

Recommended Public Health Strategies for Hepatitis B in China

by

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Abstract

Hepatitis B virus attacks the liver, which is also one of the most serious liver infections worldwide. Currently for chronic hepatitis B patients, only functional cure can be achieved when the viral load is low if the patient has good adherence with antiviral treatment. Several effective interventions in hepatitis B prevention include the three-dose hepatitis B vaccine that is given at infancy and pregnancy screening. In China, the overall percentage of hepatitis B carriers has been reduced significantly with the successful universal vaccination program. However, due to the large population, the absolute number of chronic hepatitis B carriers in China is still large and this is of great concern. The World Health Organization proposed a goal to eliminate hepatitis B in 2030, including reducing new infections by 90% and mortality by 65%. There are some remaining gaps in hepatitis B care because of the age distribution of hepatitis B carriers, the association between low-income regions and high hepatitis incidence, the discrimination and stigma against hepatitis B carriers, and lagging standards in diagnosis and initiation of hepatitis B treatment. To help China achieve the WHO goal of elimination of hepatitis B by 2030, this essay will propose two major improvements from a public health standpoint that could be done to improve the hepatitis B screening, prevention, and treatment programs, strategies, as well as policies, increasing awareness about hepatitis B among all people in China will lead more hepatitis B carriers to undergo screening for hepatitis B and start the antiviral treatment sooner. Furthermore, the discrimination and stigma against hepatitis B carriers will be reduced.

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Preface

In 1999, my mother, Dr. Xiaoling Wu, began her master's program in medicine and started doing research study in liver diseases. I grew up in a family with a medical background and I developed interest in learning more about medicine. In 2002, Dr. Wu completed her master's program. 20 years later, I am completing my master's program as well. For many years, Dr. Wu has been an awesome GI doctor that has done her best to help her patients. Before I began the master's program in infectious disease and microbiology, I have always been enthusiastic about helping the people in my home country, China. With the large population, it is more difficult to solve most health-related problems. Dr. Wu encouraged me to study more about infectious GI diseases that she has studied for years. She also taught me that public health and medicine work together in improving the overall health of the population.

I would like to express my great appreciation to Dr. Toan Ha from the School of Public Health at the University of Pittsburgh for his support during the school program. I would also like to express my great appreciation to Dr. Graham Snyder for his help and support both with infection prevention practicum and suggestions for this essay. Their knowledge and experiences in academic field helped me improved the contents, the logic, and the structure of the essay.

Eliminating hepatitis B might sound too optimistic, but it is possible to achieve with the efforts of public health prevention and intervention in combination of clinical treatment.

1.0 Introduction

1.1 Introduction of Hepatitis B

Hepatitis B virus (HBV) is an infectious virus that attacks the liver. The hepatitis B virus was discovered in 1965 by Dr. Baruch Blumberg. Hepatitis B virus can cause both acute and chronic disease (CDC, 2021). However, not all people with acute HBV infection have symptoms. The presence of signs and symptoms varies by age. Most children <5 years of age and newly infected immunosuppressed adults are generally asymptomatic, whereas 30%–50% of people age ≥ 5 years have signs and symptoms, which include fever, fatigue, abdominal discomfort, nausea, vomiting, loss of appetite, or jaundice. Acute infection ranges from asymptomatic or mild disease to fulminant hepatitis, although the latter occurs only rarely. Acute hepatitis B infection is more severe among adults age >60 years. (CDC, 2021) Chronic hepatitis B is more concerning because people at early stage of hepatitis B are often not aware of the symptoms. The risk for chronic infection varies according to the age at infection and is greatest among young children. Approximately 90% of infants and 25% to 50% of children aged 1 to 5 years will remain chronically infected with HBV. On the other hand, approximately 95% of adults recover completely from HBV infection and do not become chronically infected. (CDC, 2021) When severe symptoms, such as jaundice or ascites, are present, the patients are often in the late phase of chronic hepatitis B infection. In the late stage of chronic hepatitis B infection, some of the patients may require liver transplant. For people with chronic hepatitis B infection, the risk of developing liver failure, liver cancer, or liver cirrhosis significantly increased. Patients with

hepatitis B cannot be cured. However, with the latent infection, current treatment combined with supportive care can help the patients achieve functional cure. (Mayo Clinic)

In endemic regions, most chronic hepatitis B infections are transmitted from mother to child. (CDC, 2021) Other ways of transmission include exposure to infected blood or other bodily fluids in situations such as using contaminated needles during tattooing or piercing, as well as unprotected sexual intercourse with hepatitis B carriers. The horizontal infections of hepatitis B usually cause acute infections. While the vertical transmission of hepatitis B from mother to child generally causes chronic infections, which lead to about 95% of chronic infection cases. (WHO)

Four years after discovering the hepatitis B virus, Drs. Blumberg developed the first hepatitis B vaccine together with microbiologist Dr. Irvin Millman. The original hepatitis B vaccine was a heat-treated form of the virus. In 1981, the first commercial hepatitis B vaccine was approved by the U.S. FDA and in use until the current recombinant hepatitis B vaccine was developed in 1986. (History of Hepatitis B, 2022) It is recommended by the WHO that all infants should receive the hepatitis B vaccine within 24 hours after birth. For people at higher risk of hepatitis B infection and have not had the complete 3 doses of hepatitis B vaccine, it is recommended for them to receive the hepatitis B vaccine as well in order to reduce the risk of infection. (WHO, 2022)

1.2 Epidemiology of Hepatitis B

The World Health Organization (WHO) estimates that 296 million people were living with chronic hepatitis B virus infections in 2019, with 1.5 million new infections each year. In 2019, hepatitis B infections resulted in an estimated 820,000 deaths, mostly from cirrhosis and

hepatocellular carcinoma (primary liver cancer) (WHO, 2019). Hepatitis B causes both economic and health burdens worldwide, especially in developing countries where health resources are less accessible.

1.3 Interventions for HBV Prevention

1.3.1 Neonatal Vaccination

Vertical transmission of HBV is defined as transmission occurring during pregnancy and in the perinatal period from the HBV-infected mother to the fetus or to the child, resulting in positivity at 6-12 months of life of the hepatitis B surface antigen (HBsAg) or HBV DNA in infants. (Veronese, 2021) The three-dose series of hepatitis B vaccine given at birth and during infancy have been proved to provide more than 90% protection to people who get the vaccine. (OIDP, 2022) Furthermore, for people that have not been vaccinated during infancy, receiving the three-dose hepatitis B vaccine is also effective in preventing the infection, especially for people in high-risk groups, such as sex workers, intravenous drug users, and men who have sex with men.

1.3.2 Prenatal Maternal Screening

Neonatal vaccination is important in preventing the vertical transmission of hepatitis B from mother to child. The prenatal maternal screening that occurs during a woman's pregnancy is also important. With the screening, the HBV viral load of the pregnant woman can be assessed, and antiviral treatment can be initiated as needed. If the viral load is lowered to a safer range with

the help of antiviral treatment, the possibility of an infant receiving full coverage from the hepatitis B vaccine will increase.

1.3.3 Screening in Specific Populations

In China, all patients that will receive a gastrointestinal medical procedure and people that will onboard food-related jobs are required to have screening for hepatitis B. According to the current recommendations, students attending schools and people onboarding all other employments are not recommended to have hepatitis B screening to prevent discrimination. Screening in some populations is necessary, such as people that use intravenous drugs, homeless people, migrant workers that are from a region with higher hepatitis B incidence, sex workers, and men who have sex with men, because they are at an elevated risk of having hepatitis B infections or transmission of HBV.

1.3.4 Interventions in Healthcare Settings

Screenings for patients that will be admitted to inpatient units, especially the patients that will receive gastrointestinal medical procedures will be helpful in preventing the spread of HBV between other patients and to healthcare workers. Furthermore, annual screening for healthcare workers will help prevent the spread of infectious pathogens including HBV to the patient population as well. When taking care of patients diagnosed with infectious diseases, it is important to educate the healthcare workers and families of the patients about the hand hygiene, personal protective equipment (PPE), and vaccination.

1.4 HBV Policies and Programs in China

1.4.1 Epidemiology of HIV in China

In China, there are 87 million chronic hepatitis B carriers, accounting about one-third of all chronic hepatitis B carriers worldwide. Based on information from the WHO website, less than 25% of chronic hepatitis B and C carriers are diagnosed in China. However, only 10% of people who need hepatitis B treatment in China are currently receiving it. (WHO, 2022.)

1.4.2 Universal Vaccination Program

In 1985, China's immunization strategy was implemented including the hepatitis B vaccine. In 1992, the hepatitis B vaccine was replaced with a recombinant vaccine which could provide long-term protection against hepatitis B with three doses given at birth and during infancy. However, parents needed to pay the cost for hepatitis B vaccine out-of-pocket. In 2002, the Chinese government started the Expanded Program on Immunization, which includes hepatitis B vaccine. All newborns and children up to 14 years old could receive the hepatitis B vaccine at no cost. (Cui, 2017) Because of this, the prevalence of hepatitis B surface antigen has been significantly reduced from 9.8% in 1992 to 7.2% in 2006, with about 130 million population growth. (Bian, 2013) Furthermore, the reported coverage of three doses of hepatitis B vaccine for infants has increased from 30% in 1992 to 99.6% in 2015. (Liu, 2018)

1.4.3 Pregnancy Screening

In 2011, the National Health Committee in China launched a program to prevent mother-to-child transmission (PMTCT) of multiple infectious diseases including human immunodeficiency virus (HIV), syphilis, and hepatitis B virus (HBV). (Cui, 2017) The HBV serologic marker, hepatitis B surface antigen (HBsAg), was used as part of the screening. If the HBsAg test was positive, the pregnant woman was considered to have maternal HBV infection and the whole set of HBV serologic marker would be tested again to assess the status of HBV infection. (Hou, 2019) The pregnant care for HBV positive women would be performed together with an obstetrician for the well-being of the fetuses and by a hepatologist/gastroenterologist for the status of HBV infection during pregnancy. Follow-up care and evaluation for the mother and the child would be required as well. (Hou, 2019) The PMTCT program was expanded nationwide in 2015 with 1.4 billion Chinese Yuan (CNY) invested by the Chinese government each year to provide free screening. (Liu, 2018)

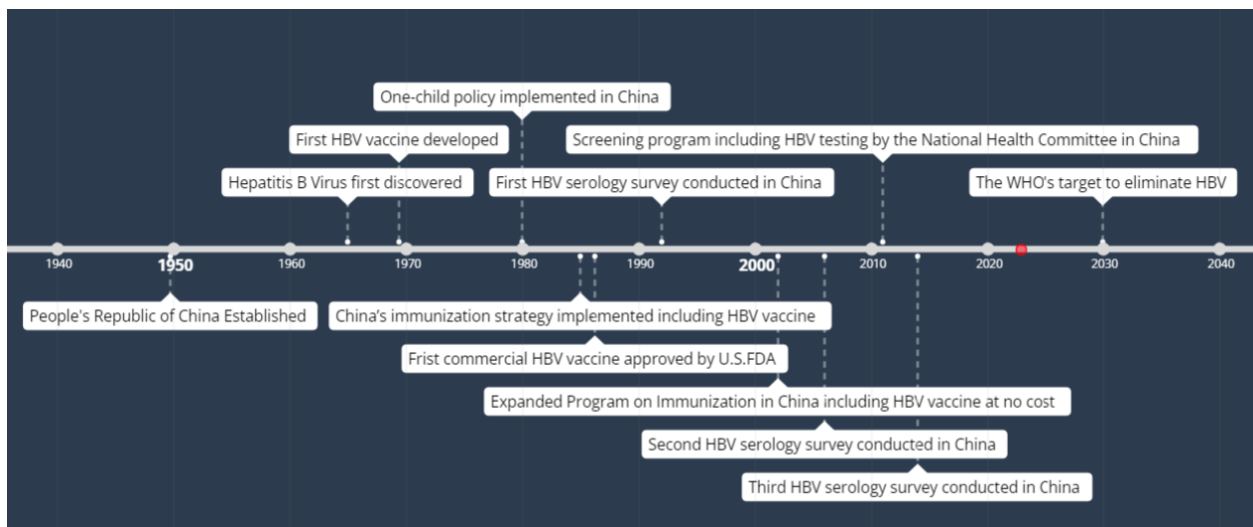


Figure 1. Timeline of Hepatitis B Policies and Programs in China

1.5 Remaining Gaps in Care

Before entering colleges or universities, the Chinese students have limited classes taught at school that address the importance of infectious diseases. There is also limited information about comprehensive sexual education at schools. Once a Chinese student enters college, the course requirements vary by majors and courses about infectious diseases are also limited if the student does not study medicine-related majors. Thus, many people in China have insufficient background knowledge in the modes of transmission, the symptoms, the effective prevention methods, and the treatment for hepatitis B.

In China, chronic hepatitis B is the leading cause of liver cirrhosis, hepatocellular carcinoma (HCC), and liver transplants. Patients with chronic hepatitis B are generally from low-income regions, where education about hepatitis B prevention and the importance of receiving hepatitis B vaccine is also insufficient. The screening for hepatitis B virus is also insufficient in the low-income regions in China. Thus, the diagnoses of the chronic hepatitis B carriers are often delayed. Furthermore, patients with late chronic hepatitis B infection often cannot afford antiviral treatment or liver transplants. People at elevated risk for hepatitis B virus infections are stuck in this “dead loop”.

Due to the one-child policy implemented in 1980, people that were born between 1980 and 2002 might have higher risk of developing chronic hepatitis B because they did not have access to free HBV vaccine at their birth. They also face heavier financial burden from the family because they needed to take care of the parents without support from siblings, and have higher risk of transmitting HBV to their children if they do not have HBV screening. The Chinese government has made efforts to lower the cost of hepatitis B antiviral treatment. However, the information is

not well-known and many residents from low-income regions still consider hepatitis B infection not affordable.

1.6 Public Health Significance

The liver is the largest solid organ in the human body, and functions to maintain healthy blood. (The Liver and its Function, n.d.) Due to the latent infection of chronic hepatitis B virus, the hepatitis B pandemic is also called a silent pandemic. Among all viral hepatitis deaths globally, 48% were due to hepatitis B infections and 47% were due to hepatitis C. (Bhadoria, 2022) With the largest number of hepatitis B carriers in the world, China should put more effort in providing care to chronic hepatitis B carriers before they develop hepatitis, liver cancer, or liver cirrhosis.

From a public health standpoint, it is important to increase awareness of hepatitis in the general populations by educating people about the risk, modes of transmission, symptoms, and life-threatening conditions of hepatitis B. In this way, more people would be willing to undergo hepatitis B screening and the chronic hepatitis B carriers could start antiviral treatment as soon as possible. Furthermore, with increased screening of hepatitis B, more HBV carriers will be notified about their status and hopefully start the antiviral treatment sooner to suppress the hepatitis B viral load to a safer level that will not cause disease progression.

2.0 Objectives

The primary aims of this paper are to 1). Review current hepatitis B, policies, strategies and programs in China; 2). Examine the barriers and challenges to improve hepatitis B prevention and treatment programs in China 3) Propose recommended strategies and policies to improve hepatitis B prevention and treatment programs as well as priority actions for eliminating hepatitis B in China.

3.0 Method

Articles published within the last 10 years were reviewed and selected for this article. The terms used for searching were “Hepatitis B”, “China”, and “epidemiology”. There were 2,042 articles with search terms published since 2012. Search terms “Hepatitis B” and “guidelines” were used to collect the latest prevention and treatment guidelines from the American Association for the Study of Liver Diseases (AASLD), the European Association for the Study of the Liver (EASL), Korean Association for the Study of the Liver (KASL), Asian Pacific association for the study of liver (APASL), the World Health Organization (WHO), and the Chinese Society of Hepatology from the Chinese Society of Infectious Diseases and Chinese Medical Association (CMA). The latest guidelines for the prevention and treatment of chronic hepatitis B of AASLD, EASL, and CSH were published in 2018, 2017, and 2019, accordingly. For the guidelines for prevention and treatment for chronic hepatitis B (2019 version) published by the CSH, the original guidelines were published in Chinese. The essential information discussed in this article was translated by the author.

4.0 Results

4.1 Age Distribution of HBV Carriers

The Chinese population grew significantly and approached the one-billion mark by the end of late 1970s. Due to the large population growth, the Chinese government implemented the “one-child policy” in 1980 to slow down the rapid population growth. The one-child policy was officially ended in the mid-2010s. For people that were born during the “one-child policy” and before the free hepatitis B vaccination program in 2002, they have a higher risk of having chronic hepatitis B infections while being the only child in the family.

Based on Figure 2, in 2018, the age groups with the highest hepatitis B surface antigen (HBsAg) prevalence were the 20s to 40s and people over 60 years old. From the ancient Chinese history, people have been taught that “of all virtues, filial piety is the most important”. Because of this, Chinese adults normally take care of their parents if their parents have no financial income after retirement. The age distribution of HBsAg is concerning that people aged 20 to 40 are considered the main support of the entire family. As the only child of the family, people aged 20 to 40 do not have support from siblings when they need to take care of their parents and children. If hepatitis B virus levels continue to increase in people of these age groups and symptoms of late infections develop, they may need to quit job to receive antiviral treatment, or even receive the more expensive liver transplant surgery if liver cancer develops. It will be a huge burden to the family both financially and mentally. If the problem continues, the financial burden will rise to a societal level, impacting the development of the country eventually.

Another issue that is associated with the age distribution of hepatitis B carriers in China is that women at ages 20 to 40 are likely to have their children. Even with the mandatory screening introduced by PMTCT, many women do not know that they should continue to be on treatment during pregnancy. If the HBV level is too high, the newborn is likely to not have successful protection from the hepatitis B vaccine after birth. Then, those children will become chronic hepatitis B carriers as well.

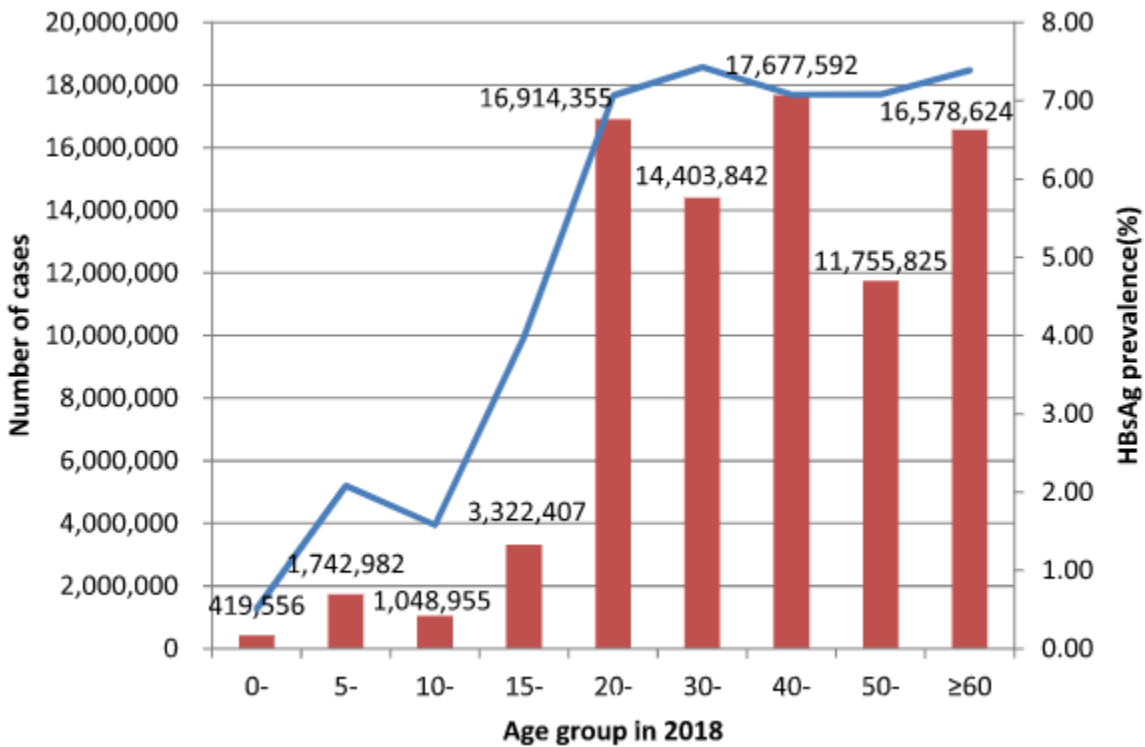


Figure 2. Estimated Hepatitis B Surface Antigen (Hbsag) Prevalence and Extrapolation of The Number of People Living With HBV in The General Population of China According to Age in 2018 (Wang, 2019)

4.2 Relation Between Economic Status and Number of HBV Carriers

Currently, the most effective treatment against chronic hepatitis B infection is antiviral treatment. However, the hepatitis B virus cannot be eliminated from the patient completely and antiviral treatment is typically a lifelong commitment. Several oral antiviral medicines including entecavir, tenofovir, lamivudine, adefovir, and telbivudine have replaced less effective injectable interferon therapy and can suppress viral replication and slow the ability to damage the liver. (Mayo clinic, 2022) If drug-resistance occurs, it is recommended to switch to another antiviral medicine, to combine two of these medications or to take one of the antiviral medicines with interferon to improve treatment response. (Mayo clinic, 2022) In 2016, 51.2%, 18.8%, 16.1%, 12.5%, and 1.4% patients receiving nucleoside analogues therapy were taking entecavir, lamivudine, adefovir, telbivudine, and tenofovir. (Liu, 2018) Higher compliance rate will increase the higher successfulness of suppressing the virus below upper limits of normal (ULN). However, compliance is influenced by treatment affordability as well. From 2009 to 2014, the Chinese government expanded the healthcare insurance coverage to reach 1.3 billion people and established a national essential medicines system. In 2017, tenofovir from the antiviral medicines was added to the system and the average daily cost for tenofovir reduced significantly from ¥49.0 (~\$6.84) to ¥16.6 (~\$2.32, calculated based on 1CNY=0.14USD). (Liu, 2018) Currently, all of the antiviral medicines recommended by the Chinese treatment guidelines are included in the national basic medical insurance reimbursement list that the patients pay partial out-of-pocket expenses. The insurance coverage of antiviral medicines contributed to the improvement in treatment coverage and affordability. (Liu, 2018)

However, even with the advanced coverage of antiviral medicines, the income level varies greatly between the eastern and the western regions/provinces in China. Since the eastern region in China is coastal, there are more opportunities for eastern regions to have foreign trade with other countries. Also, the eastern region has plain geographical distribution that is ideal for transportation such as trains and buses. These two factors made the eastern region have more job opportunities and higher income level. The economic level also reflects the accessibility and value of healthcare provided in the region/province. Figure 3 shows that the eastern regions, especially the coastal provinces, represented the highest income regions in China in 2010, while the western regions had much lower income levels (Li, G 2016).

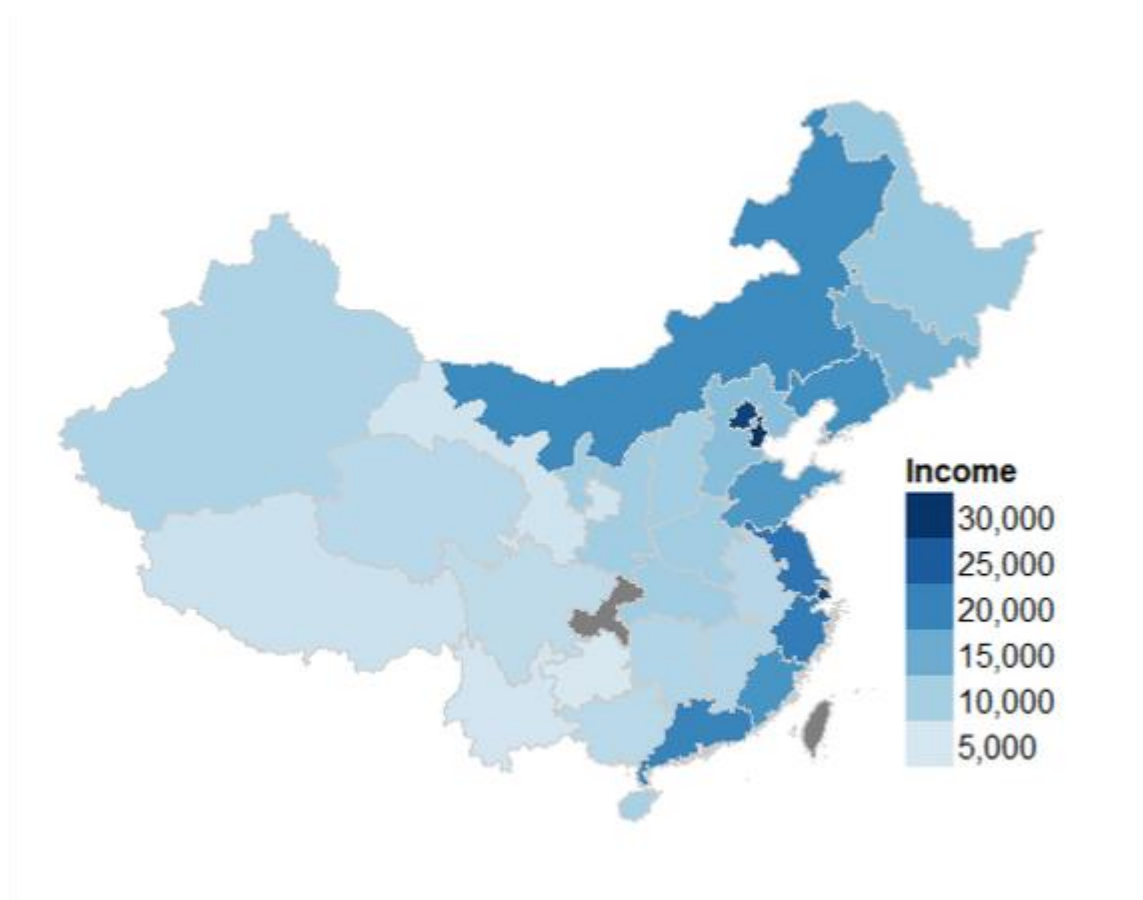


Figure 3. The Regional Distribution of Income in China (Real GDP Per Capita in 2010) (Li, G., 2016)

From Figure 4, the distribution of hepatitis B incidence in China showed great disparities between the northwestern regions and the eastern regions. Even with relatively smaller population in every province in the northwestern region, the mean reported incidence of hepatitis B is greater than 125 per 100,000 in those provinces.

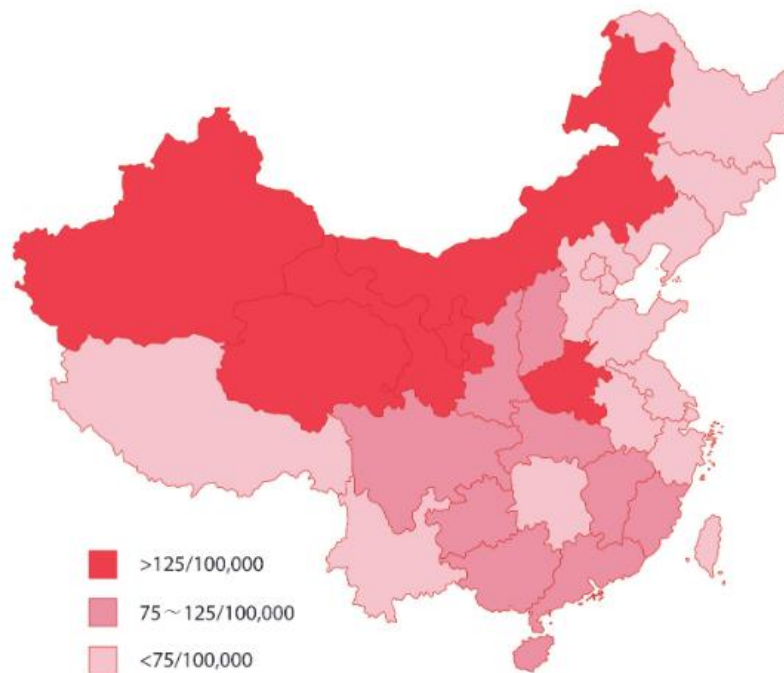


Figure 4. Distribution of Mean Reported Incidence of Hepatitis B in 31 Provinces of China Between 2005 and 2010 (Yan, 2014)

A study conducted in 2022 by Wang used data of pregnant women from the PMTCT program from 2013 to 2020. Calculation of concentration index was used to create the Lorenz curve that showed the relationship between economic status, represented by the cumulative percentage of population ranked by GDP per capita, and HBV infection, represented by cumulative percentage of HBV infection. As shown in Figure 5, the curve was above the equity line, with a negative value of the concentration index of -0.027. This indicated that there was economic-related

health disparities in the distribution of HBV infection. The study also found out that the trends of concentration index on HBsAg prevalence has declined from 2013 to 2020, indicating the economic-related inequalities have been narrowing. (Wang, 2022)

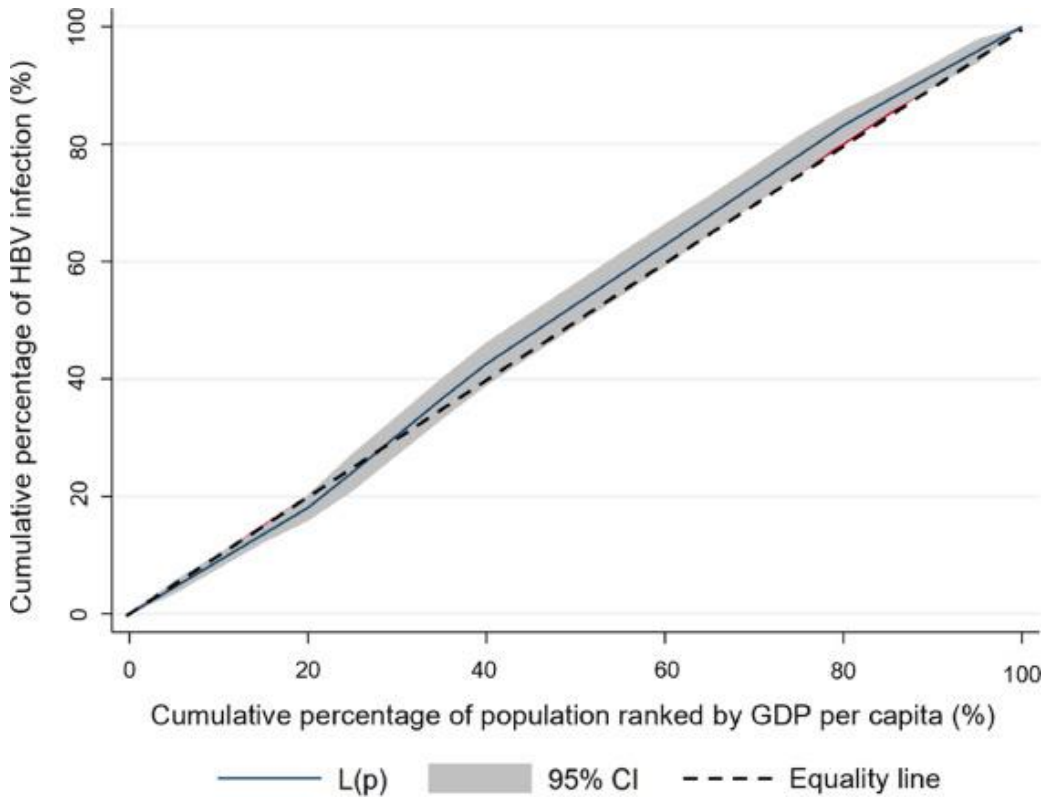


Figure 5. Lorenz Curve of HBV Infection (Wang, 2022)

4.3 Discrimination and Stigma Against HBV Carriers

Discrimination and stigma issues have been associated with all types of infectious diseases. For blood borne infectious diseases such as human immunodeficiency virus (HIV) and hepatitis B, the discrimination and stigma are even worse. In terms of public health, it is difficult to address the importance in preventing the transmission of infectious diseases while not introduce stigma

and discrimination against patients or carriers. For HBV, the social stigma with negative preconceptions or stereotypes would be the assumption that a person living with HBV injects drugs or has unsafe sexual behaviors. (Smith-Palmer, et al. 2020) Structural stigma related to HBV has been reported in China as well. In 2007, the anti-discrimination legislation was introduced to prevent the denial or termination of employment with a positive HBV test. In 2010, testing for HBV prior to employment onboarding and entrance to school or university is banned. (Smith-Palmer, 2020) In fact, the major transmission route of HBV in China is the vertical transmission from mother-to-child, as well as in other Asian countries. The introduction of vaccination programs has helped decline the incidence of vertical transmission of HBV. (Smith-Palmer, 2020) However, previous discrimination has already existed for many years and reducing testing in the target population may seem not beneficial in reducing the pre-existed discrimination.

A recent study by J Li, et al. in 2021 analyzed the discrimination against people with hepatitis B virus in villages of different provinces in China. The questionnaire included questions about people's opinions and attitudes regarding people with hepatitis B:

- (1) "Are you willing to accept gifts from hepatitis B (HB) positive patients or carriers?"
- (2) "Are you willing to shake hands with or hug HB patients or carriers?"
- (3) "Are you willing to have dinner with HB patients or carriers?"
- (4) "Do you think parents should let their children play with HB-infected children?"
- (5) "Do you think parents should accept their child marrying a HB-infected person?"

The answers were recorded on a score basis including "Yes=0", "Depends on the situation=1", and "No=2". The discrimination scores against people with hepatitis B virus ranged between 0 to 10 points, with scores closer to 0 indicating a lower level of discrimination and scores closer to 10 points indicating a higher level of discrimination (J Li, 2021). Based on Figure 5, in

most villages selected for the study, the discrimination level against people with hepatitis B was high (7-10), because the pie charts were composed of large portions in red. This result suggests that the knowledge of hepatitis B in low-income regions, represented as villages in the study, is insufficient which caused high discrimination. What is more, higher levels of discrimination would become a barrier for people with hepatitis B to start treatment or look for care. Discrimination against hepatitis B will also prevent people from getting tested, which will lead to more potential hepatitis B virus carriers.

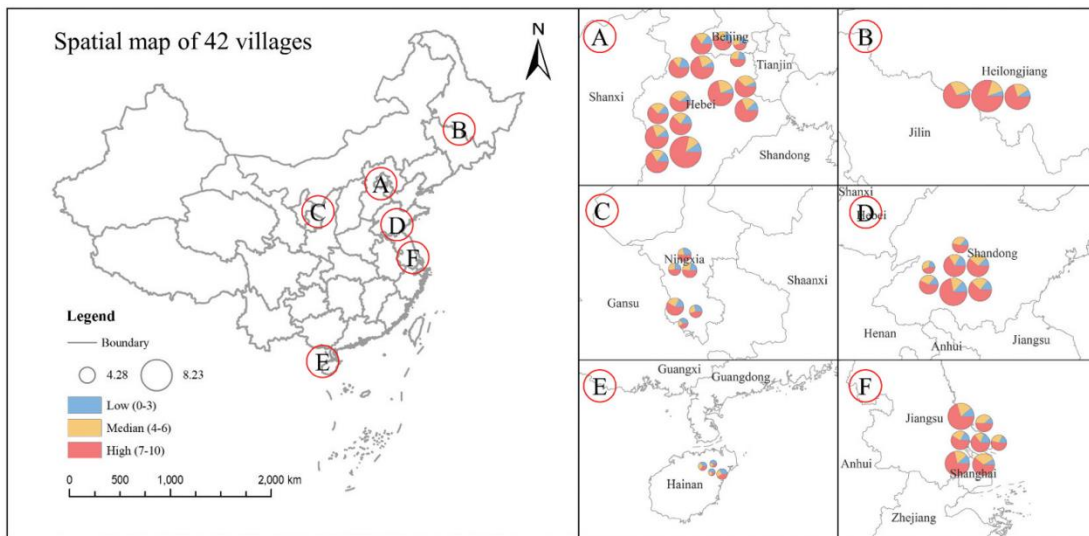


Figure 6. Spatial Distribution of Discrimination Across 42 Villages (Li, J., 2011)

There are several limitations of the study which included that the regions selected for the survey were mostly in the northeastern area of China. According to Figure 5, these regions had a lower prevalence of HBsAg compared to the western regions. In villages in the northwestern regions, the discrimination issue might be worse than the result from this study. The questions asked in the study also reflected the understanding of the mode of transmission of the hepatitis B virus. The results indicated that many rural populations lacked knowledge regarding hepatitis B.

4.4 Treatment Standard of Hepatitis B in China

The guidance statements on counseling of pregnant women, recommended HBV screening population, and the treatment indication from different guidelines published by various liver associations across the world were collected and organized into Table 1. The latest version of the guidelines of prevention and treatment for hepatitis B in China was published in 2019. Multiple changes have been made compared to the previous edition of guidelines published in 2014. Compared to the last version, the treatment standard for hepatitis B has been widened to make more hepatitis B virus carriers start treatment as soon as possible. In patients positive for hepatitis B virus without treatment, the ALT (alanine aminotransferase) level is a useful tool to determine the initiation of antiviral treatment. In the guidelines of prevention and treatment for hepatitis B 2019 version, it was not clearly indicated the ALT level to start hepatitis B treatment in China. From the expert opinion published by You H in 2022, the authors mentioned that generally males with ALT >50 U/L and females with ALT >40 U/L would be recommended to start antiviral treatment in China. However, compared to the guidelines published by the AASLD and the EASL, the general treatment standard in China in terms of the ALT levels is in the upper reference region (You H, 2022). In the guidelines published by AASLD in 2007 and 2016, the suggested ALT level as an indicator to start antiviral treatment was 30 U/L for males and 19 U/L for females. Multiple clinical studies in different countries have shown that increased ALT level is associated with a higher risk of HCC (You H, 2022).

Table 1. Comparison of HBV Recommendations Worldwide

	<i>Guidance Statements on Counseling of Women in Pregnancy</i>	<i>HBV screening population</i>	<i>Treatment indication</i>
<i>CMA, 2019</i>	not immune to or infected with HBV should receive vaccine series, recommended 0, 1, 2m fast sequence; HBV DNA >200,000IU/ml in the second trimester should consider treatment	Except the screening for school admission, job onboarding. All other clinical required screening.	ALT > ULN 50 for male, 40 for female
<i>WHO 2020</i>	All pregnant women should be tested for HIV, syphilis and HBsAg at least once and as early as possible. HBV DNA >200,000 IU/mL should be treated from 28w	All adults in $\geq 2\%$ HBsAg seroprevalence in the general population	ALT > ULN
<i>AASLD 2018</i>	Not immune to or infected with HBV should receive vaccine series. HBV DNA >200,000 IU/mL in the second trimester should consider treatment	All persons born in countries with HBsAg $\geq 2\%$; US-born not vaccinated whose parents were born in regions with HBV $\geq 8\%$	ALT > ULN, 35 for male, 25 for female
<i>EASL 2017</i>	HBV DNA levels >200,000 IU/ml antiviral prophylaxis with TDF should start at week 24–28 of gestation and continue for up to 12 weeks after delivery	all first-degree relatives and sexual partners of subjects with chronic HBV infection	ALT > ULN
<i>KASL 2022</i>			ALT > 2ULN, 34 for male, 30 for female
<i>APASL 2021</i>	HBV DNA $\geq 200,000$ IU/ml 24–28 to 28–32 weeks of gestation, from stopping at delivery to 12 weeks postpartum		ALT > ULN

5.0 Discussion

In the past two decades, successful progress has been made in China to prevent hepatitis B infections such as the Expanded Program on Immunization and the pregnancy screening for infectious diseases. Hepatitis B vaccine has been made available and provided at no cost nationwide across China. The new hepatitis B incidence has been significantly reduced by 90%. The hepatitis B vaccination rate for infants has reached 95%. (WHO, 2022) However, there are several remaining challenges and gaps in the prevention and intervention of hepatitis B in China. In terms of public health strategies, there are two main categories that China needs to focus in the future in order to achieve hepatitis B-free

5.1 Increase HBV Screening

An effective way to get more chronic hepatitis B carriers to start antiviral treatment is to increase HBV screening. There were three seroepidemiological survey for hepatitis B conducted in 1992, 2006, and 2014. Since the last national seroepidemiological survey conducted in 2014, the Chinese population increased by 49 million (China Population). The hepatitis B vaccination rate and HBsAg prevalence rate both need to be updated after 8 years. Considering the great disparities in distribution of HBsAg prevalence in China, the survey sampling can be separated into different sections depending on the region. Also, it is important to consider and to include both urban and rural populations in the survey. Furthermore, based on the result from Figure 2, the population of age 20 to 50 should be focused more in the seroepidemiological survey.

After having a positive HBsAg test, it is better to perform a follow-up polymerase chain reaction (PCR) test to test the HBV viral load of the chronic HBV carrier. Previously, there was an issue associated with the seroepidemiological survey. In many rural regions, there was no sufficient equipment and funding to perform HBV PCR tests. This indicates that even with a positive HBsAg test, many chronic HBV carriers have not started the treatment because they did not have a PCR test to assess the viral load.

According to the current HBV screening in China, all patients receiving medical procedures and having inpatient clinical stays must have HBV screening before the procedure or inpatient charge. Also, employees working in food-related industries such as restaurants and supermarkets, need to have HBV screening before job onboarding. However, it is not recommended for children entering kindergarten, schools (including elementary, middle, and high school), and college to receive HBV screening in order to “avoid discrimination against hepatitis B carriers in school”. A potential issue with this recommendation is that children born to a hepatitis B positive mother who does not know the hepatitis B virus level during pregnancy and after delivery may not know that they are at higher risk of being chronic hepatitis B carriers. Even though PMTCT is available nationwide, many women do not know that they should start treatment after they have a positive screening result. If the HBV level of the mother is too high at the time of delivery, the child might not have successful protection from the hepatitis B vaccine. Children born to hepatitis B carriers should be screened for hepatitis B level even if they have had the hepatitis B vaccine at birth and infancy.

In December 2019, the first case of SARS-CoV-2 in China was reported. Since 2019, the COVID-19 pandemic has been ongoing for three years. Because of the large population base and the high mortality of the COVID-19 infection, the China CDC has shifted most of the attention

from other infectious diseases to the prevention of COVID-19. On the China CDC official website, most articles, information, and news are related to COVID-19 and then HIV. The information regarding hepatitis B is limited and can only be found under sub-tabs. As more attention has been shifted from other infectious diseases to COVID-19, the vaccination rate, as well as screening tests for other infectious diseases significantly decreased since 2019. It has been a controversial topic that the Chinese government has spent a great effort in COVID-19 testing. Many Chinese citizens complain about the requirement of having a negative COVID-19 test every 48 hours in order to go to work or travel to other cities. However, these COVID-19 tests in China are PCR tests that are collected through pharyngeal swabs or nasal swab. If some of the PCR testing technologies and facilities can be used in hepatitis B testing, more HBV carriers, especially those in the rural areas as discussed previously, can be found out. Furthermore, hepatitis B virus infection, along with other hepatitis virus infections, is known as “the silent infections.” It is important to pay attention to chronic virus infections even during the COVID-19 pandemic in order to maintain the successful efforts made in the past.

5.2 Increase Education About Hepatitis B

For Chinese students that do not have a medical background, educational materials regarding hepatitis B, as well as other infectious diseases, are limited. The great stigma and discrimination against all infectious pathogen carriers, including HBV carriers, people living with HIV, etc. exist because people only consider infectious diseases serious and deadly. Many people do not know that there is antiviral treatment that can achieve functional cure for chronic hepatitis B carriers. With increased education provided to the general population, they will raise the

awareness to receive HBV screening, protect themselves from getting infected, reduce the stigma and discrimination against HBV carriers, and eventually make more HBV carriers start receiving antiviral treatment as soon as possible.

To increase the education about hepatitis B, public awareness raising and communication campaigns should be conducted across the country. In addition, activities like putting posters be put at community clinics, schools, and especially obstetrics and gynecology department should be conducted. Pregnant women should be provided with HBV information when they visit antenatal care so they will pay more attention to the hepatitis B level during pregnancy and after delivery. The Chinese government should implement new policies like those that have been done in the United States in which students entering colleges or universities are required to provide the immunization record to ensure that hepatitis B vaccine, as well as other necessary vaccines, are administered, especially if a student is from a rural region or was born before the hepatitis B vaccine was offered free for all in China.

From the clinical aspect, the guidelines of prevention and treatment of hepatitis B should be updated to keep up with the standard in AASLD and EASL. The earlier that a chronic hepatitis B patient is put on treatment, the greater possibility that the viral load of hepatitis B would be controlled without developing further symptoms or hepatocellular carcinoma. Furthermore, gastroenterologists should be trained to inform the patient about receiving hepatitis B vaccine if the patient is unvaccinated. They should also be trained to understand the importance of starting early treatment of patients with hepatitis B. They could also make the patients aware that the treatment of hepatitis B is currently accessible and affordable in China. Financial issues should not be a barrier to preventing patients from receiving care. Given that the chronic hepatitis B population is much larger compared to other countries and the antiviral treatment is available and

affordable in China, the guidelines of prevention and treatment for hepatitis B in China need to be updated again to match some treatment standards globally to get more chronic hepatitis B carriers on antiviral treatment as soon as possible. Furthermore, for gastroenterologists from non-urban cities or regions, it is important to educate them with the latest recommendations of treatment standard of hepatitis B, especially because they may not have the access to the updated information or newest research findings in hepatitis B both nationally and globally.

The latest guideline of prevention and treatment of hepatitis B was published in 2019. It is unlikely to have another updated one published in the next few years. More researches should be conducted to analyze a better ALT level as the indicator to start hepatitis B treatment. The standards in AASLD, EASL, and other liver study associations globally can be used as references. Findings from future studies can cooperate into new treatment guidelines. Also, the information about treatment guidelines should be made available to the gastroenterologists in rural areas so that they can notify their patients to start antiviral treatment according to the newest guidelines or direct their patients to other hospitals that have advanced treatment in other larger and urban cities.

In conclusion, the Chinese government has made a significantly successful impact on reducing new hepatitis B virus infections by adding the hepatitis B vaccine into the vaccination program, making the vaccine free to newborns and infants, and providing mandatory screening for prevention of mother-to-child transmission during pregnancy. Compared to the progress made since 1992, it seems like the government has slowed down or was satisfied enough with the results that no new progress was made in the recent years, especially with no new policies set or surveys conducted after the goal was set by WHO in 2016. With the enormous number of hepatitis B virus carriers and the potential hepatitis B patients in China, the goal of eliminating hepatitis B in 2030 is still yet far from being accomplished. In terms of infectious diseases, the treatment provided

from the clinical side and the prevention and control strategies published from the public health side should work together to improve the overall health of the population.

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