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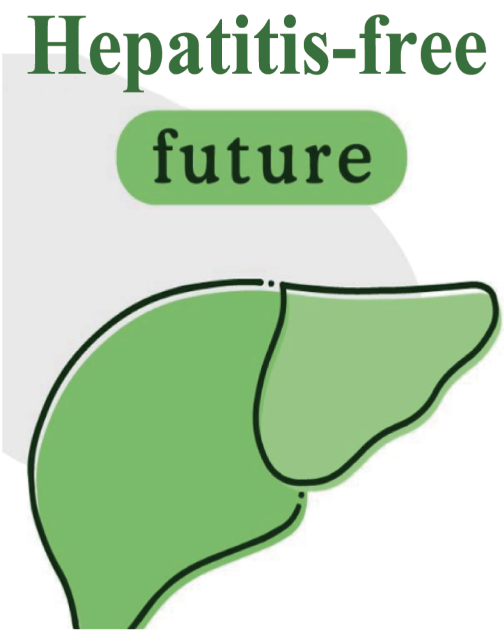

World Hepatitis Day 2020

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Announcements

The 10th World Hepatitis Day 2020 — July 28, 2020

Zundong Yin[1,#]

Viral hepatitis represents one of the most serious public health threats in the world today. World Hepatitis Day takes place on July 28 every year and is an opportunity to step up national and international efforts to control and prevent viral hepatitis and to encourage action and engagement by individuals, partners, and the general public. July 28 was chosen for the World Hepatitis Day because it is the birthday of Nobel-prize-winning scientist Dr. Baruch Blumberg, who discovered hepatitis B virus (HBV) and developed a diagnostic test and vaccine for it (*1*). The World Health Organization (WHO)'s theme for World Hepatitis Day 2020 is "Hepatitis-Free Future."

China has the heaviest burden of viral hepatitis in the world. In 1979, approximately 9% to 10% of people in China had chronic hepatitis B infection (*2*); in 1992, 3.2% of the population had hepatitis C (*3*); and in the pre-hepatitis-A-vaccine era, outbreaks of hepatitis A occurred frequently throughout the country. Hepatitis B and hepatitis A vaccines were integrated into China's National Immunization Program in 2002 and 2008, respectively, with prompt increases in coverage (*4–5*). Screening of pregnant women for hepatitis B surface antigen (HBsAg) — a marker of infection that is capable of transmitting hepatitis B virus during childbirth — was started at the end of 2010 (*6*). In addition to the dose of hepatitis B vaccine that all newborn infants in China receive at birth, babies born to HBsAg-positive mothers are also given hepatitis B immunoglobulin (HBIG) during their first day of life (*7*). Because hepatitis B virus (HBV) and hepatitis C virus (HCV) can be readily transmitted by blood, blood donors began to be screened for these 2 viruses in 1998 (*8*), and by 2015, universal HBV and HCV nucleic acid testing has been implemented by all blood banks (*9*). During 2006 to 2017, the National Plan for Hepatitis B Prevention and Control, 2006–2010 (*10*), and the Plan for the Prevention and Control of Viral Hepatitis in China, 2017–2020, have been continuously updated and re-issued (*11*).

Through these and other active efforts, chronic HBV infections among children under 5 years of age have decreased 97% from the pre-vaccine era prevalence to the current prevalence of 0.32% (*12*). Small-molecule, direct-acting hepatitis C antiviral agents were included in China's national medical insurance program last year (*13*). With properly-administered antivirals, hepatitis C can be cured more than 90% of the time (*14*). Prior to the introduction of universal hepatitis A vaccination, most people were infected as children, but the incidence of hepatitis A declined markedly following the introduction of the hepatitis A vaccine and improvements in sanitation and hygiene (*15*).

Although these achievements are impressive, there are major challenges remaining for prevention and control of viral hepatitis in China. There are many adults in China living with hepatitis B because they were infected during their birth or early childhood — before the widespread availability of hepatitis B vaccine. Since perinatal hepatitis B infection is usually asymptomatic and therefore difficult to detect, most infected babies and children become adults without realizing they are carriers of hepatitis B virus. Without antiviral treatment, many individuals with chronic hepatitis B and hepatitis C infection will go on to have liver cirrhosis and liver cancer. There are still areas with weak routine immunization programs, resulting in new hepatitis B infections and outbreaks of hepatitis A or hepatitis E.

Theme for the Hepatitis Day 2020 in China is "Active prevention, positive detection, standardized treatment, and comprehensive containment of the hazards of hepatitis" — the same theme as in 2018 and 2019. In the future, we must strengthen vaccination programs to completely stop hepatitis A and hepatitis B infections, and we need to determine the most effective way to use hepatitis E vaccines to prevent or stop outbreaks of hepatitis E. It is critically important to encourage and incentivize individuals with chronic hepatitis B and hepatitis C infection and those at high risk of infection to seek testing at medical institutions so they can receive treatment if infected.

For this special issue of *China CDC Weekly*, we invited experts from China CDC's National

Immunization Program and National Center for AIDS/STD Control and Prevention, Peking University's School of Public Health and Beijing Friendship Hospital to describe key viral hepatitis research and global strategic plans.

We hope that these articles will help readers understand more about viral hepatitis and its key challenges and will illuminate pathways forward to stronger prevention, control, and management of this enormous public health problem. Let us work together for a hepatitis-free future.

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Vital Surveillances

Acute Hepatitis B — China, 2005–2019

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ABSTRACT

Introduction: Hepatitis B is a major public health threat in China. Detailed subtyping of acute hepatitis B (AHB) has been reported to China's National Notifiable Disease Reporting System (NNDRS) since 2005. We divided the years since NNDRS reporting started into three stages: a "primary stage" (2005–2008), a "catch-up stage" (2009–2012), and an "AHB surveillance pilot stage" (2013–2019). We evaluated characteristics of AHB and progress towards AHB control in these three stages.

Methods: We obtained data on cases reported to NNDRS between January 1, 2005 and December 31, 2019 and compared the annual incidence of reported AHB in each of the three stages by region, age, and gender.

Results: The incidence of reported AHB declined from 7.52 per 100,000 in 2005 to 3.21 per 100,000 in 2019 — a decrease of 57.31%. The annual incidences of AHB in the primary stage, the catch-up stage, and the AHB surveillance pilot stage were 7.45 per 100,000, 5.78 per 100,000, and 4.26 per 100,000, respectively; 7 provincial-level administrative divisions (PLADs) had an annual incidence of more than 10 per 100,000 in the primary stage, 5 PLADs in the catch-up stage, and 1 in the AHB surveillance pilot stage. The group aged 20–29 years old had the highest annual rate of reported AHB in the primary stage (14.35 per 100,000) and in the catch-up stage (10.42 per 100,000), and the group aged 30–39 years old had the highest annual rate in the surveillance pilot stage (5.89 per 100,000). AHB affected males and females in all age groups.

Conclusions and Implications for Public Health Practice: The incidence of AHB had decreased significantly since the start of the NNDRS reporting in 2005, but additional action is needed to eliminate AHB in China. Hepatitis B vaccine (HepB) coverage in adults should be increased to reduce new AHB cases among people over 20 years old, epidemiological investigations of AHB cases should be conducted to identify risk factors for infection, and prevention of mother-to-child transmission needs to be strengthened.

INTRODUCTION

Hepatitis B is a major public health threat in China as China has over 30% of the hepatitis B surface antigen (HBsAg)-positive individuals in the world (*1*). In 2018, 12% of the global burden of liver cancer was among men in China (*2*). The combined incidence of acute and chronic hepatitis B increased from 75.57 per 100,000 in 2005 to 89.00 per 100,000 in 2007, and subsequently decreased to 68.74 per 100,000 in 2016 (*3*). However, the epidemiological characteristics of acute hepatitis B (AHB) are not clearly known, and the morbidity of AHB may reflect recent infections and impact of hepatitis B vaccination.

Hepatitis B cases have been reported to China's National Notifiable Disease Reporting System (NNDRS) since 1990, and detailed subtyping (acute and chronic) of cases has been available since 2005. The hepatitis B vaccine (HepB) was included into the Expanded Program on Immunization in 2002; a HepB catch-up campaign was conducted among children under 15 years of age during 2009–2011 to increase HepB coverage of adolescents; and an AHB surveillance pilot project was started in 2013 to improve the accuracy of AHB NNDRS reporting by standardizing diagnostic and reporting procedures and promoting IgM anti-HBc testing to help distinguish acute hepatitis B from flare-ups of chronic hepatitis B. For this study, we divide prevention and control of AHB into three stages: a "primary stage" (2005–2008), a "catch-up stage" (2009–2012), and an "AHB surveillance pilot stage" (2013–2019).

We obtained reported AHB case-based data from the NNDRS and analyzed the epidemiological characteristics of AHB and assessed progress towards AHB control in China.

METHODS

We obtained AHB case and incidence data reported to the NNDRS between January 1, 2005 and December 31, 2019. The NNDRS is a national, hospital-based, passive surveillance system that includes all county and township hospitals. In 2004, China revised NNDRS by establishing a web based, real-time, data sharing surveillance platform. Data included in this study were from the mainland of China.

We compared the reported annual incidences of AHB in the three stages by geographical region and age and gender of patients. AHB cases were divided into 9 age groups: <9 years, 10–19, 20–29, 30–39, 40–49, 50–59, 60–69, 70–79, and ≥80 years old. We analyzed characteristics and morbidity of AHB by stage, age, and gender using Microsoft Excel (version 2007); we determined the spatial distribution of AHB reports with ArcGIS (version 10.4; Esri Institute).

RESULTS

The reported incidence of AHB in China declined from 7.52 per 100,000 in 2005 to 3.21 per 100,000 in 2019 (Mean=5.52), a 57.31% decrease. The annual number of reported cases in the primary, catch-up, and AHB surveillance pilot stages were 97,755, 77,520, and 58,396, respectively, and the annual incidences of AHB in the three stages were 7.45, 5.78, and 4.26 per 100,000. The annual incidence in the AHB surveillance pilot stage was 42.82% and 26.30% less than in the primary and catch-up stages. (Figure 1)

In the primary stage, there were 7 provincial-level administrative divisions (PLADs) with annual incidences over 10 per 100,000: Guangxi Zhuang Autonomous Region (22.18 per 100,000), Hainan Province (16.22), Gansu Province (14.97), Ningxia Hui Autonomous Region (14.12), Fujian Province (12.15), Inner Mongolia Autonomous Region (10.77), and Guizhou Province (10.30). In the catch-up stage, there were 5 PLADs with annual incidences over 10 per 100,000: Guangxi (21.72), Fujian (19.13), Hainan (12.12), Shanxi Province (10.92), and Xinjiang Uyghur Autonomous Region (10.39). In the AHB surveillance pilot stage, 1 PLAD had an annual incidence over 10 per 100,000: Guangxi at 14.72 per 100,000. (Figure 2)

During the primary stage, the 3 age groups with the highest annual incidence of reported AHB were aged 20–29 years old (14.35 per 100,000), 30–39 years old (9.75), and 40–49 years old (7.49). During the catch-up stage, the 3 age groups with the highest annual incidences were aged 20–29 years old (10.42 per 100,000), 30–39 years old (7.87) and 40–49 years old (6.41). In the AHB surveillance pilot stage, the 3 age groups with the highest annual incidence were aged 30–39 years old (5.89 per 100,000), 20–29 years old (5.77), and 50–99 years old (5.26). (Figure 3)

Compared with the primary stage, the 2 age groups with the largest decreases in annual incidence in the catch-up stage were aged 10–19 years old (a 52.29% decrease) and 0–9 years old (a 48.58% decrease). Compared with the catch-up stage, the 2 age groups with the largest decreases were aged 10–19 years old (a 55.02% decrease) and 20–29 years old (a 44.67% decrease). (Figure 3)

AHB affected males and females in all age groups. In the primary stage, there were 67,657 reported annual AHB cases among males (10.06 per 100,000 population) and 30,095 reported annual cases among females (2.29 per 100,000). In the catch-up stage, there were 52,223 reported annual AHB cases among males (7.60 per 100,000) and 25,297 reported annual cases among females (1.89 per 100,000). In the AHB surveillance pilot stage, there were 37,598 reported annual AHB cases among males (5.36 per 100,000)

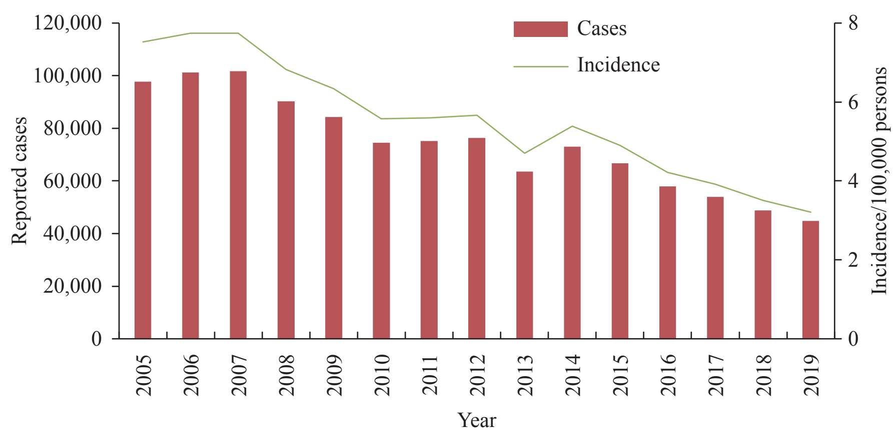

FIGURE 1. Reported cases and incidence of acute hepatitis B (AHB), in China, 2005–2019.

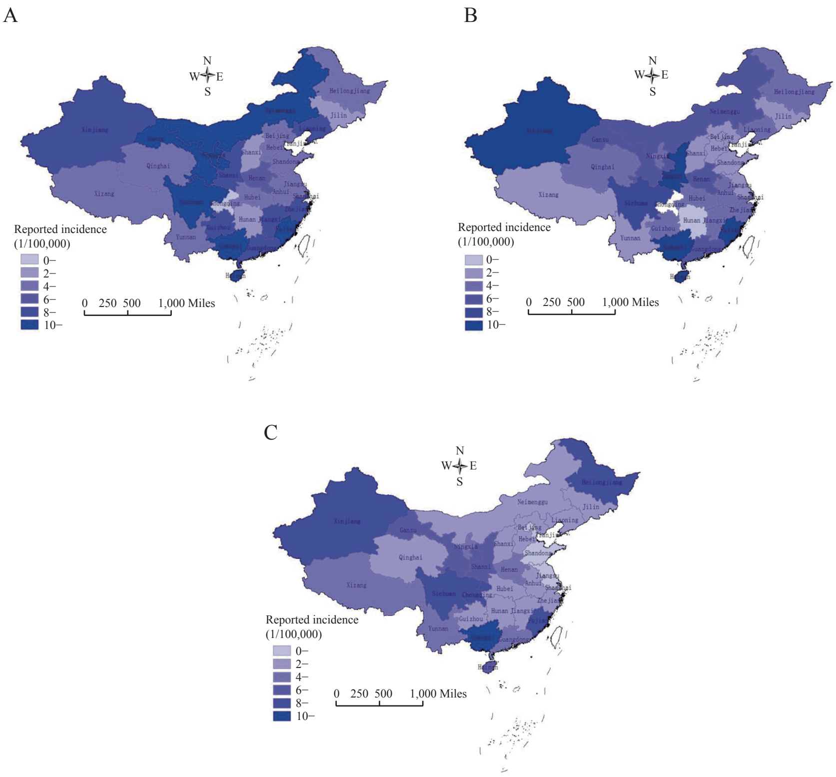

FIGURE 2. Geographical distribution of the reported acute hepatitis B (AHB) in China, 2005–2019. (A) Primary stage. (B) Catch-up stage. (C) Acute hepatitis B (AHB) surveillance pilot stage.

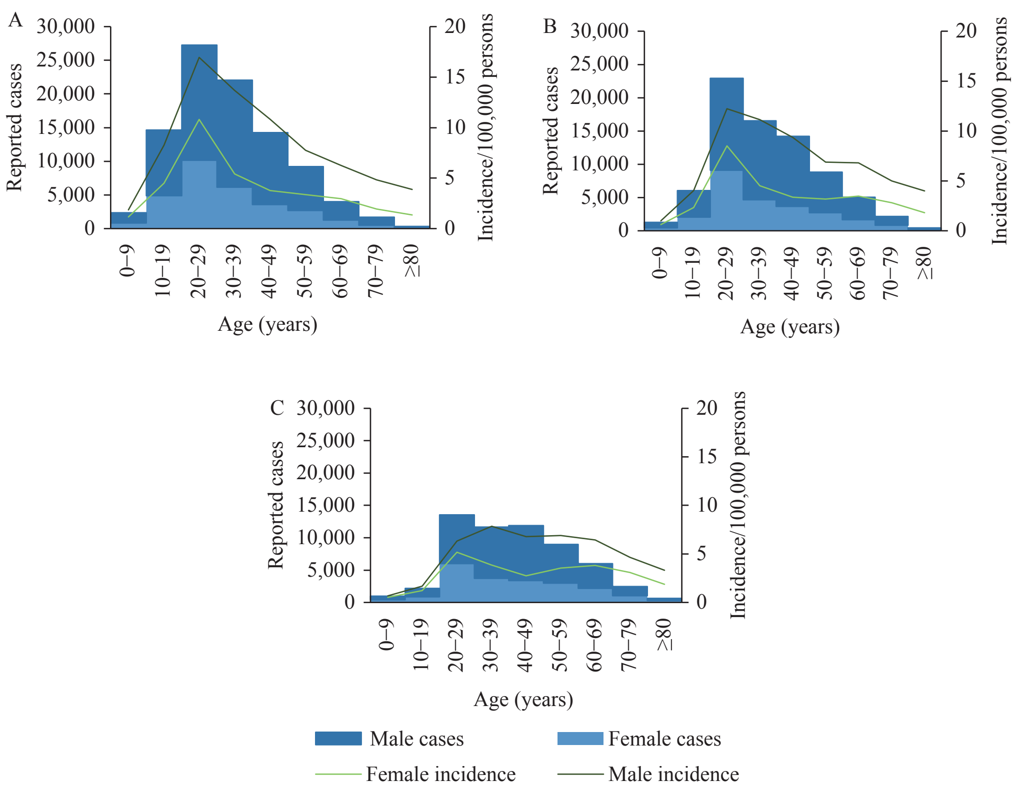

FIGURE 3. Age-specific and gender-specific cases and incidence of acute hepatitis B (AHB) in three stages in China, 2005–2019. (A) Primary stage. (B) Catch-up stage. (C) Acute hepatitis B (AHB) surveillance pilot stage.

and 20,797 reported annual cases among females (1.52 per 100,000). (Figure 3)

DISCUSSION

The World Health Organization (WHO)'s global health sector strategy on viral hepatitis (*4*) aimed to eliminate viral hepatitis as a major public health threat by 2030, specifically targeting reduction of the incidence of new hepatitis B infections. In China, coverage of HepB among newborns had consistently been over 95% since 2009 (*5*), and chronic hepatitis B caused by early childhood infections has been effectively controlled. China has continued to take measures to decrease the incidence of AHB. Our study showed that the annual reported incidences in the catch-up stage and AHB pilot stage were 20.69% and 40.26% lower than those in the primary stage.

In the catch-up stage (2009–2011), China conducted a HepB catch-up campaign for children <15 years of age who were born during 1994–2001. This campaign reached approximately 68 million children. As a result, the largest decrease in AHB was among those under 20 years of age during the catch-up stage — a decrease of 50.34% compared with the primary stage. In the AHB surveillance pilot stage, standardized diagnostic and reporting procedures for clinicians, based on national diagnostic criteria, were promoted to improve the accuracy of AHB reports from 200 sentinel counties. At the same time, AHB surveillance guidance encouraged hospitals to use IgM anti-HBc testing to help distinguish acute from chronic hepatitis B (*6*–*8*). These efforts led to a 26.30% decrease in AHB incidence compared with the catch-up stage.

Guangxi had the highest AHB incidence among all PLADs during all three stages, although incidence decreased over time. Several factors likely contributed to Guangxi's high incidence: first, sero-epidemiological studies conducted in 2006 (*9*) and 2014 (*10*) showed that the HBsAg prevalence in Guangxi was more than 8% higher than other PLADs; second, the HBsAg prevalence among women of childbearing age was approximately 10% in Guangxi, which may have led to infection of the spouses through sexual transmission without effective protection measures (*11*); and third, sexual transmission (*12*) and dental treatment in private clinics may also be contributing factors (*13*).

This study had strengths and limitations. A strength was that this study was the first to analyze the characteristics of AHB cases reported from all 31 PLADs of mainland China. Our study was limited by variation in laboratory capacity in reporting hospitals as not all hospitals conducted IgM anti-HBc testing. Diagnosis of AHB should be based on positive IgM anti-HBc and HBsAg tests along with symptoms related to hepatitis B. However, IgM anti-HBc was present in approximately 10%–15% (*14*–*16*) of patients with chronic hepatitis B — especially in CHB with an acute flare-up. Therefore, the reported AHB incidence was higher than the true incidence. Another limitation was that differences in the diagnostic ability of each PLAD for AHB affected the reported incidence in each PLAD.

In summary, the incidence of AHB cases decreased significantly since 2005. Although much progress has been made in AHB control, creative work remains to be done in China. First, HepB coverage should be increased among adults to reduce AHB among people over 20 years old. Second, epidemiological investigations of reported AHB cases need to be conducted to identify risk factors for infection and develop effective strategies for prevention. Finally, a post-vaccination serological testing (PVST) recommendation for HBV-exposed newborns is crucial for the prevention of vertical transmission of hepatitis B virus.

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Conflicts of interest: No conflicts of interest were reported.

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Preplanned Studies

Global Trends and Regional Differences in Hepatitis C Virus Infection Prevalence and Implications for Prevention — Worldwide, 1990–2017

Wenzhan Jing[1]; Jue Liu[1]; Min Liu[1,#]

Summary

What is already known on this topic?

The global prevalence of hepatitis C virus (HCV) infection in 2015 has been modeled to assess the disease burden in 21 Global Burden of Disease (GBD) regions. However, there is no study to clarify the global long-term trends and regional differences in HCV infection prevalence.

What is added by this report?

This report clarified the global temporal trends and regional differences in HCV infection prevalence. Global HCV infection age-standardized prevalence rate (ASR) gradually decreased from 1990 to 2017 except in Eastern Europe, and liver cancer due to hepatitis C ASR increased worldwide with drastic shifts in low-middle Socio-Demographic Index (SDI) regions in the last decade.

What are the implications for public health practice?

HCV is still prevalent worldwide despite the development of highly effective direct-acting antivirals (DAAs) and showed a reemergence concurrent with the opioid crisis. HCV infection prevention might involve at least 3 aspects: first, prohibiting HCV widespread transmission among general populations; second, increasing global DAAs coverage; and third, continuously investing in the development of the HCV vaccine.

Hepatitis C virus (HCV) infection is a major public health problem worldwide (*1*). It is necessary to clarify the global trends and regional differences in HCV infection prevalence to make tailored prevention strategies. The HCV infection burdens from 1990 to 2017 were collected from the Global Burden of Disease (GBD) Study 2017. Relative changes in HCV cases and estimated annual percentage changes (EAPCs) of age-standardized prevalence rate (ASR) with 95% confidence intervals (CIs) were used to quantify temporal trends of HCV infection. HCV infection ASR decreased by an average of 0.67% (95% CI: 0.64%–0.70%) per year from 2,043.42 per 100,000 in 1990 to 1,728.04 per 100,000 in 2017, while the number of HCV cases increased by 28.82% from 105.15 million in 1990 to 135.45 million in 2017. Against the global background of HCV infection prevalence decreasing, the ASR increased in Eastern Europe (EAPC=0.78, 95% CI: 0.56–0.99). Liver cancer due to hepatitis C increased drastically in the low-middle Socio-Demographic Index (SDI) regions in the last decade. There is no vaccine for hepatitis C, therefore, prevention should be focused on reducing exposure risk to HCV by safe injections, harm reduction, screening, and treatment.

About 55%–85% of infected persons develop chronic HCV infection without treatment, and 15%–30% of those with chronic infections develop complications within 20–30 years (*2*). Global incidence of HCV infection was 23.7 per 100,000 population in 2015 with 1.75 million new infections (*3*). About 71.1 million people were living with HCV, accounting for 1% of the population (*1*), and approximately 399,000 people died from cirrhosis and hepatocellular carcinoma (HCC) due to hepatitis C in 2016 (*2*). A watershed moment came in 2014 with the development of highly effective direct-acting antivirals (DAAs) for HCV infections (*4*). DAAs can not only cure those treated, thereby reducing death risk from cirrhosis and HCC, but also reduce HCV transmission and therefore its prevalence (*5*). Advances in HCV therapeutics prompted World Health Organization (WHO) member states to set targets for HCV elimination. However, only 20% of persons with hepatitis C know their diagnosis, and 15% of those with known hepatitis C have been treated (*1*). The global epidemic may continue to expand in magnitude in the absence of scaled-up interventions because new infections outnumbered the individuals dying from end-stage HCV infections and those who were cured.

The HCV infection burden, including acute hepatitis C, cirrhosis and other chronic liver diseases due to hepatitis C, and liver cancer due to hepatitis C from 1990 to 2017 by age group, region, and country, was collected from GBD 2017 (*6*). Specific methods of the estimation process for HCV infection prevalence were described elsewhere (*6*). First, anti-HCV seroprevalence data from population-based studies and surveys were reviewed to estimate the acute hepatitis C prevalence using DisMod-MR 2.1 model. Second, total cirrhosis and total liver cancer prevalence were modelled using hospital data and cause-specific mortality rate estimates. Third, the proportions of cirrhosis and liver cancer due to underlying etiologies such as hepatitis B, hepatitis C, and alcohol use were estimated by meta-regression. Finally, the prevalence of cirrhosis and liver cancer due to hepatitis C was estimated according to total cirrhosis and total liver cancer prevalence and the proportion attributable to hepatitis C.

The 195 countries and territories were divided into 5 SDI regions according to total fertility rate under 25 years old, years of education for those aged 15 and older, and lag distributed income per capita and were separated into 21 GBD regions based on their epidemiological homogeneity and geographical contiguity. The ASR calculated by the direct method and absolute number of HCV cases were used to show HCV epidemic status. Relative changes in HCV cases and EAPCs of ASR with 95% CIs were calculated to quantify the temporal trends of HCV infection from 1990 to 2017. Change in HCV cases was defined as $\frac{\text{HCV } cases_{2017} - \text{HCV } cases_{1990}}{\text{HCV } cases_{1990}} \times 100\%$. A regression line was fitted to the natural logarithm of ASR, for instance, $y = \alpha + \beta x + \varepsilon$, where y=ln(ASR) and x=calendar year, EAPCs=$100 \times (e^{\beta} - 1)$. All statistical analyses were conducted by R statistical software (version 3.5.1; The R Foundation for Statistical Computing, Vienna, Austria). Statistical significance was attributed to p values ($p<0.05$).

The HCV infection ASR was unevenly distributed worldwide with the highest in Egypt (Figure 1). HCV cases in China and India accounted for one third of the global HCV infections. The HCV infection ASR decreased by 0.67% (95% CI: 0.64%–0.70%) per year globally from 2043.42 per 100,000 in 1990 to 1728.04 per 100,000 in 2017 (Table 1); while the number of HCV cases increased by 28.82% from 105.15 million in 1990 to 135.45 million in 2017, and increased significantly among individuals aged 50–69 years old and 70 years old above by 63.87% and 76.53%, respectively (Supplementary Figure S1 available in http://weekly.chinacdc.cn/). Against the global trend of ASR falling, an increasing trend was reported in Eastern Europe (EAPC=0.78, 95% CI: 0.56–0.99). Meanwhile, the number of HCV cases only decreased in Central and Western Europe. Over 99% of HCV infections were cirrhosis and other chronic liver diseases (Supplementary Figure S1), and the global trends and regional differences of which were similar to those of global HCV infections (Supplementary Figure S2 available in http://weekly.chinacdc.cn/).

The highest acute hepatitis C ASR was observed in Central Asia and the lowest in Western Europe (Supplementary Figure S3 available in http://weekly.chinacdc.cn/). The acute hepatitis C ASR decreased by 0.62% (95% CI: 0.59%–0.65%) per year from 9.50 per 100,000 in 1990 to 8.05 per 100,000 in 2017; while the number of acute hepatitis C cases increased by 8.63% from 0.54 million in 1990 to 0.59 million in 2017. The acute hepatitis C ASR increased in Eastern Europe (EAPC=0.65 95% CI: 0.45–0.86), and the number of acute hepatitis C cases decreased distinctly in Central Europe (30.47%) and East Asia (22.5%) (Supplementary Figure S3).

Liver cancer due to hepatitis C ASR was distributed heterogeneously worldwide with the highest in high-income Asia Pacific Region (14.39 per 100,000 in 2017) (Figure 2). Globally, liver cancer due to hepatitis C ASR increased by 0.87% (95% CI: 0.80%–0.94%) per year from 3.38 per 100,000 in 1990 to 4.54 per 100,000 in 2017. Meanwhile, the number of liver cancer due to hepatitis C increased by 159.40% from 0.14 million in 1990 to 0.37 million in 2017, and significantly increased by 253.15% among those over 70 years old (Supplementary Figure S1). Remarkably, liver cancer due to hepatitis C ASR increased drastically in low-middle SDI regions in the last decade, and increases were also observed in middle SDI regions (Supplementary Figure S4 available in http://weekly.chinacdc.cn/). The liver cancer due to hepatitis C ASR increased enormously in Australasia (EAPC=4.66, 95% CI: 4.24–5.08) and high-income North America (EAPC=4.47, 95% CI: 3.99–4.95), and the number of cases also increased by 521.99% and 455.62%, respectively (Figure 2).

DISCUSSION

HCV infection ASR decreased globally except in

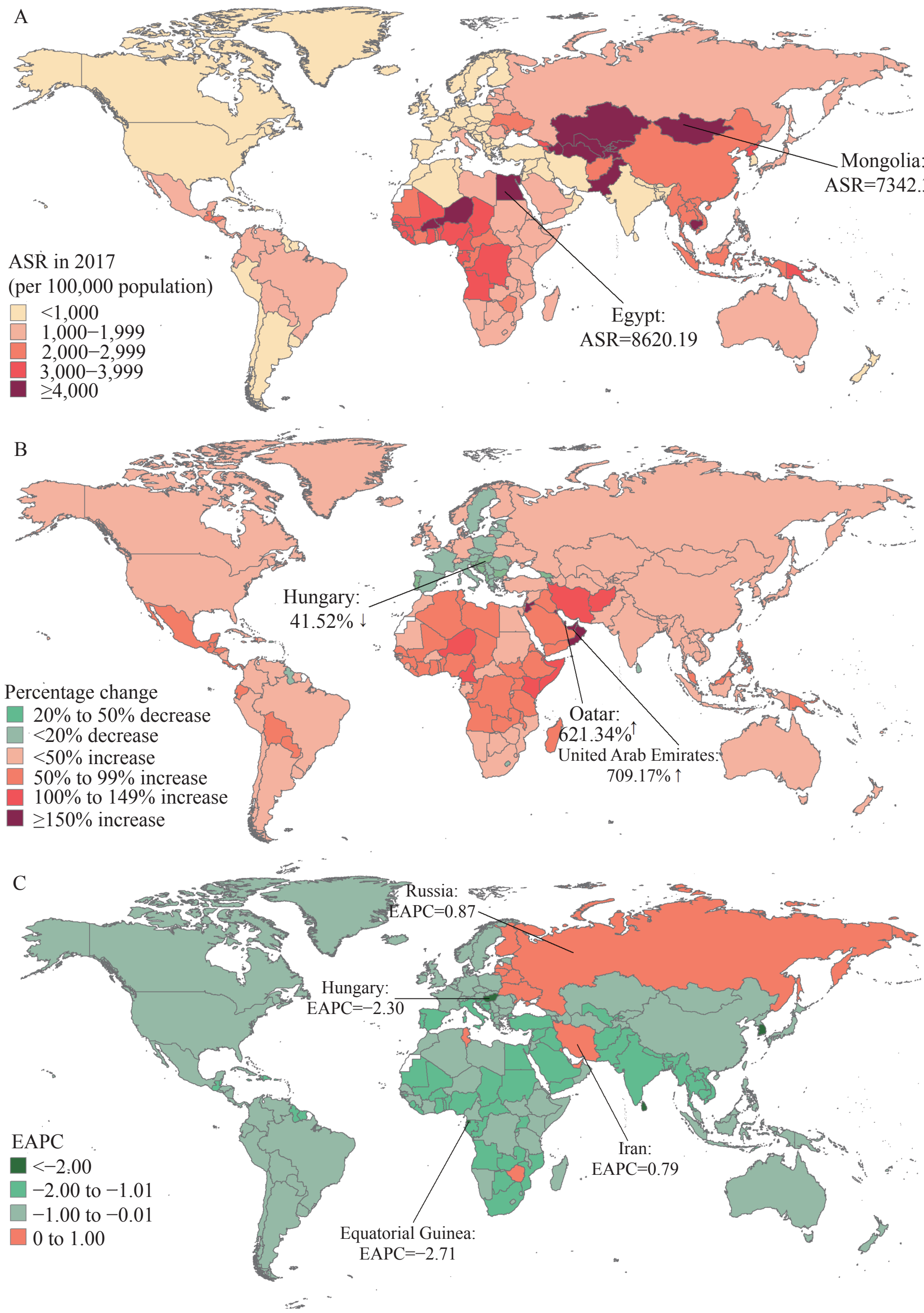

FIGURE 1. The global trends of HCV infection burden in 195 countries and territories. (A) The age-standardized prevalence rate (ASR) of HCV infection in 2017; (B) The percentage change in HCV cases between 1990 and 2017; (C) The estimated annual percentage changes (EAPCs) of age-standardized prevalence rate of HCV infection from 1990 to 2017.

Eastern Europe, and liver cancer due to hepatitis C ASR increased worldwide with drastic shifts in low-middle SDI regions in the last decade. The reduction of HCV infection ASR was partly due to the increased mortality due to liver-related causes and an ageing population. Similar with previous studies, Egypt had the highest HCV prevalence with 6.3% of the population living with HCV due to endemic schistosomiasis treatment by unsafe healthcare injections from the 1950s to 1980s, and subsequently inadequate infection control and interfamilial transmission (*7*). Over 1 million people in Egypt, the first country to negotiate an alternative price of DAAs, were treated from 2015 to 2017; however, treatment

TABLE 1. The estimated annual percentage changes (EAPCs) of the age standardized prevalence rate (ASR) of acute hepatitis C, cirrhosis, and other chronic liver diseases due to hepatitis C, liver cancer due to hepatitis C, and total HCV infections from 1990 to 2017 by region.

Characteristics	EAPCs of ASR (95%CI)			
	Acute hepatitis C	Cirrhosis and other chronic liver diseases due to hepatitis C	Liver cancer due to hepatitis C	Total HCV infections
Global	−0.62(−0.65 to −0.59)	−0.67(−0.70 to −0.64)	0.87(0.80 to 0.94)	−0.67(−0.70 to −0.64)
Socio–Demographic Index				
Low	−0.57(−0.64 to −0.50)	−0.79(−0.83 to −0.76)	−0.63(−0.67 to −0.59)	−0.79(−0.82 to −0.76)
Low–middle	−0.59(−0.61 to −0.56)	−0.87(−0.93 to −0.82)	0.64(0.57 to 0.71)	−0.87(−0.92 to −0.82)
Middle	−0.89(−0.93 to −0.86)	−0.94(−0.98 to −0.90)	0.19(−0.01 to 0.38)	−0.94(−0.98 to −0.89)
High−middle	−0.78(−0.82 to −0.73)	−0.61(−0.67 to −0.56)	1.24(0.94 to 1.53)	−0.61(−0.67 to −0.55)
High	−1.04(−1.12 to −0.97)	−0.71(−0.76 to −0.67)	1.34(1.13 to 1.55)	−0.71(−0.75 to −0.66)
Global Burden of Disease Region				
High−income Asia Pacific	−1.51(−1.64 to −1.38)	−1.01(−1.06 to −0.97)	−0.57(−0.75 to −0.38)	−1.01(−1.05 to −0.96)
Central Asia	−0.34(−0.46 to −0.23)	−0.63(−0.74 to −0.52)	0.17(0.08 to 0.26)	−0.63(−0.74 to −0.52)
East Asia	−0.66(−0.75 to −0.57)	−0.67(−0.74 to −0.6)	0.85(0.56 to 1.13)	−0.67(−0.74 to −0.59)
South Asia	−0.68(−0.75 to −0.61)	−1.04(−1.14 to −0.94)	1.16(1.12 to 1.20)	−1.04(−1.14 to −0.94)
Southeast Asia	−0.77(−0.79 to −0.75)	−0.84(−0.86 to −0.82)	0.09(0.00 to 0.18)	−0.84(−0.86 to −0.82)
Australasia	−0.30(−0.36 to −0.24)	−0.51(−0.57 to −0.44)	4.66(4.24 to 5.08)	−0.50(−0.56 to −0.44)
Caribbean	−1.07(−1.10 to −1.03)	−1.00(−1.05 to −0.95)	−0.51(−0.63 to −0.39)	−1.00(−1.05 to −0.95)
Central Europe	−0.74(−0.87 to −0.61)	−0.96(−1.02 to −0.90)	0.57(0.40 to 0.74)	−0.96(−1.02 to −0.90)
Eastern Europe	0.65(0.45 to 0.86)	0.78(0.56 to 1.00)	−0.18(−0.32 to −0.04)	0.78(0.56 to 0.99)
Western Europe	−1.33(−1.44 to −1.23)	−1.06(−1.13 to −0.98)	2.38(2.02 to 2.73)	−1.04(−1.12 to −0.97)
Andean Latin America	−0.51(−0.54 to −0.47)	−0.69(−0.73 to −0.65)	0.27(0.11 to 0.44)	−0.69(−0.72 to −0.65)
Central Latin America	−0.94(−1.01 to −0.86)	−0.63(−0.66 to −0.60)	−0.63(−0.70 to −0.57)	−0.63(−0.66 to −0.60)
Southern Latin America	−0.86(−0.93 to −0.78)	−0.65(−0.71 to −0.59)	−0.40(−0.52 to −0.29)	−0.65(−0.71 to −0.59)
Tropical Latin America	−0.48(−0.64 to −0.32)	−0.48(−0.69 to −0.27)	0.00(−0.17 to 0.17)	−0.48(−0.69 to −0.27)
North Africa and Middle East	−1.08(−1.12 to −1.03)	−1.34(−1.43 to −1.26)	1.10(0.91 to 1.29)	−1.34(−1.42 to −1.25)
High−income North America	0.01(−0.08 to 0.11)	−0.19(−0.34 to −0.05)	4.47(3.99 to 4.95)	−0.18(−0.32 to −0.03)
Oceania	−0.30(−0.39 to −0.21)	−0.32(−0.38 to −0.25)	0.32(0.27 to 0.38)	−0.32(−0.38 to −0.25)
Central Sub−Saharan Africa	−0.64(−0.89 to −0.40)	−0.70(−0.88 to −0.52)	−1.22(−1.40 to −1.04)	−0.70(−0.88 to −0.52)
Eastern Sub−Saharan Africa	−0.85(−0.95 to −0.74)	−0.77(−0.87 to −0.68)	−0.83(−0.95 to −0.72)	−0.77(−0.87 to −0.68)
Southern Sub−Saharan Africa	−0.90(−1.08 to −0.72)	−0.96(−1.12 to −0.79)	−0.94(−1.41 to −0.47)	−0.96(−1.12 to −0.79)
Western Sub−Saharan Africa	−0.99(−1.07 to −0.92)	−1.07(−1.11 to −1.02)	−1.17(−1.2 to −1.14)	−1.07(−1.11 to −1.02)

numbers stagnated and finding those undiagnosed remained the biggest challenge (*7*). Being unaware of HCV infection can lead to serious health outcomes and increase HCV transmission risk (*8*). Consistent with this study, the WHO reported that hepatitis C was found in less than 0.5% of the population in Western, Northern, and Central Europe and as high as 3%–6% in many countries of Eastern Europe and Central Asia, and Eastern Europe suffered from an increasing trend of HCV infection due to sharing of needles and syringes (*9*).

Nowadays, even in areas where HCV infections were low, an increase in HCV transmission may occur (*3*). Consistent with our study, surveillance in the United States showed a reemergence of new HCV infections with reported acute hepatitis C rates increasing threefold from 0.3 per 100,000 population in 2009 to 1.2 per 100,000 population in 2018 concurrent with the nation's opioid crisis; and increasing rates among reproductive-aged persons put multiple generations at risk for chronic hepatitis C (*8*). Prevention should be focused on reducing exposure risk because no vaccine

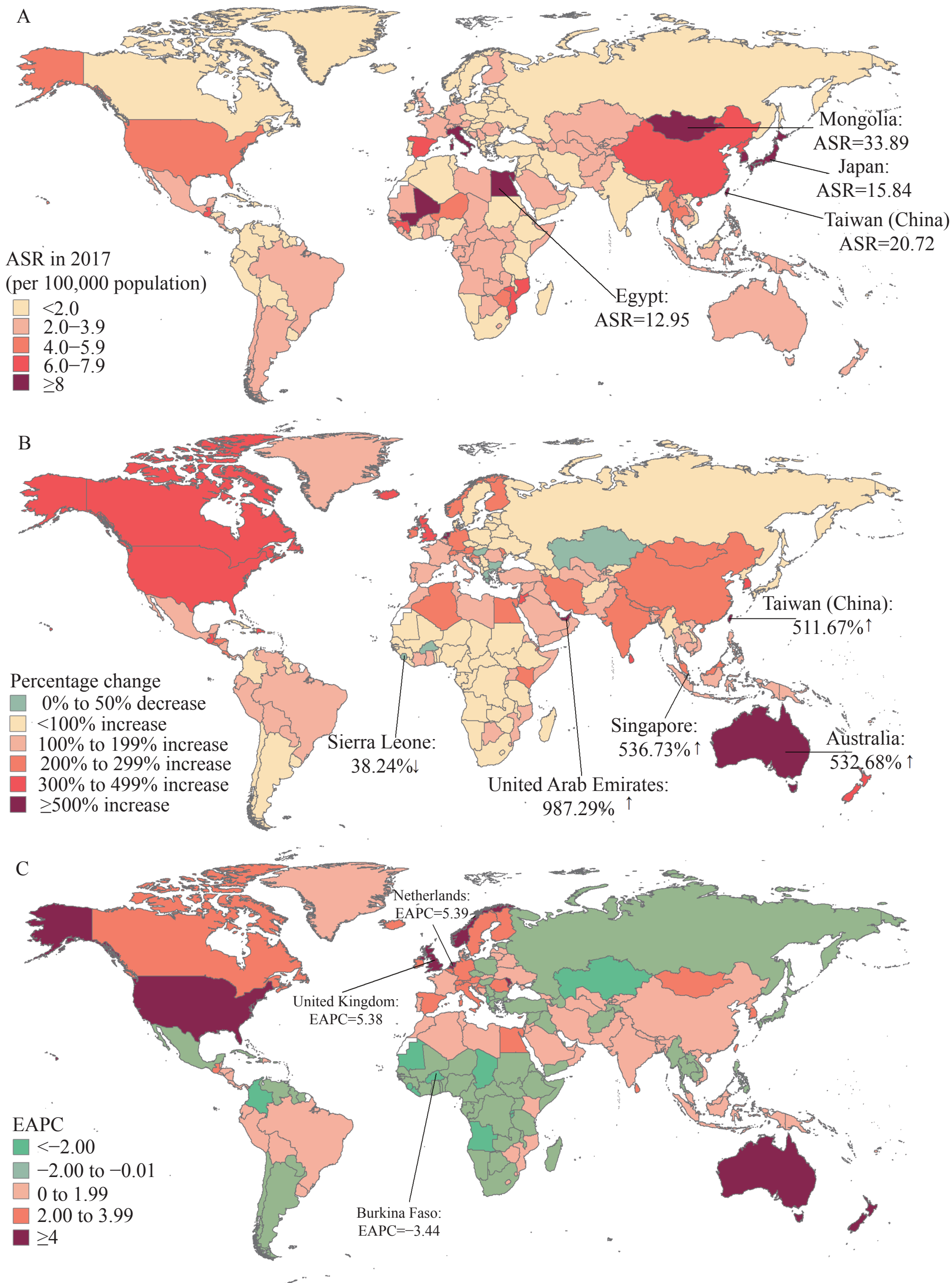

FIGURE 2. The global trends of liver cancer due to hepatitis C in 195 countries and territories. (A) The age-standardized prevalence rate (ASR) of liver cancer due to hepatitis C in 2017; (B) The percentage change in the number of liver cancer due to hepatitis C between 1990 and 2017; (C) The estimated annual percentage changes (EAPCs) of age-standardized prevalence rate of liver cancer due to hepatitis C from 1990 to 2017.

exists for hepatitis C (*9*). The protection of safe injections and harm reduction and screening are key points to prevent new infections worldwide.

The global liver cancer due to hepatitis C ASR displayed increases and remarkably increased in most high-income regions probably due to the longer life expectancy and higher ageing population. To some extent, the increases were also driven by the increasing of obesity, diabetes, and steatosis, since these diseases could increase risk of advanced fibrosis among chronic HCV infections (*10*). A prospective cohort study reported DAA treatment reduced risk for mortality and HCC, therefore, DAAs should be considered in all chronic HCV infections (*5*). A global mathematical model estimated a comprehensive package of HCV prevention, screening, and treatment could result in a 61% reduction in mortality compared with the 2015 baseline (*4*). However, the prices of DAAs remained high in high-income countries and those middle-income countries where generic drugs were unable to access and licensing agreements were not covered (*3*).

To our knowledge, this is the first assessment of the global landscape, long-term trends, and regional differences in HCV infection prevalence using GBD study data. HCV is still prevalent worldwide despite the development of DAAs, and a reemergence of HCV was concurrent with the opioid crisis. HCV infection prevention might involve at least 3 aspects: first, prohibiting HCV widespread transmission among general populations; second, increasing global DAAs coverage; and third, continuously investing in the development of an HCV vaccine. Public health gains can be made in low-resource contexts, provided there is strong government will, budgetary commitments, and smart drug procurement to make life-saving treatments affordable.

Several limitations remained. First, availability of data and quality of available data in different regions might be incomparable and limit accuracy and robustness of HCV infection estimates in the modeling, evaluation of which was not listed due to limited space. Second, different regional governments had different priorities in HCV treatment, prevention, and healthcare policies. Third, EAPCs and change of HCV cases from 1990 to 2017 might mask the short-term trends that reflected the effectiveness of recent prevention interventions.

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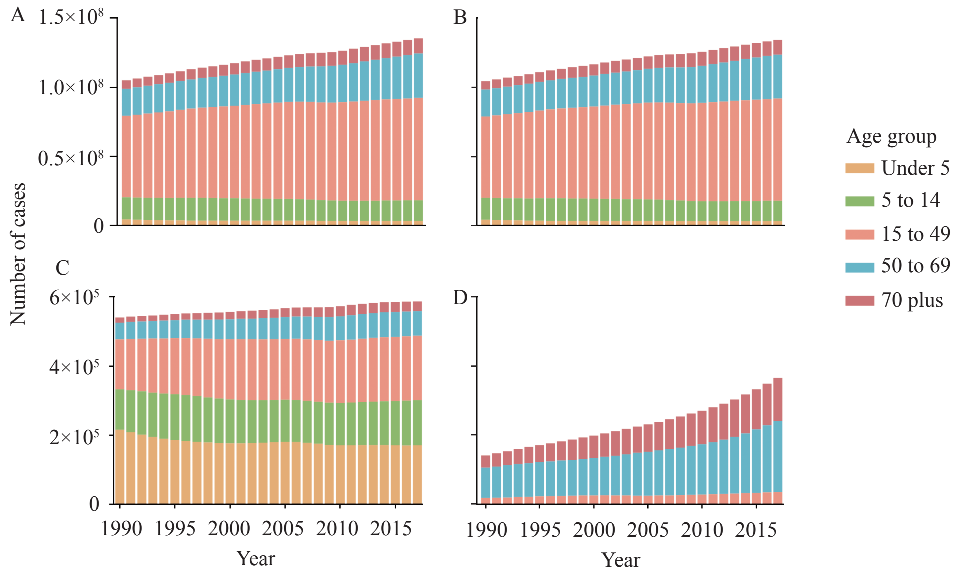
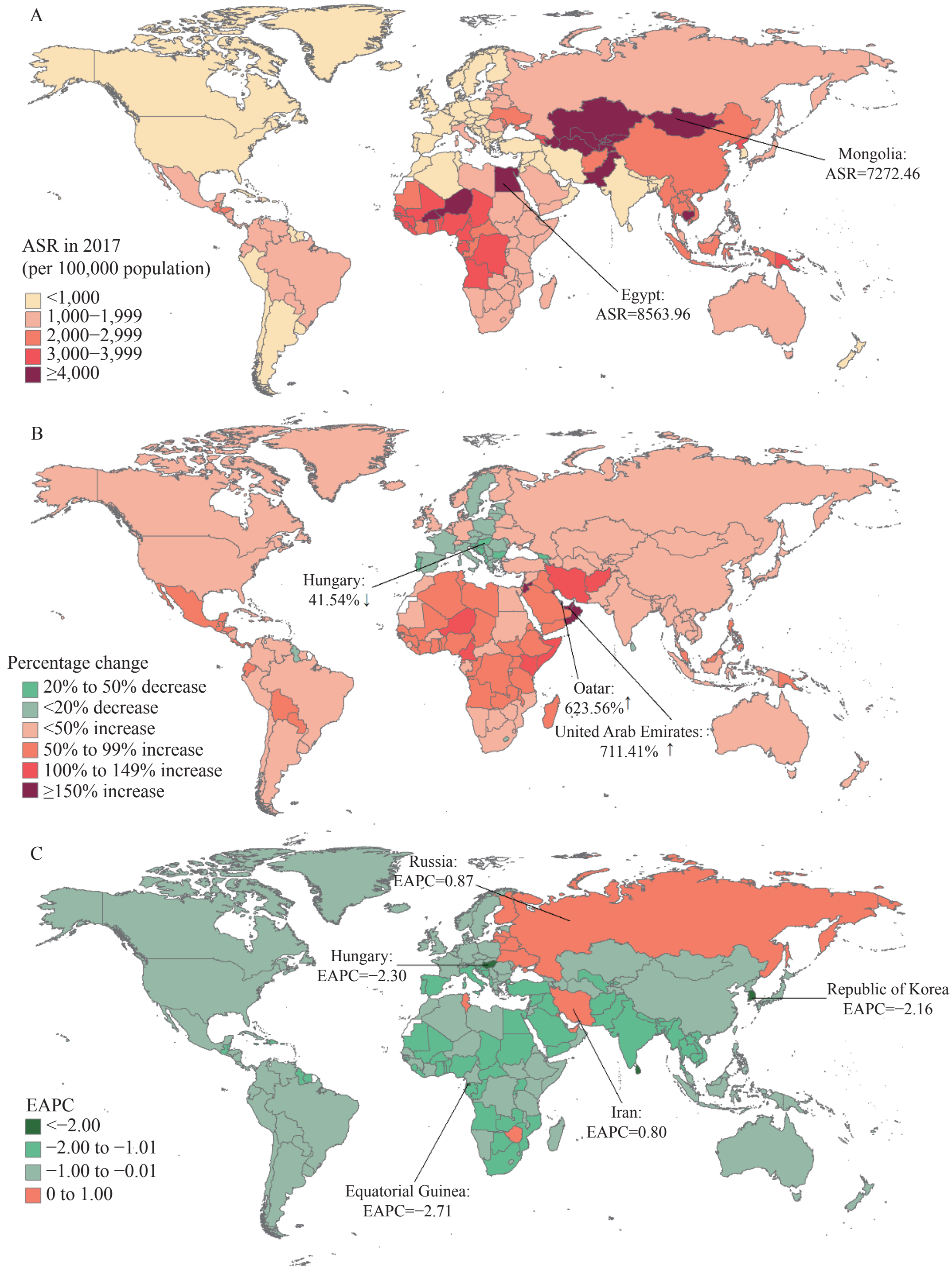
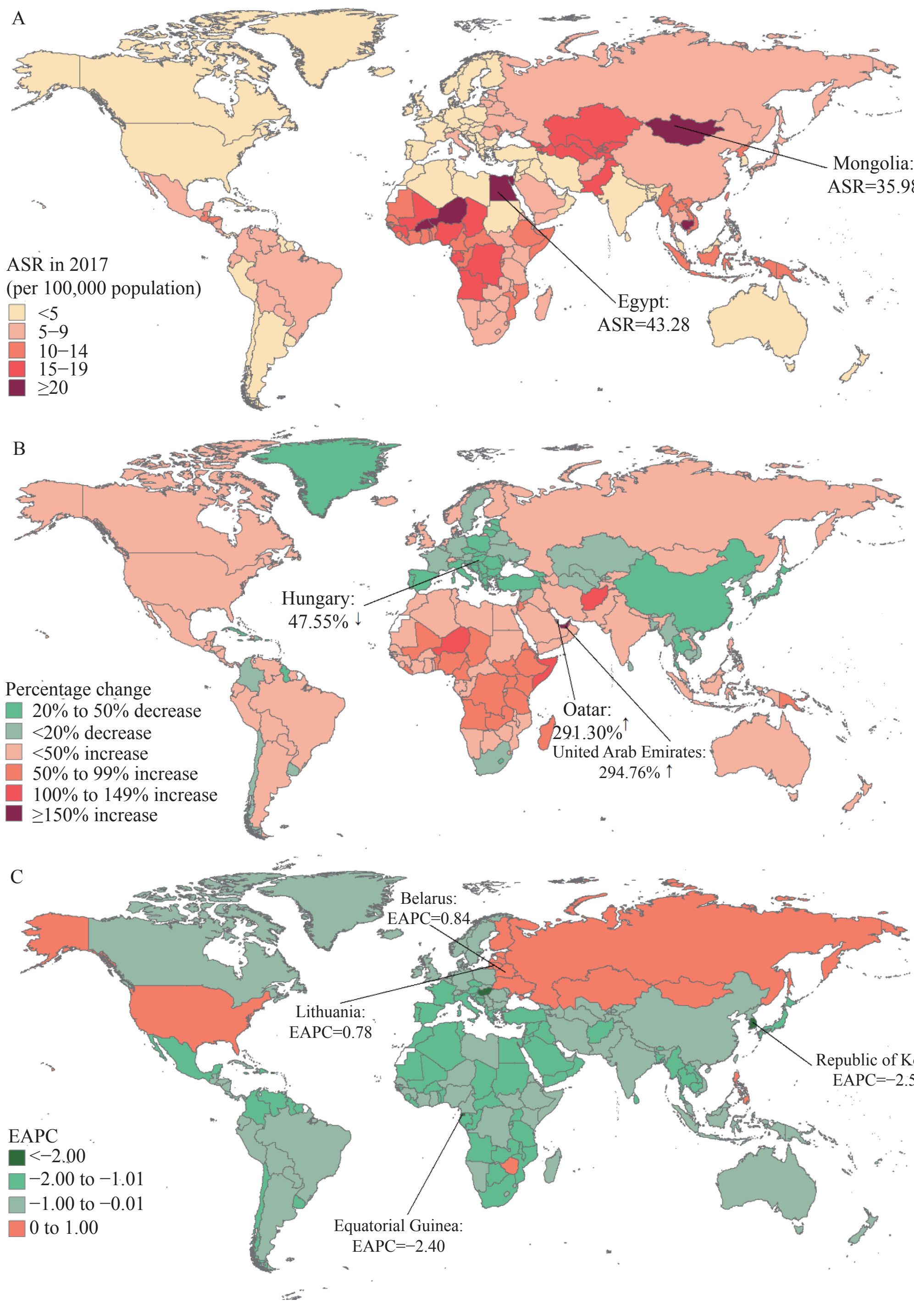


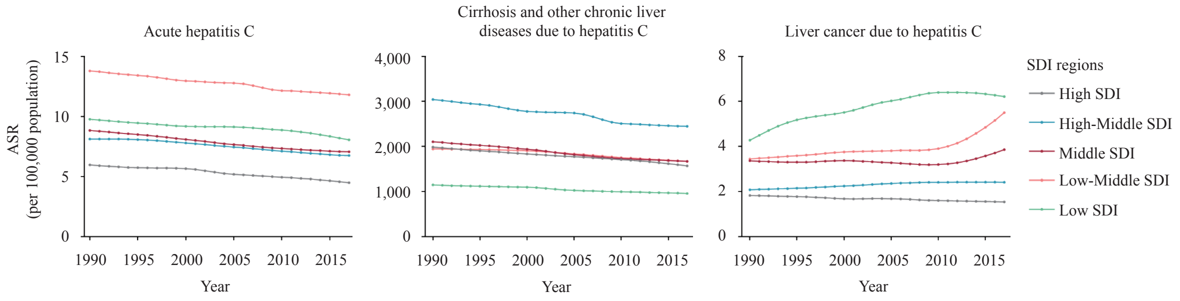
SUPPLEMENTARY FIGURE S1. The global burden of HCV infection by age group from 1990 to 2017, worldwide. (A) Total HCV cases. (B) Cirrhosis and other chronic liver diseases due to hepatitis C. (C) Acute hepatitis C. (D) Liver cancer due to hepatitis C.



SUPPLEMENTARY FIGURE S2. The global trends of cirrhosis and other chronic liver diseases due to hepatitis C in 195 countries and territories; (A) the age-standardized prevalence rate (ASR) of cirrhosis and other chronic liver diseases due to hepatitis C in 2017; (B) the percentage change in the number of cirrhosis and other chronic liver diseases due to hepatitis C between 1990 and 2017; (C) the estimated annual percentage changes (EAPCs) of age-standardized prevalence rate of cirrhosis and other chronic liver diseases due to hepatitis C from 1990 to 2017.



SUPPLEMENTARY FIGURE S3. The global trends of acute hepatitis C in 195 countries and territories; (A) the age-standardized prevalence rate (ASR) of acute hepatitis C in 2017; (B) the percentage change in acute hepatitis C cases between 1990 and 2017; (C) the estimated annual percentage changes (EAPCs) of acute hepatitis C age-standardized prevalence rate from 1990 to 2017.



SUPPLEMENTARY FIGURE S4. The age-standardized prevalence rate (ASR) of acute hepatitis C, cirrhosis and other chronic liver diseases due to hepatitis C, and liver cancer due to hepatitis C from 1990 to 2017, by Socio-demographic Index (SDI) region.

Outbreak Reports

An Epidemic of Hepatitis A — Liaoning Province, 2020

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Summary

What is already known about this topic?

Hepatitis A (HA) is caused by acute hepatitis A virus (HAV) infection and was once very common in China. Following the 2008 introduction of the HA vaccine into the national Expanded Program on Immunization (EPI), the incidence of reported HA in China decreased markedly. However, HA epidemics still occur in Liaoning Province every 3–5 years, although with far fewer cases than in the pre-HA-vaccination era.

What is added by this report?

Between January 1, 2020 and March 18, 2020, the number of reported cases of HA in Dalian and Dandong cities of Liaoning Province increased significantly compared with the same period in previous years. All cases were sporadic, and cases were seen in nearly every township. The increase in HA occurred one month after local fresh seafood became available with most cases being among adults. A case-control study showed that consuming raw or undercooked seafood, clams, snapping shrimp, and oysters were significantly associated with the increase in HA.

What are the implications for public health practices?

Strengthening health education for residents to avoid consumption of raw seafood and encouraging HAV vaccination of adults aged 20 to 54 years are important to prevent periodic HAV endemic outbreaks. Further multisectoral cooperation must be emphasized on HA surveillance in areas with a high prevalence of HA.

BACKGROUND

In February 2020 compared with February 2019, there was a 138.2% increase of cases of hepatitis A (HA) reported to the National Notifiable Disease Report System (NNDRS) from Liaoning Province, and 77.6% of the cases in Liaoning were from two coastal cities — Dalian and Dandong. All cases were sporadic, and cases were seen in nearly every township of the two cities. Through an interview survey of HA cases and a case-control study, we found that consuming raw or undercooked seafood was significantly associated with the increase in HA. Local governments have taken a series of measures including health education and restriction of the sale of seafood products in markets. During March 11–16, the China CDC, Liaoning Provincial CDC, and Dalian and Dandong CDCs conducted a joint investigation and identified the consumption of raw seafood as the main risk factors associated with the HA increase. We report results of the investigation and recommendations to prevent similar epidemics.

INVESTIGATION AND RESULTS

All cases of hepatitis A were laboratory confirmed according to the *Diagnostic Criteria of Viral Hepatitis A* (WS 298-2008) (*1*). Based on date of onset, 3,511 HA cases were reported nationwide through NNDRS between January 1, 2020 and March 18, 2020, which was a decrease of 12.3% compared with the 4,003 cases reported across the nation during the same period last year. In contrast, HA cases reported from Liaoning Province in January 1 through March 18 increased from 700 in 2019 to 1,361 in 2020, accounting for approximately one-third of all cases reported nationwide. After integration of the HA vaccine into the national Expanded Program on Immunization (EPI) in 2008, HA had occurred at relatively low levels in Liaoning with periodic increases in every 3–5 years, and the most recent increase was in 2014–2016. In 2020, the number of reported HA cases increased markedly in the first 2 months of the year but began to decrease on March 4 (Figures 1 and 2).

There were 426 and 586 cases reported from two coastal cities, Dalian and Dandong, which accounted for 74.36% (1,012/1,361) of all cases reported from Liaoning. Zhuanghe County of Dalian and Donggang County of Dandong reported 262 (62.50%, 262/426) and 290 (49.49%, 290/586) cases, which was more

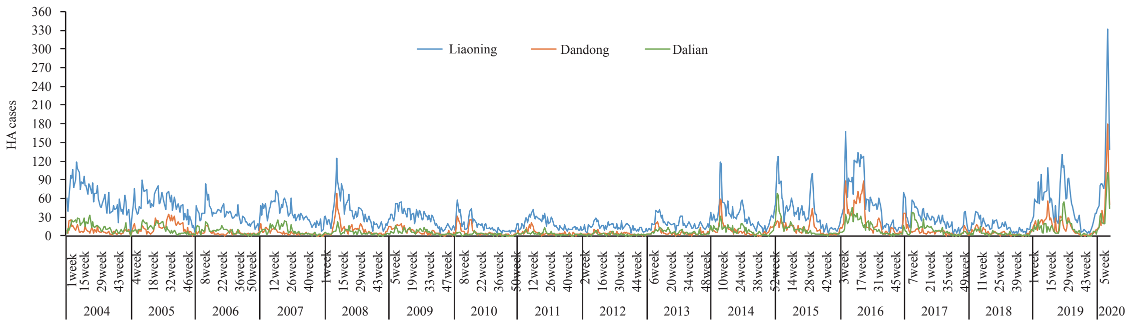

FIGURE 1. Weekly reported hepatitis A (HA) cases in Liaoning Province, 2004 through Week 11 of 2020.

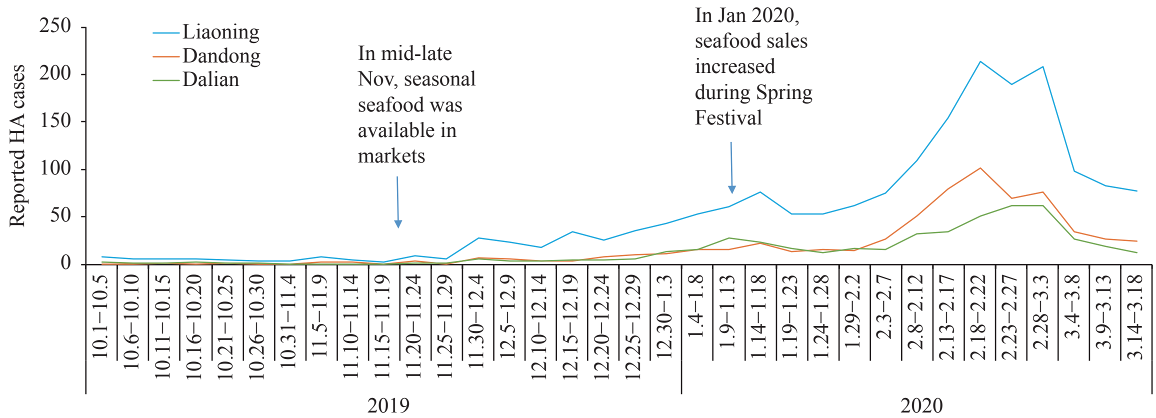

FIGURE 2. Seafood sales timeline and daily distribution of reported hepatitis A (HA) cases in Liaoning, October 1, 2019 to March 18, 2020.

than any other county (Figure 3).

Most cases were among adults that were aged 30–54 years in Dalian and aged 30–49 years in Dandong, which represented 85.4% (364/426) and 82.6% (484/586) of the cases in the two cities. There were 4 (0.39%, 4/1,012) reported cases among children less than 15 years of age, and 3 of the 4 children had no history of HAV vaccination. By occupation, 50.9% (515/1,012) of HA cases were among farmers and 31.2% (316/1,012) were among household workers or unemployed individuals.

Local CDCs conducted routine epidemiological investigations of all reported and confirmed HA cases in face-to-face or telephone interviews (n=191). The interviews focused on five themes including eating habits, drinking water, types of seafood eaten, dining-out behavior, and sources of food during their incubation period. We analyzed data from case interviews conducted between January and early March in Zhuanghe County and found that 71.2% (104/146), 36.9% (31/84), and 13.3% (2/15) of interview subjects who consumed oysters, snapping shrimp, or cockles ate them raw. During the same time in Dandong, the percent of HA cases with a history of seafood consumption in 2020 was 84.7% (287/339), which was higher than in 2018 (72.0%) and 2019 (61.0%) (local, unpublished data).

We compared sales of local seafood during the two months prior to the HA increase with sales during the HA epidemic. We found that HA case reports began to increase in December 2019, approximately one month after local seafood became available in November. Following a sharp increase of seafood sales during Spring Festival in January 2020, there was a peak of HA cases in February and early March (Figure 2).

The case-control study was conducted by Dalian CDC using face-to-face and telephone interviews. All 191 confirmed HA cases reported between January 1, 2020 and March 7, 2020 in Zhuanghe County were enrolled as the case group, and 277 healthy individuals residing in the same county were recruited for the control group. Controls were healthy adults living in the same town as a case, with no history of HA, and who had not received HAV vaccine. The questionnaire was designed, tested, and revised by Dalian CDC; all data, including eating habits, types of drinking water,

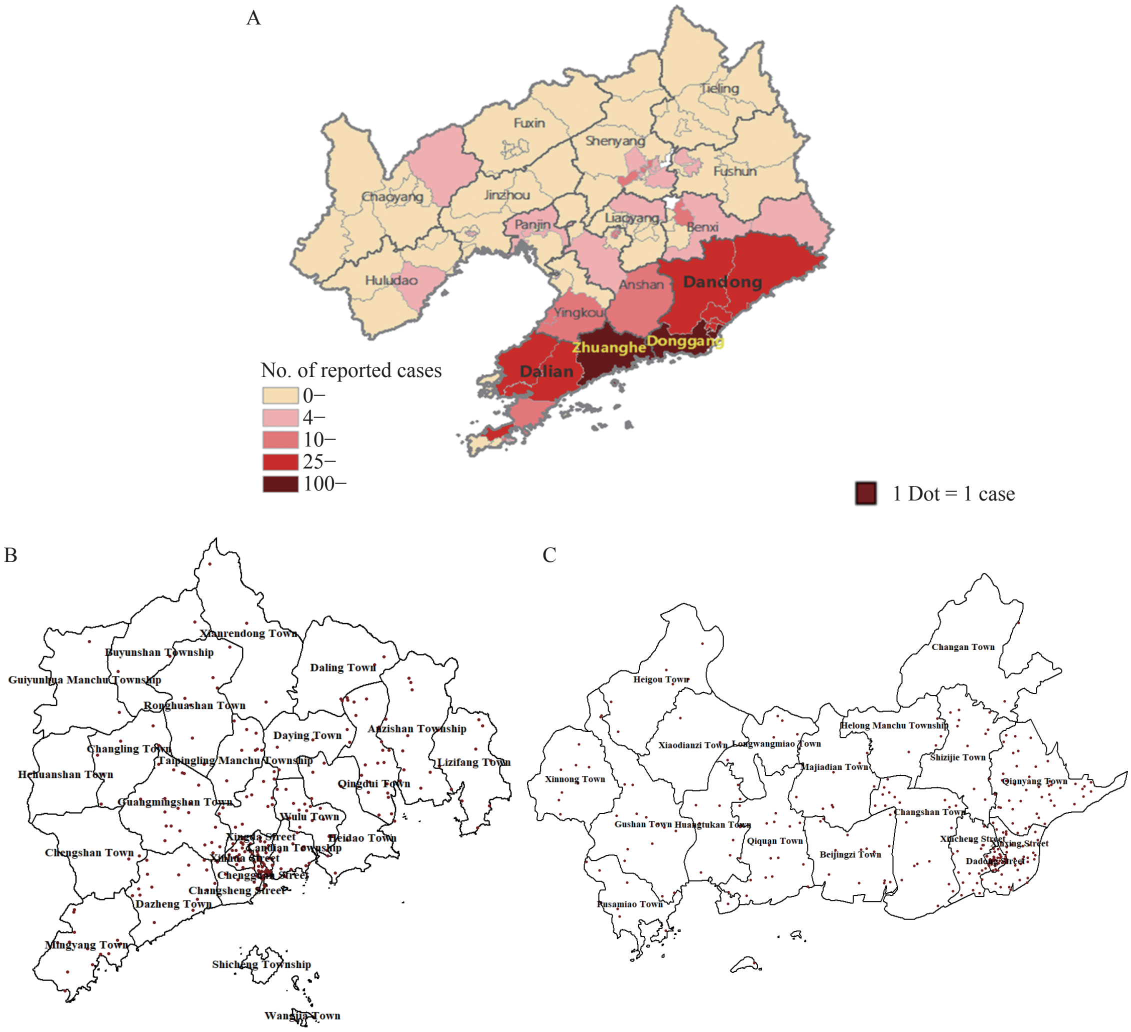

FIGURE 3. Geographic distribution of Hepetitis A (HA) reports in Liaoning Province and two local areas, January 1, 2020 to March 18, 2020. (A) County level distribution of reported HA cases in Liaoning Province. (B) Township-level distribution in Zhuanghe County, Dalian City. (C) Township-level distribution in Donggang County, Dandong City.

types of seafood eaten, food sources, and dining out behavior, were collected by trained, experienced local staff. HA risk factors were identified by univariate and multivariate logistic regression analyses. We found that consumption of raw or undercooked seafood (OR=11.1, 95% CI: 6.0–20.6), eating clams (OR=2.5, 95% CI: 1.6–5.9), eating snapping shrimp (OR=3.1, 95% CI: 1.6–6.0), and eating oysters (OR=4.6, 95% CI: 2.6–8.1) were significantly associated with HAV infection (Table 1).

In March 2020, we collected 30 samples of seafood from local markets, 23 samples of seafood from coastal areas, and 3 samples of water from the Yellow Sea estuary. The samples were sent to the National Marine Environment Monitoring Center to test for the presence of HAV. All samples were negative for HAV.

RESPONSE

Local governments took several measures in response to the HAV epidemic in Dalian and Dandong including educational, mass-media public communications about the importance of avoiding consuming raw seafood and an encouragement of HA vaccination. By March 14, 4,418 adults in Zhuanghe County of Dalian and 1,861 adults in Donggang County of Dandong were vaccinated. Local governments restricted sale of seafood products in early March to reduce HAV exposure. A total of 22 serum samples from patients with acute HAV infection were obtained and sent to Liaoning Provincial CDC's laboratory for genotyping, and the results are pending.

TABLE 1. Case-control study on risk factors of Hepetitis A (HA) in Dalian City, Liaoning Province, 2020.

Item	Cases (N=191)		Controls (N=277)		Univariate analysis	Multivariate analysis
	Number	Percentage (%)	Number	Percentage (%)	OR (95% CI)	OR (95% CI)
Consumption habits						
Eating raw seafood	64	33.5	41	14.8	12.0 (6.6–21.9)	11.1 (6.0–20.6)
Dining out	60	31.4	35	12.6	3.1 (1.9–5.1)	1.4 (0.7–2.7)
Types of seafood eaten						
Big yellow corbicula	43	22.5	23	8.3	3.5 (2.0–6.2)	1.1 (0.4–2.8)
Little yellow corbicula	31	16.2	20	7.2	2.4 (1.3–4.5)	0.3 (0.1–0.8)
White corbicula	71	37.2	62	22.4	2.0 (1.3–3.1)	1.0 (0.5–1.8)
Mixed color corbicula	22	11.5	11	4.0	3.5 (1.6–7.9)	2.5 (0.8–7.4)
Sand corbicula	72	37.7	64	23.1	2.1 (1.4–3.3)	0.9 (0.5–1.7)
Clams	41	21.5	17	6.1	4.7 (2.4–9.0)	2.5 (1.6–5.9)
Snapping shrimp	84	44.0	46	16.6	4.4 (2.6–7.2)	3.1 (1.6–6.0)
Cockle	15	7.9	9	3.2	2.5 (1.4–6.1)	1.8 (0.5–6.2)
Oysters	146	76.4	97	35.0	6.1 (3.8–10.0)	4.6 (2.6–8.1)

DISCUSSION

HAV is highly infectious and is transmitted through the fecal-oral route (*2*). HAV that exists in the environment can cause periodic HA epidemics among people if there are sufficient numbers of susceptible individuals. With improvements in health and sanitation and the widespread use of vaccines, the incidence of HA in Liaoning decreased markedly. Coastal cities like Dalian and Dandong have been highly endemic HA areas in Liaoning with endemic outbreaks characterized by adult cases and peaks in January to March, which is different than areas with endemic HA outbreaks in the summer and autumn (*3*).

We have shown that despite the increasing number of HA cases in Liaoning, from January 1 to March 18, 2020, the epidemic characteristics remained unchanged. As in the past, cases were mainly from Dalian and Dandong and were sporadic, which was inconsistent with HA outbreak criteria (*4*). The coastal areas increase in cases were believed to represent the start of a new 3–5-year epidemic cycle. Because this increase occurred during the COVID-19 virus containment activities, local health-care authorities were already prepared for case detection and reporting. After a series of public health measures taken by local governments, the number of reported HA cases declined.

Our study found that consumption of seafood before HA onset was higher than in previous years and that consumption of raw or undercooked seafood were significantly associated with HAV infection. Dalian and Dandong are located on the Liaodong Peninsula where seafood is abundant. From November to April, many types of fresh seafood are sold and consumed by residents, and most people eat raw seafood (*5*–*6*). Clams and oysters have been shown to be frequently contaminated with HAV, making HA outbreaks caused by raw seafood consumption common (*7*–*8*). A dose-response curve correlating the quantity of clams consumed to the attack rate of HA during the HA outbreak in Shanghai in 1988 (*9*).

There were two reasons why our study did not find any HAV-positive environmental or seafood samples. First, considering the incubation period of 28 days for HAV, there must be a time lag between exposure to the risk factor and the time of sample collection, which indicated the need for routine monitoring initiated early during infection. Second, the real-time RT-PCR approach has a low sensitivity for finding HAV in such samples (approximately 6%). However, studies conducted in 2002 found that local offshore seawater and shellfish were significantly contaminated with HAV (*10*). In June 2019, HAV was detected in 1 shellfish sample during routine monitoring of food safety risks in Liaoning Province. It's worth noting that the results of patients' HAV genotyping testing can only provide evidence of the HAV homology among patients rather than the likely source of infection that the patients are jointly exposed to. Therefore, our findings that reported HA cases increased one month after the initiation of sales of local seafood provides indirect support for our conclusion about the role of seafood in the HA increase this year from epidemiological evidence.

We suggest 1) strengthening health education of local residents to avoid consumption of raw or undercooked seafood, 2) encouraging HAV vaccination of adults aged 20 to 54 years to close population immunity gaps and prevent periodic HAV endemic outbreaks, 3) restarting routine immunization and catching up of children who missed vaccinations due to the COVID-19 epidemic, and 4) establishing multisectoral partnerships for HA surveillance in areas with a high prevalence of HAV infections to monitor HAV and its genotypes in patients, the environment, and food with the objective of providing data for updating HA prevention and control strategies.

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Commentary

Exporting China's Successes in Vaccine Preventable Hepatitis

Lance E. Rodewald[1,#]

Almost four decades of science, innovation, and programmatic effort to control and prevent vaccine-preventable viral hepatitis have paid off spectacularly well in China. In the pre-vaccine era, nearly 10% of children were infected by hepatitis B virus (HBV) — especially during childbirth — causing them to be lifelong carriers of HBV, able to infect others, and in great danger of liver cancer and cirrhosis as adults (*1*). Most young children were infected by hepatitis A virus (HAV), with a lifetime infection rate of 90%, keeping this virus in circulation and causing outbreaks among older children and adults who could become quite ill from hepatitis A (*2*).

Fast-forward to the present day, and the landscape is markedly changed for the better. The current generation of children in China is the first generation to be almost completely free of hepatitis B and protected for life (*3*); the incidence of hepatitis A is extremely low in China as vaccine-induced immunity has replaced infection-induced immunity among children; and a third viral hepatitis — hepatitis E — is now preventable by vaccines developed and licensed in China (*4*).

Vaccines can take partial credit for these successes since they could not have been achieved without vaccines, but the vaccines were deployed in the context of a strategic strengthening of maternal and child health and childbirth practices — for hepatitis B prevention — and improvements in sanitation — for hepatitis A and hepatitis E prevention. Integration of vaccination and health system and sanitation improvement was not only essential for control of these infections, but also brought benefits beyond viral hepatitis prevention and control. For example, China was an early participant in the United Nations International Children's Fund (UNICEF)-coordinated Safe Motherhood Initiative that improved childbirth practices in many countries around the world (*5*). Bringing childbirth into birthing centers and hospitals in China not only made childbirth safer, preventing potentially deadly post-partum hemorrhage and significantly reducing the maternal mortality rate, but also provided an effective platform for administration of a timely birth dose of hepatitis B vaccine to the newborn infant. More hygienic birthing practices also enabled elimination of maternal-neonatal tetanus — a major accomplishment that was verified in 2012 by the World Health Organization (WHO) (*6*).

There is critically important remaining work for prevention and control of these three vaccine preventable diseases (VPDs) in China. Most importantly, the nearly 90 million individuals living with HBV infection, who were born before hepatitis B vaccine was widely available in China, are in need of identification and clinical management to prevent progression to cirrhosis, liver cancer, and premature death (*7*). Although there has been a 97% reduction in maternal-to-child transmission of HBV, there are an estimated 50,000 breakthrough chronic infections of newborn infants every year (*3*), which necessitates tightening the program and providing antivirals during pregnancy for certain HBV carriers to prevent transmission during childbirth. The rapid decline in the incidence of hepatitis A following introduction of hepatitis A vaccine in 2007 resulted in many children born in the years immediately prior to the vaccine's introduction to be neither infected nor vaccinated — allowing a gap in population immunity among 10-to-20-year-olds in China that leaves some people susceptible to HAV infection (*2*). The public health significance of this immunity gap is yet to be determined but will be important to understand and possibly act upon. Finally, because there is insufficient experience with the relatively new hepatitis E vaccine, the roles of the hepatitis E vaccine in outbreak responses and routine immunization have not been fully determined (*8*). Although Hepatitis E vaccine is eligible for WHO prequalification, it has not yet been submitted for prequalification, limiting its use overseas and depriving much of the world of this prevention tool.

Even though there is much work to be done, China has clearly traveled a great distance in the prevention and control of vaccine preventable hepatitis. China's comprehensive approaches to the prevention and control of hepatitis B and hepatitis A can serve as evidence-based models for countries that are at earlier points in this journey. For example, many countries have yet to embrace the timely birth dose of hepatitis B vaccine to prevent perinatal hepatitis B infection. Ninety percent of perinatal infections become chronic infections that cause direct suffering and perpetuate HBV transmission. Although the WHO recommends the birth dose for all newborn infants, only 11% of the WHO African Region's newborn infants receive the timely birth dose (*9*). Hepatitis B vaccine could become an added-value pillar to strengthen and improve maternal child health. As another example, countries that have been highly endemic for hepatitis A may be able to look to the experience in China of introducing hepatitis A vaccine in the context of improvements in sanitation practices. A domestically-developed inactivated hepatitis A vaccine was prequalified by WHO in 2017 and is contributing to the global vaccine supply for immunization programs (*10*).

Chinese scientists and health professionals have worked with the WHO, UNICEF, and other countries for many years to support viral hepatitis prevention and control — including serving on advisory committees, supporting epidemiological studies, and providing vaccines. Indeed, a characteristic of China's effort to control and prevent viral hepatitis has been longstanding collaborations with international organizations such as the WHO, UNICEF, Gavi the Global Alliance on Vaccines and Immunization, and US CDC.

But now is a good time for accelerating China's global support for hepatitis prevention and control. The WHO has a health sector strategy to eliminate viral hepatitis as a public health problem by 2030 (*11*). China CDC could become a WHO Collaborating Center for Viral Hepatitis, supporting the WHO effort with experience, expertise, and vaccines. As a WHO Collaborating Center, the number of opportunities to contribute to the elimination of viral hepatitis will greatly increase. In a bit of good timing, Gavi recently approved support of the hepatitis B birth dose and will begin investing in the birth dose in Gavi-eligible countries in 2021 (*12*). China's comprehensive approach to hepatitis B prevention through strengthening the maternal health system could be highly relevant in many Gavi-eligible countries. Viral hepatitis prevention and control could become a focus of the Belt and Road Initiative on health, which includes many Gavi-eligible countries. In short, exporting China's successes on prevention and control of vaccine preventable hepatitis can and will make the world a healthier and safer place for all.

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Profiles

Huaqing Wang, China CDC's Chief Expert in National Immunization Program

Peter Hao[1,&]; Ying Zhang[1,&]; Zhenjun Li[1]; Jingjing Xi[1,#]; Feng Tan[1,#]

Huaqing Wang has had a long and distinguished career in developing and implementing immunization programs to protect China's people. After graduating from Harbin Medical University in 1986 with a major in preventive medicine, Huaqing Wang was assigned to Heilongjiang Provincial CDC and has dedicated his career to infectious disease control and immunization.

In 1986, China's National Immunization Program (NIP) was experiencing rapid development and progress as multiple sectors of public health workers were hard at work achieving the first nationwide coverage goal of at least 85% of children in every provincial-level administrative division (PLAD) receiving all NIP vaccines. The Chinese government prioritized childhood immunization with the State Council of China approving and establishing the NIP and specifying April 25 every year as "National Child Vaccination Day." With the government's support and sponsorship from the United Nations International Children's Fund (UNICEF), China's vaccine cold chain — a system of storing and transporting vaccines at recommended temperatures to preserve the vaccines' efficacy — was established and perfected. Simultaneously, immunization services were gradually being aligned with international technical standards with the support of the World Health Organization (WHO).

By the end of 1986, Huaqing Wang became greatly impressed by an epidemiological investigation of poliomyelitis that caused him to become engaged with the NIP for over 30 years. In the winter of 1986–1987, Huaqing Wang and his senior colleagues discovered that many children with polio had not been reported or were misreported during local CDC investigations. The issue was significant and urgent as poliomyelitis could cause lifelong disability or, in severe cases, could cause patients and survivors to lose any ability to care for themselves as no medications can treat polio, leaving immunization as the only strategy capable of stopping polio from harming children. In Qitaihe City of Heilongjiang Province, Huaqing Wang saw a 2-year-old boy suffering from severe poliomyelitis and having extremely limited muscle strength — grade 1 to 2 out of 4. This child being immobile and bedridden due to missed or unavailable poliovirus vaccinations left an important image in his heart and mind and inspired his continuing work with the NIP.

The NIP continued to focus on vaccine accessibility and elimination of polio, and China successively achieved planned targets of 85% childhood coverage with NIP vaccines at the provincial-level in 1988, the county-level in 1990, and the township-level in 1995. In 2000, China was certified as polio-free by the WHO Western Pacific Region, and Huaqing Wang received individual honors from China NIP in 1999 and was recognized as a National Advanced Polio Eradication Leader in 2001.

In addition to this domestic work, Huaqing Wang also studied advanced molecular biology for one year with the virology group in the Department of Medicine of Niigata University in Japan to enrich his knowledge and understanding of molecular biology in 1998. Following this, he obtained a master's degree in epidemiology from 1999 to 2001 and began doctoral studies on disease etiology at the University of Tokushima in Japan in 2002. By 2005, Huaqing Wang was transferred to the Department of the National Immunization Program of the recently established China CDC and had several major accomplishments.

As the technical director, Huaqing Wang introduced the ideas and methods of evidence-based medicine into China's Expanded Program on Immunization (EPI 2007) and included evidence-based recommendations for a live, attenuated Japanese-encephalitis vaccine and hepatitis A vaccine, both of which were independently developed by China. He and a group of senior colleagues also led the development of China's Adverse Events Following Immunization (AEFI) Monitoring System from 2011 to 2014, which eventually passed WHO assessments to allow vaccines produced in China to be internationally recognized. In addition, over 100 national-level programs and guidelines such as the widely used "Work Specifications for Vaccinations" were developed under his leadership and guidance.

Beyond this work, Huaqing Wang also personally leads responses to public health events. Media coverage of vaccines can sometimes cause worry and doubt in recipients, parents, or general citizens and require a disciplined, scientific response to curb harm to societal perception of vaccines. For instance, the Shanxi Province "high temperature" incidents in 2008 and 2010, the measles vaccine incident in 2010, the hepatitis B vaccination child death incident in 2013, and the Shandong Province "illegal" vaccine incident in 2016 showcased the continued need for professionals to carry out cohort investigations and causal inference analysis on deaths, diseases, or symptoms that are related with vaccines. The technical support for the conclusion of the vaccine incidents is critical for maintaining public trust and averting panic.

Huaqing Wang also directs response to emerging and existing outbreaks of infectious diseases. In 2009, Huaqing Wang also led the development and implementation of the "Guidance for the Clinical Trial of H1N1 Influenza Vaccine (2009, China)" helping China become the first country to launch an H1N1 influenza vaccine. In addition, during a polio epidemic in Xinjiang Uyghur Autonomous Region, he and a team of senior colleagues led joint analyses of polio surveillance that examined the main population, age structure, regional distributions, and time distribution of polio cases to yield an epidemiologically-based emergency immunization strategy. The adopted strategy included specified areas, age ranges, vaccination timing, and dosing and was precise enough to require only two months to control the epidemic. Later, the WHO recognized this response as a model for global control of polio.

As the Chief Expert for Immunization Program of China CDC, Huaqing Wang plays a crucial role in guiding China's immunization programs, in responding to outbreaks and emergencies, in technical analysis, and in provision of immunization services in disasters.

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