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Assessing the effectiveness of the expanded hepatitis A vaccination program in China: an interrupted time series design

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ABSTRACT

Introduction China initialised the expanded hepatitis A vaccination programme (EHAP) in 2008. However, the effectiveness of the programme remains unclear. We aimed to comprehensively evaluate the effectiveness of EHAP in the country.

Methods Based on the provincial data on the incidence of hepatitis A (HepA), the population and meteorological variables in China, we developed interrupted time series (ITS) models to estimate the effectiveness of EHAP with the autocorrelation, seasonality and the meteorological confounders being controlled. Results were also stratified by economic zones, age groups and provinces.

Results We found a 0.9% reduction (RR=0.991, 95% CI: 0.990 to 0.991) in monthly HepA incidence after EHAP, which was 0.3% greater than the reduction rate before EHAP in China. Across the three economic regions, we found a 1.1% reduction in HepA incidence in both central and western regions after EHAP, which were 0.3% and 1.2% greater than the reduction rates before EHAP, respectively. We found a decreased reduction rate for the eastern region. In addition, we found generally increased reduction rate after EHAP for age groups of 0–4, 5–14 and 15–24 years. However, we found decreased reduction rate among the 25–64 and ≥65 years groups. We found a slight increased rate after EHAP in Shanxi Province but not elsewhere.

Conclusion Our finding provides comprehensive evidence on the effectiveness of EHAP in China, particularly in the central and western regions, and among the population aged 0–24 years old. This study has important implications for the adjustment of vaccination strategies for other regions and populations.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Early analyses mostly found that the incidence of hepatitis A (HepA) decreased more slowly after the expanded HepA vaccination programme (EHAP) in China.

⇒ These findings have raised significant debates about the effectiveness of EHAP in China.

WHAT THIS STUDY ADDS

⇒ When we account for data distribution and confounding factors, our comprehensive analysis of 3 economic regions, 31 provinces and 5 age groups of China found the reduction rate after EHAP mostly increased, illustrating the effectiveness of EHAP.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study provides more accurate evidence for the amendment of HepA prevention and control programmes in China, which covers more than 20% of the world's population.

⇒ This study has important implications for the adjustment of vaccination strategies for other regions and populations in China.

INTRODUCTION

Hepatitis A (HepA) is an acute, usually self-limiting liver infection caused by the HepA virus. HepA is mainly spread through the fecal–oral route,[1] such as drinking contaminated water or eating undercooked food. And it is a frequent cause of foodborne infections worldwide, resulting in sporadic cases, outbreaks or epidemics.[2] HepA is highly endemic in most developing countries and usually occurs in early childhood.[3] Severe cases can result in jaundice, acute hepatitis and even death. Currently, there are no highly effective antiviral drugs available on the market for treating HepA.[4] Therefore, the prevention of HepA relies mostly on the HepA vaccine.

HepA vaccine is highly effective in preventing HepA and reducing disease transmission. Recent research from Argentina, Israel, Alaska, the USA and Brazil[5–9] showed that childhood vaccination against HepA significantly reduced the incidence of HepA in all age groups, resulting in significant health and economic benefits for these countries. HepA vaccine has been used in China since 1992,[10] but it was entirely self-funded by citizens. Since 2008, with the implementation of the expanded HepA vaccination programme (EHAP), all infants at 18 months of age can receive free HepA vaccination. With the availability of vaccines, the coverage of target children increased. Since then, the effectiveness of EHAP in China has become a research hotspot. Tang *et al*[11] found a lower reduction rate of HepA incidence after EHAP in China compared with the before rate. Liu *et al*[12] and Zhang *et al*[13] investigated the effectiveness of EHAP in Chongqing Province and Huzhou City, and found that reduction rate of HepA incidence slowed down after EHAP.

However, the existing research evidence faces the following challenges. First, the existing research evidence was lacking in assessing the effectiveness of EHAP on different age groups and provinces in China. Second, the incidence data of HepA in the existing research followed a log-normal distribution. But they mostly did not take the logarithm of the HepA incidence and instead directly used a simple linear regression model, which may lead to an overestimate of the reduction rate of HepA incidence before EHAP. Third, the existing research mostly used years as time points in the model, which resulted in an insufficient number of data points. The interrupted time series (ITS) analysis requires at least 20 data points before and after the intervention. The more time points there are, the higher the efficacy of the ITS analysis will be.[14]

Therefore, we quantitatively assessed the effectiveness of EHAP among different economic regions, age groups and provinces in China. We used ITS design based on the monthly reported incidence data of HepA in China from 2004 to 2018. The results will improve the evidence-base of effectiveness of EHAP, and can inform the development of immunisation strategies to reduce the incidence of HepA in the future.

METHODS

Data source

The monthly reported incidence data of HepA by provinces and age groups in China from 2004 to 2018 were from the Infectious Disease Reporting System of the Chinese Center for Disease Control and Prevention. The annual population data by provinces and age groups were from the China Statistical Yearbook published by the National Bureau of Statistics of China and the public database.[15] The monthly temperature and precipitation data were obtained from the Institute for Health Metrics and Evaluation.[16] The temperature data were the monthly mean surface temperature at 2 metres above the ground in Celsius, and the precipitation data were the monthly mean daily precipitation in millimetres.

Measures

Outcomes: the changes in the monthly HepA incidence

First, we focused on the changes in the monthly HepA incidence from 2004 to 2018 in China overall. Second, we explored the changes by different economic regions. According to the National People's Congress, the provinces of China were divided into three regions: the eastern region, the central region and the western region, representing high (east), medium and low (west) levels of socioeconomic development (online supplemental methods). Finally, we examined the changes across different age groups. The entire population was divided into five age groups: 0–4, 5–14, 15–24, 25–64 and≥65 years groups.

We could only use the 2004–2018 data as the monthly data of the reported HepA incidence during the COVID-19 era has not yet been released. Furthermore, during the COVID-19 era, China government took strict public health measures to control the pandemic, such as compulsory lockdown and disinfection. These measures greatly reduced the mobility of the population, leading to a significant reduction in the incidence rate of most infectious diseases.[17 18] The exclusion of the COVID-19 era could avoid the overestimation of the effectiveness of EHAP.

Exposure: the expanded HepA vaccination program

We defined relevant policy interventions of interest, EHAP, as effective from 2008 onwards. We modelled this intervention with the assumption that it may have a short-term (ie, level change) and a long-term (ie, slope change) effect according to literature.[14] The preintervention period was defined as from January 2004 to December 2007, while the postintervention period was from January 2008 to December 2018.

Statistical analysis

We performed a quasi-experimental ITS analysis in order to assess the effectiveness of EHAP. We first established a basic model, which consisted of three parts: the slope before the intervention, the short-term level change after the intervention based on the preintervention trend and the slope change from preintervention to postintervention. ITS requires that the time series have no autocorrelation. The Durbin-Watson (DW) test is the most commonly used method to test for the autocorrelation in the data sequence, with a DW value close to 0 or 4 indicating an autocorrelation and a value close to 2 indicating the independence. The DW test was conducted on the time series of HepA (online supplemental tables S1 and S2). To control for autocorrelation, our model included a first-order lag of the residuals. We also incorporated Fourier terms (a matrix of sine and cosine functions) in the basic model to adjust for seasonality. The model we developed was

$$log(Y) = \beta_0 + \beta_1 \text{pretime} + \beta_2 \text{intervention} + \beta_3 \text{posttime} + \sum \beta_p \text{covariates} + \text{lag}\left(\text{residuals}\right) + \text{seasonality} + \varepsilon$$

where, Y was the main outcome indicator, which represented the incidence of HepA. Pretime was a time indicator variable before EHAP (with values of 1, 2, 3,…,48 for the period before EHAP, and a value of 49 for the after). Intervention was a dummy variable (with a value of 0 for the period before EHAP, and a value of 1 for the after). Posttime was a time variable indicating the period after EHAP (with a value of 0 for the period before EHAP, and values of 0, 1, 2, 3,…,132 for the after) (online supplemental table S3). Temperature and precipitation were also covariates being controlled. β_0 was the constant term, representing the average HepA incidence at the beginning of the study. β_1 was the slope of the logarithmic change in HepA incidence before EHAP. It can be interpreted as the relative risk ($RR_1 = e^{\beta_1}$) of HepA incidence associated with 1 month increase before EHAP, representing the underlying before-EHAP trend. β_2 was the instantaneous change in the level of logarithmic incidence of HepA after EHAP. It can be explained as the RR ($RR_2 = e^{\beta_2}$) after EHAP using before-EHAP as a reference, representing the short-term change in HepA incidence after EHAP. β_3 was the slope after EHAP. It can be interpreted as the RR ($RR_3 = e^{\beta_3}$) of HepA incidence associated with 1 month increase after EHAP, representing the underlying after-EHAP trend. β_p reflected the effect of confounders on the logarithmic incidence of HepA. ε represented the residual of the model. The analysis was conducted using R V.3.4.2. All tests are two-sided, and p<0.05 indicates statistical significance.

RESULTS

HepA incidence and ITS analysis in China

Before EHAP, the average reported incidence of HepA in China was 0.501/100 000 per month, with the highest average incidence in August at 0.585/100 000 and the lowest in December at 0.355/100 000. After EHAP, the average reported incidence decreased to 0.178/100 000 per month, with the highest in August at 0.302/100 000 and the lowest in December at 0.204/100 000. Online supplemental figure S1A shows the decreasing trend of HepA incidence in China from 2004 to 2018, particularly after EHAP. The incidence showed a clear seasonal trend, usually peaking in spring and summer. However, the seasonal pattern of HepA incidence weakened after EHAP.

The ITS results showed that after EHAP, the HepA incidence decreased by 28.5% (RR=0.715, 95% CI: 0.657 to 0.778) in a short time. And the incidence of HepA decreased by 0.9% per month (RR=0.991, 95% CI: 0.990 to 0.991), which was 0.3% greater than the reduction rate before EHAP (0.6%, RR=0.994, 95% CI: 0.991 to 0.997). Therefore, EHAP had both short-term and long-term impact on the incidence of HepA. After EHAP the incidence of HepA showed a faster downward trend than before. The result of ITS analysis in China is shown in table 1. The segmented linear regression graph of China is shown in figure 1A.

HepA incidence and ITS analysis in three economic regions

From January 2004 to December 2007, the monthly average incidence was 0.970/100 000 for the western region, 0.430/100 000 for the central region and 0.263/100 000 for the eastern region. From January 2008 to December 2018, the incidence decreased to 0.360/100 000, 0.139/100 000 and 0.098/100 000 in these regions. Overall, the HepA incidence in China was more concentrated in the central and western regions. After EHAP, the HepA incidence in the western region decreased the fastest, followed by the central region, while the incidence in the eastern region decreased relatively slowly. The trends in the incidence in these regions are shown in online supplemental figure S1A.

The ITS results showed that after EHAP, the HepA incidence in the eastern, central and western regions decreased by 21.5% (RR=0.785, 95% CI: 0.704 to 0.876), 25.4% (RR=0.746, 95% CI: 0.674 to 0.825) and 30.9%

Table 1 The result of ITS analysis of China overall, eastern region, central region and western region

Region	Variable	RR	95% CI	Trend*
China	Intervention	0.715	0.657 to 0.778	
	Pretime	0.994	0.991 to 0.997	Decrease faster
	Posttime	0.991	0.990 to 0.991	
Eastern region	Intervention	0.785	0.704 to 0.876	
	Pretime	0.982	0.979 to 0.986	Decrease slower
	Posttime	0.995	0.995 to 0.996	
Central region	Intervention	0.746	0.674 to 0.825	
	Pretime	0.992	0.988 to 0.995	Decrease faster
	Posttime	0.989	0.989 to 0.990	
Western region	Intervention	0.691	0.616 to 0.774	
	Pretime	1.001	0.997 to 1.004	Decrease faster
	Posttime	0.989	0.988 to 0.990	

This table was created by Yueqian Wu.
*The change in the trend of HepA incidence between before and after EHAP.
EHAP, expanded HepA vaccination program; HepA, hepatitis A.

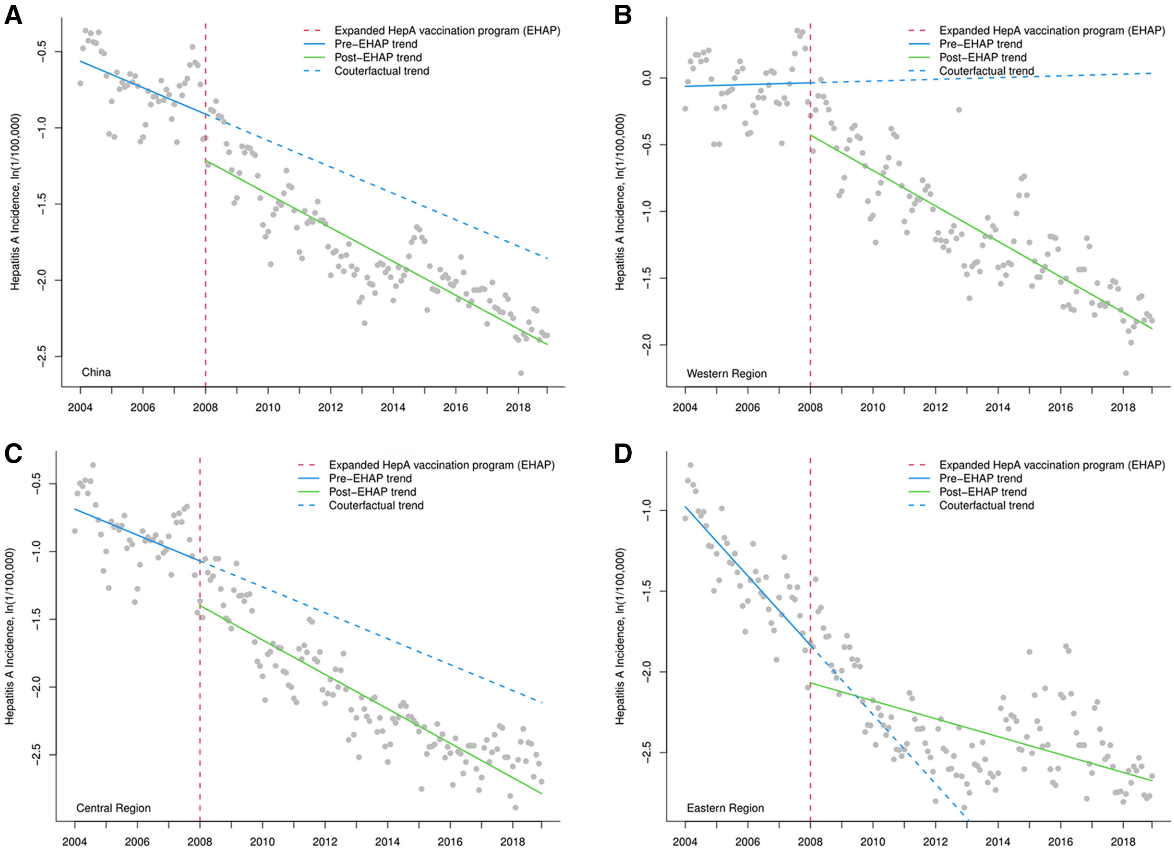

Figure 1 The segmented linear regression graph of the logarithm of the HepA incidence in China and three economic regions from 2004 to 2018. (A) China, (B) western region, (C) central region and (D) eastern region. This figure was created by Yueqian Wu. HepA, hepatitis A.

(RR=0.691, 95% CI: 0.616 to 0.774) in a short time. In addition, after EHAP, the HepA incidence in the eastern region decreased by 0.5% (RR=0.995, 95% CI: 0.995 to 0.996) per month, which was 1.3% less than the reduction rate before EHAP (1.8%, RR=0.982, 95% CI: 0.979 to 0.986). In contrast, the reduction rate was 1.2% and 0.3% greater in the western and central regions. Overall, EHAP had both short-term and long-term impact on the incidence in three economic regions. After EHAP, the incidence of HepA showed a faster downward trend than before in the central and western regions, while a slower downward trend than before in the eastern region. The results of ITS analysis in three economic regions are shown in table 1. The segmented linear regression graphs of three regions are shown figure 1B–D.

HepA incidence and ITS analysis in five age groups

Before EHAP, the monthly average incidence of HepA in age groups of 0–4, 5–14, 15–24, 25–64 and ≥65 years were 0.622/100 000, 0.846/100 000, 0.398/100 000, 0.447/100 000 and 0.374/100 000, respectively. After EHAP, they were 0.249/100 000, 0.208/100 000, 0.124/100 000, 0.169/100 000, 0.209/100 000, respectively. Generally speaking, the age groups of 0–4, 5–14 and 15–24 years had a greater reduction rate in the HepA incidence than the remaining two groups, although the incidence in each age group showed a significant downward trend. The peak incidence age shifted from younger age groups towards older age groups (online supplemental figure S1B).

The ITS results showed that after EHAP, the HepA incidence in age groups of 0–4, 5–14, 15–24, 25–64 and ≥65 decreased by 40.8% (RR=0.592, 95% CI: 0.497 to 0.704), 35.1% (RR=0.649, 95% CI: 0.589 to 0.754), 16.1% (RR=0.839, 95% CI: 0.752 to 0.937), 16.3% (RR=0.837, 95% CI: 0.765 to 0.915) and 0.9% (RR=0.991, 95% CI: 0.901 to 1.089) in a short time. Furthermore, after EHAP, the age groups of 0–4, 5–14 and 15–24 years showed a faster downward trend in the HepA incidence than before, while the age groups of 25–64 and ≥65 years showed a slower downward trend than before. The results of ITS analysis in five age groups are shown in table 2.

HepA incidence and ITS analysis in different provinces

We found the province with the highest monthly incidence of HepA was Xinjiang Autonomous Region, while the province with the lowest average incidence was Tianjin Province during the periods before and after EHAP. The nationwide incidence trend is shown in figure 2.

The ITS results showed that 12 provinces mainly in the western and central regions (Gansu, Guangxi, Hebei, Henan, Jiangxi, Tibet, Guizhou, Hunan, Ningxia, Qinghai, Xinjiang and Yunnan) showed faster reduction rates of HepA incidence after EHAP compared with the

Table 2 The result of ITS analysis of five age groups in China

Group	Variable	RR	95% CI	Trend*
0–4	Intervention	0.592	0.497 to 0.704	
	Pretime	1.009	1.003 to 1.014	Decrease faster
	Posttime	0.989	0.988 to 0.990	
5–14	Intervention	0.649	0.589 to 0.754	
	Pretime	1.007	1.002 to 1.012	Decrease faster
	Posttime	0.978	0.977 to 0.979	
15–24	Intervention	0.839	0.752 to 0.937	
	Pretime	0.994	0.990 to 0.997	Decrease faster
	Posttime	0.985	0.984 to 0.986	
25–64	Intervention	0.837	0.765 to 0.915	
	Pretime	0.986	0.984 to 0.989	Decrease slower
	Posttime	0.993	0.992 to 0.993	
≥65	Intervention	0.991	0.901 to 1.089	
	Pretime	0.987	0.984 to 0.990	Decrease slower
	Posttime	0.997	0.996 to 0.997	

This table was created by Yueqian Wu.
*The change in the trend of HepA incidence between before and after EHAP.
HepA, hepatitis A; EHAP, expanded HepA vaccination programme.

before period. Fifteen provinces mainly in the eastern regions (Anhui, Beijing, Fujian, Guangdong, Hainan, Heilongjiang, Hubei, Jilin, Jiangsu, Inner Mongolia, Shandong, Shaanxi, Sichuan, Zhejiang and Chongqing) showed lower reduction rates after EHAP. The changes in the incidence in Liaoning, Shanghai and Tianjin did not have statistical significance. Surprisingly, Shanxi showed an increasing trend in HepA incidence after EHAP (online supplemental table S4). The results of ITS analysis for 31 provinces are shown in figure 3.

DISCUSSION

We used ITS design to conduct a comprehensive assessment of the effectiveness of EHAP in China and across different economic regions, age groups and provinces. Our research found that after EHAP, the rate of decline in HepA incidence in China accelerated, particularly in the western and central regions. The age groups of 0–4, 5–14 and 15–24 years in China experienced a faster decline in the incidence relative to others. Among 31 provinces in China, 12 provinces experienced a faster decline in the incidence after EHAP, most of which were concentrated in the relatively less developed central and western regions. Fifteen provinces exhibited a slower decline, primarily located in the economically developed eastern region. Surprisingly, we found that Shanxi province experienced an increase in HepA incidence after EHAP.

The effectiveness of EHAP in China

After EHAP, we observed a decrease in HepA incidence in China in the short term, and a more pronounced long-term decrease, indicating the effectiveness of EHAP. China has used two types of HepA vaccines: the inactivated HepA vaccine (I-HepA) available globally and the

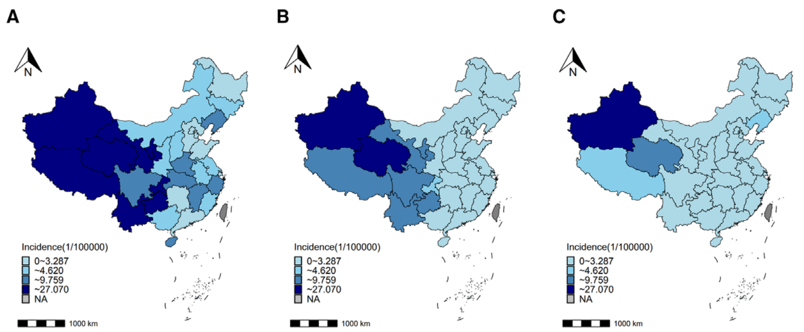

Figure 2 The spatial distribution of the HepA incidence in 31 provinces of China from 2004 to 2018. (A) 2004 to 2008. (B) 2009 to 2013. (C) 2014 to 2018. The thresholds were the quartiles of HepA incidence in China during the study period. This figure was created by Zhicheng Du. HepA, hepatitis A.

Figure 3 The change in the trend of HepA incidence between before and after EHAP of 31 provinces in China. This figure was created by Zhicheng Du. EHAP, expanded HepA vaccination programme; HepA, hepatitis A.

attenuated HepA vaccine (L-HepA) produced exclusively in China and available in several developing countries including India. It has been reported that the seroprotection rate against HepA virus can reach about 95% within 14–30 days after the first dose of I-HepA.[19] The serum protection rates of I-HepA and L-HepA are similar for children and adults after one dose.[20 21] This may explain the observed short-term effectiveness of EHAP in reducing HepA incidence. Otherwise, the long-term effectiveness may be attributed to the sustained immunity gained after vaccination, which can effectively protect the body from HepA for several years. A longitudinal cohort study followed up subjects who received the first dose of L-HepA for 17 years, and found that individuals would have long-term immunity, including antibody persistence and immunological memory, after receiving L-HepA.[22] Mathematical models suggested that at least 95% of the vaccinated individuals can maintain immunity for at least 33 years after two doses of I-HepA.[23]

Our results underscored the importance of national-level immunisation programmes in controlling the spread of infectious diseases, both in the short and long terms, and provided a successful preventive strategy model for other countries. And, it is crucial to continuously provide free HepA vaccinations in the future and to promote the effectiveness of the HepA vaccine to encourage timely vaccination among more people, ultimately reducing HepA incidence to a lower level.

The effectiveness of EHAP in three economic regions

We found that the reduction in HepA incidence in the eastern region slowed down after the programme. The most possible reason may be that the HepA incidence in the eastern region had already been reduced to a relatively low level before 2008. The HepA vaccine was introduced into China since 1992, but before its inclusion in EHAP, residents had to pay for it. From 2004 to 2007, 18–22 million doses of the HepA vaccine were administered, primarily to school-age children.[24] Residents in the wealthier provinces of the eastern region (such as Beijing, Tianjin) were more likely to receive the HepA vaccine, with approximately 80% being children. This resulted in a lower initial incidence of HepA in the eastern region compared with the central and western regions, which is consistent with previous research findings.[25–27] After EHAP, the incidence of HepA in the eastern region decreased to an even lower level in the short term, making it difficult to assess the effectiveness of EHAP on HepA incidence. WHO also pointed out that interventions had little effectiveness on the HepA incidence in areas with very low prevalence, and the efficacy of vaccine may be overlooked.[28]

However, we also found that the central and western regions experienced a faster reduction in the incidence of HepA in the long term and the incidence of HepA decreased in three economic regions in the short term after EHAP. The most plausible interpretations may be that the HepA vaccine has been included in EHAP since 2008, making it free for all the newborns. And children aged 18 months and older have universally started to receive the vaccine, significantly reducing the unequal distribution of healthcare resources in the three regions.[29]

These findings suggested that in economically developed areas, where the incidence of HepA had already been reduced to a certain extent, free vaccination of children for HepA showed pronounced short-term effect, but the long-term impact was relatively less noticeable. This may lead to insufficient utilisation of resources. In contrast, for disadvantaged areas, the policy was significantly effective, capable of rapidly and sustainably reducing the incidence of HepA. To achieve a consistent low incidence of HepA disease, the government should still pay attention to the disadvantaged areas. And it is of great importance to reconsider the follow-up vaccination plans in economically developed areas. It is necessary for the government to pay more attention to populations other than children in these areas.

The effectiveness of EHAP in five age groups

Our research found that EHAP led to a short-term reduction in HepA incidence across five age groups. Among the age groups of 0–4, 5–14 and 15–24 years, the HepA incidence declined more rapidly over time. While the remaining two age groups of 25–64 and ≥65 years experienced the opposite trend. The change of immunisation coverage of HepA vaccine is the most plausible interpretation for what we found. Since 2010, the coverage rate of HepA vaccine has been beyond 97% in China.[29] The EHAP programme ensures high HepA vaccine coverage, regardless of regional socioeconomic development, thus, the regional differences are relatively small.[30] The faster decline in HepA incidence over time for the age groups of 5–14, and 15–24 years indicated a clear indirect protective effect, which has also been observed in other studies.[31]

The decreasing trend for the age groups of 25–64, and ≥65 years flattened over time, possibly due to a lower natural infection rate in the older age groups which led to an accumulation of susceptible individuals. Additionally, the older age groups did not receive free vaccination at birth and may be less willing to receive the subsequent self-paid vaccination. As a result, the peak incidence of HepA shifted towards the older age groups, causing a slower decline in HepA incidence over time.

Overall, EHAP can significantly reduce the HepA incidence in children. Moreover, vaccinating children with the HepA vaccine had a direct or indirect impact on the incidence of HepA across all age groups. In the future, it is essential to continuously increase the vaccine coverage among eligible children. However, it is most crucial to reconsider the high-risk groups for HepA and to focus on unvaccinated adults, particularly those over the age of 65. This age group maintained a relatively higher incidence rate compared with other groups, and targeting on these ones could further reduce the incidence of HepA in the general population.

The effectiveness of EHAP in Shanxi province

When analysing various provinces nationwide, we found that Shanxi Province, after EHAP, experienced a short-term decrease in the incidence of HepA infection. However, in the long term, the HepA incidence in this province shifted from a declining trend to a slight increasing trend, after EHAP. The reason may be that HepA vaccine was low at 18 months when children were mostly susceptible to HepA infection due to HepA circulation in the communities of Shanxi Province,[32] failure to vaccinate or vaccine failure. Otherwise, the effectiveness of EHAP may not be fully realised due to vaccine hesitancy.[33] In Shanxi Province, despite the availability of vaccination services, delays in vaccine uptake or vaccine refusal, influenced by factors such as complacency, convenience and confidence, contributed to low vaccination rates. Additional analysis is needed on the influencing factors of the incidence of HepA in this province. This will enable the implementation of appropriate intervention measures tailored to this province after adjustments, to better control the incidence of HepA. Our finding further demonstrated that while the programme was beneficial overall, active and passive surveillance, as well as timely evaluation, were crucial for different provinces.

Strengths and limitations

Our study has three strengths. First, for the first time, this study comprehensively evaluated the trends of HepA incidence over time, and more importantly, the impact of incorporating HepA vaccine into the expanded programme on immunisation in the country which covers more than 20% of the world's population. Furthermore, with the ITS approach, we controlled for pre-existing time trends and provided more robust estimation results by comparing the short-term and long-term changes in outcome indicators before and after policy implementation. This study provides more accurate evidence for the amendment of HepA prevention and control programmes in China. Finally, this study is based on the high-quality data of different economic regions and age groups in China and could provide insights for more countries to formulate HepA vaccine immunisation plans in the future.

However, there are some limitations in our study. First, as an ecological and observational study, this research could not clarify the causal relationship between the expanded vaccination programme and the temporal trend of HepA incidence. Second, the reported incidence of HepA used in our study is inevitably subject to under-reporting and misreporting, although it is a notifiable disease in China and subject to mandatory reporting. Finally, the incidence of HepA may be affected by other factors such as land use/land cover changes, detection differences, improvements in health conditions, the mobility and migration, and so on, which were not included in this descriptive study.

CONCLUSION

The incidence of HepA changed from high levels to very low levels in China after introduction of HepA vaccine into EHAP. EHAP showed better effectiveness in provinces which are mostly located in the central and western regions, as well as among the age group of 0–24 years. More attention should be paid to EHAP performance in the provinces located in the eastern region and age groups of ≥25 years, and the adjustment of vaccination strategies should be considered.

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Contributors YH: conceptualisation; YWu: conceptualisation, data curation, formal analysis, methodology, software, validation, visualisation, writing—original draft, writing—review and editing; PW: resources, writing—review and editing; JC: writing—review and editing; YC: writing—review and editing; JL: writing—review and editing; YWang: formal analysis, writing—review and editing; YHao: conceptualisation, investigation, supervision, writing—review and editing; WZ: conceptualisation, investigation, supervision, writing—review and editing; ZD: conceptualisation, funding acquisition, investigation, supervision, writing—review and editing. ZD is responsible for the overall content of the manuscript as guarantor. All authors approved the final version for submission and agreed to be accountable for all aspects of the work.

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Competing interests 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.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval Analyses were conducted at aggregate level and no confidential information was involved. The research study protocol was approved by the Institutional Review Board of the School of Public Health, Sun Yat-sen University (approval number: 2023-076). All analyses were performed in accordance with the principles of the Declaration of Helsinki.

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Data availability statement Data are available in a public, open access repository. The authors do not have permission to share data. The monthly reported incidence data of HepA are publicly available at https://www.phsciencedata.cn/Share/en/index.jsp. The annual population data by age groups are publicly available at https://ourworldindata.org/age-structure. The annual population data by provinces are publicly available at http://www.stats.gov.cn/sj/ndsj/2022/indexch.htm. The monthly temperature and precipitation data are publicly available at https://cds.climate.copernicus.eu.

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