the work.

Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.vaccine.2019.07.067>.

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