Preplanned Studies

Changing Patterns of Mortality in Viral Hepatitis — China, 1987–2021

Chen Chen[1,&]; Zuliyaer Talifu[2,&]; Yu Wu[1]; Binbin Su[3,#]; Wanwei Dai[4,#]

Summary

What is already known about this topic?

Viral hepatitis continues to present a major global public health challenge, with China shouldering the heaviest burden of this disease worldwide.

What is added by this report?

This study examined evolving trends and assessed the impacts of age, period, and cohort on viral hepatitis mortality from 1987 to 2021 in both urban and rural settings across China.

What are the implications for public health practice?

This research provides critical insights, enabling policymakers to develop precise and effective intervention strategies that are specifically tailored to address the needs of high-risk older adults.

Viral hepatitis (VH) continues to pose a substantial global health concern, attributed to roughly 1.34 million fatalities each year. China, in particular, shoulders the most substantial VH burden worldwide. In response, significant strategies have been executed, leading to notable advancements in VH prevention (*1*). However, significant gaps remain in evidence pertaining to the efficacy of these prevention efforts and the influence of age, period, and cohort on evolving VH patterns. To address these gaps, we performed an extensive analysis of VH mortality from 1987 to 2021, investigating the effects of these three factors. Our analysis seeks to equip policymakers with essential insights to develop strategic intervention plans. Our study illustrates a significant decline in VH mortality representative of the considerable success of applicable prevention strategies. However, it also underscores a prominent emerging challenge specific to older adults, necessitating amplified focus and the formulation of targeted intervention strategies.

This research sourced VH mortality data by age, gender, and urban-rural sectors from 1987 to 2021 from the National Health Commission (1954–2013, Ministry of Health; 2013–2018, National Health and Family Planning Commission) of China's death registration system. To compute the age-standardized mortality rate per 100,000, we employed the direct standardization method utilizing the World Standard Population as a basis. To identify significant fluctuations and ascertain the independent effects of age, period, and cohort, we utilized both joinpoint regression and the age-period-cohort (APC) model (the age-standardized mortality rate per 100,000, we employed the direct standardization method utilizing the World Standard Population as a basis. To identify significant fluctuations and ascertain the independent effects of age, period, and cohort, we utilized both joinpoint regression and the APC model (*2*).

This research explored changing patterns and evaluated the effects of age, period, and cohort on VH mortality from 1987 to 2021 in both urban and rural areas throughout China.

Figure 1 highlights the evolving trends in VH mortality from 1987 to 2021. Over this period, a consistent downward trend is observed in both urban and rural cohorts. More specifically, VH mortality in urban populations decreased from 2.76 per 100,000 individuals in 1988 to 1.36 per 100,000 in 2021. Similarly, in rural areas, these statistics saw a reduction from 2.59 to 1.81. The detailed analysis indicates that regardless of the location, whether urban or rural, VH mortality demonstrated a consistent diminishing trend up until 2004. However, between 2004 and 2015, there was a resurgence, which then subsided and recommenced the initial declining trend through to 2021. With regards to gender disparities, higher VH mortality rates were observed in men as opposed to women, a pattern consistent in both urban and rural settings.

Table 1 presents the findings of the joinpoint regression analysis displaying the decrease in VH mortality in both urban and rural areas, with a higher rate of decrease observed in urban areas. The table also shows the trends for different periods and highlights a gender difference, noting a greater decline in VH mortality for women compared to men.

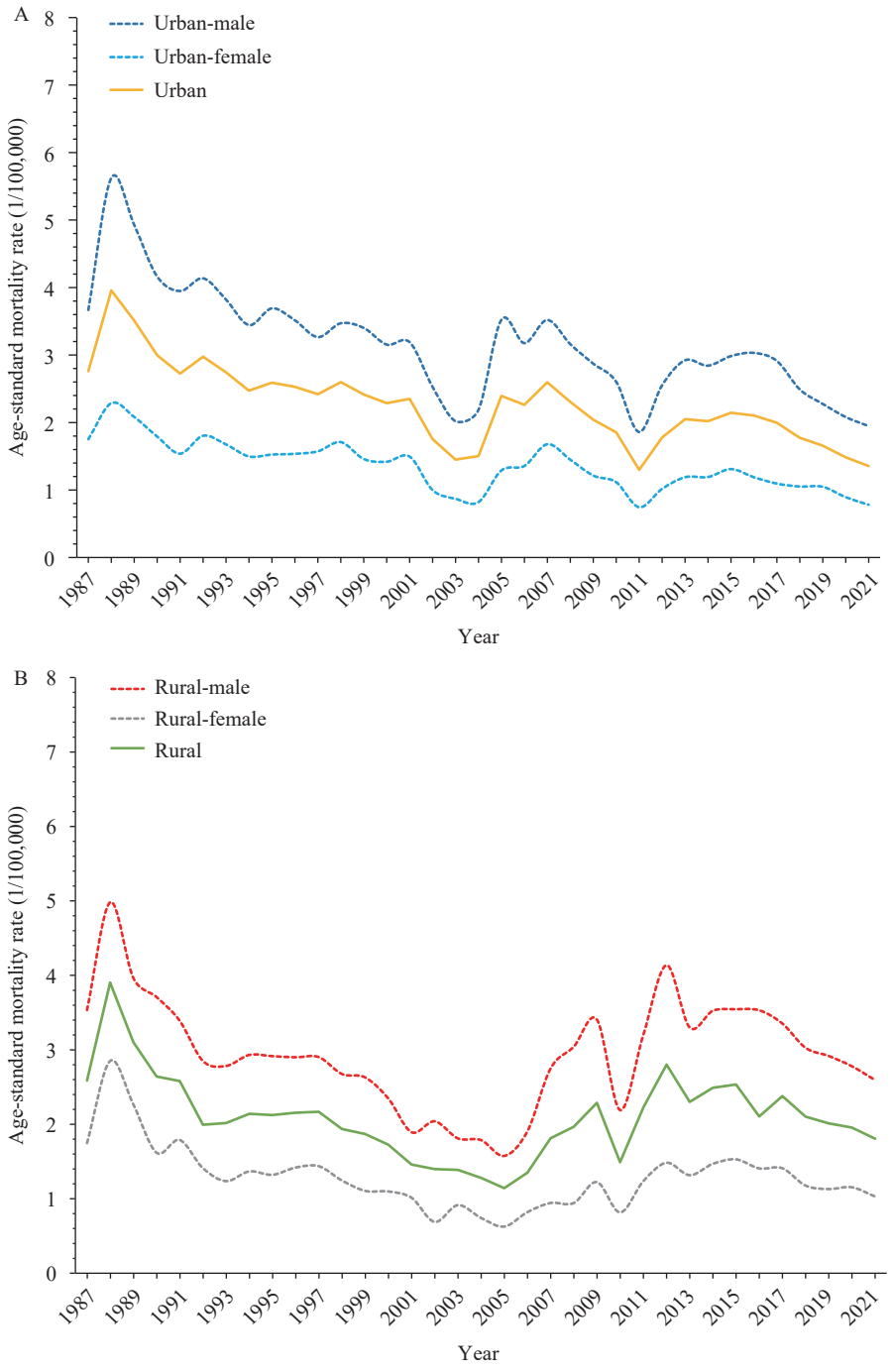

FIGURE 1. Temporal trend of age-standardized mortality of viral hepatitis in (A) urban and (B) rural China from 1987 to 2021.

Figure 2 presents the findings of the APC model analysis. Across both urban and rural parameters, mortality rates for VH were shown to increase with age. This trend is more pronounced in rural areas compared to urban ones. When stratified by gender, men consistently displayed a higher risk compared to women, regardless of geographical categorization.

With respect to period effect, a general decrease was observed throughout the study period in both urban and rural demographics. However, there was a noticeable resurgence during 2004–2009 for urban areas and 2004–2015 for rural areas. These resurgences did not exhibit significant gender discrepancies.

Observation of the cohort effect indicated a conserved pattern in urban and rural populations; both showed an initial risk increase followed by a decrease.

TABLE 1. Joinpoint analysis of age-standardized mortality rate of viral hepatitis in urban and rural areas.

Viral hepatitis		Total study period (1987–2021)		Period 1		Period 2		Period 3	
		AAPC (%)	95% *CI*	Years	APC (%)	Years	APC (%)	Years	APC (%)
Urban	Total	−2.7*	(−4.5, −0.8)	1987–2003	−3.5*	2003–2017	0.2	2017–2021	−9.3
	Men	−2.7*	(−4.4, −0.9)	1987–2003	−3.4*	2003–2017	0.3	2017–2021	−9.5
	Women	−2.5	(−6.3, 1.5)	1987–2004	−4.0*	2004–2007	8.7	2007–2021	−2.9*
Rural	Total	−1.5	(−3.0, 0.1)	1987–2005	−4.9*	2005–2012	10.6*	2012–2021	−3.4*
	Men	−1.3	(−2.8, 0.3)	1987–2005	−4.6*	2005–2012	11.5*	2012–2021	−3.8*
	Women	−2.2*	(−3.9, −0.5)	1987–2005	−6.0*	2005–2014	8.6*	2014–2021	−5.3

Abbreviation: AAPC=average annual percent change; APC=annual percent change; *CI*=confidence interval.
* Significant difference from zero (P<0.05).

Among urban cohorts, 1931 marked the peak risk period [risk ratio (*RR*)=1.53, 95% confidence interval (*CI*): 1.37–1.70], with cohorts born post-1961 evidencing lower risk. Prior to 1961, a higher risk was detected for women, but this pattern reversed in cohorts born after 1961. In the context of rural areas, maximum risk was exhibited by the 1966 cohort (*RR*=1.23, 95% *CI*: 1.10–1.39). Specifically, as cohorts approached 1961, the risk increased, while those further away displayed a decrease. Similar to the urban demographic, risk rates were higher for women before the 1961 cohort, after which the trend reversed.

DISCUSSION

This research discovered a decrease in VH mortality in China from 1987 to 2021, although a significant resurgence was observed between 2004 and 2015, affecting both urban and rural populations. Notably, distinct patterns were observed across urban and rural areas. During periods 1 and 3, a decline in VH mortality was noted, but during period 2, an increase was discernible. Remarkably, the increase in rural areas was more pronounced than that in urban areas. Across different age groups, an initial decrease in VH mortality in urban areas was replaced by a rising trend past the age of 70. Conversely, in rural areas, an upward trend was noticed before the age of 50, which then reversed. Risk factors associated with VH mortality displayed a J-shaped age distribution, a decreasing period trend, and an inverted U-shaped cohort trend. Furthermore, discrepancies between urban and rural areas were identified.

The observed shift in VH mortality trends is an important accomplishment in the prevention of VH in China. Over the last thirty years, the Chinese government has employed a variety of prevention strategies, ranging from targeted interventions, such as vaccination against hepatitis A and B, as well as free prenatal testing for VH, to more comprehensive initiatives like improving water supply and sanitation. Concurrent socioeconomic advancements and medical improvements have also positively influenced the declining VH mortality trend. However, a unique period from 2004 to 2015 diverges from this downward trajectory, where VH mortality saw a resurgence — a phenomenon corroborated by an earlier study (*3*). We speculate that this increase could be due to the escalating epidemic of hepatitis C virus (HCV) (*4*) and hepatitis E virus (HEV) (*5*), combined with a lack of effective vaccines and universal vaccination. As for gender disparities, our research indicates that men face a higher risk of VH mortality than women. This heightened risk in men could be linked to their higher exposure to behavioral and occupational risk factors (*6*).

This analysis of the impact of age on VH mortality revealed an escalating pattern as age increased, from the 5–10 years age group to those aged 85 and above. This trend, evident in both urban and rural regions, corroborates findings from a prior study (*3*). Interestingly, VH mortality among the 0–4 years age group was marginally higher than that of those aged 5–9 years. This slight uptick could potentially be due to vertical transmissions (i.e., mother-to-child) and horizontal early childhood transmissions that took place before targeted preventative measures were initiated (*1*). Additionally, our data highlighted an increased risk of VH mortality among older adults in both urban and rural areas. Based on these findings, we advocate for the creation of targeted prevention strategies that cater specifically to older adults at high risk of VH. By doing so, we may better these individuals' health prospects and improve healthy life expectancy (*7*–*8*).

Concerning the effect of time on VH mortality, our

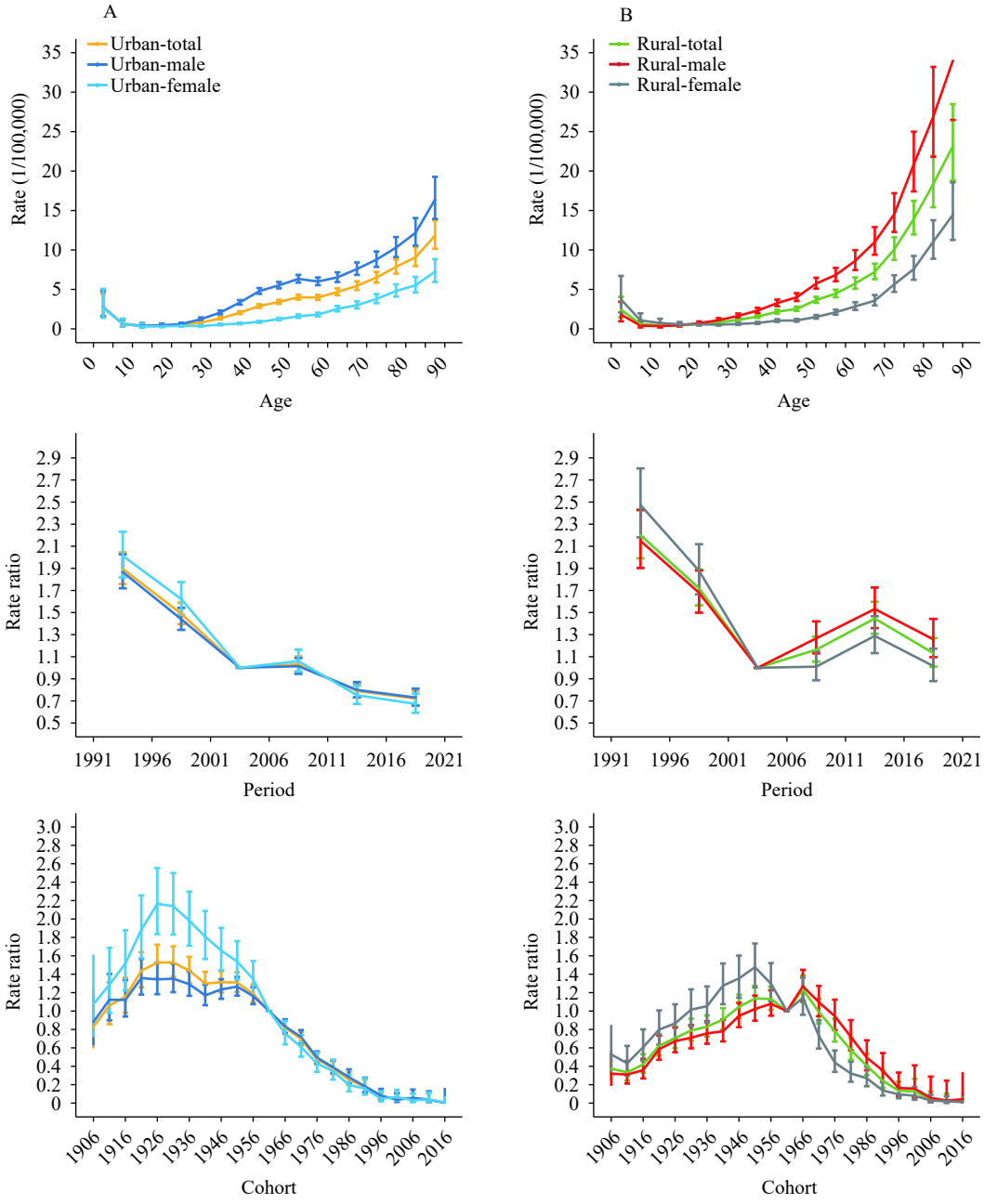

FIGURE 2. The effects of age, period, and cohort on age-standardized mortality rate of viral hepatitis in (A) urban and (B) rural China from 1987 to 2021.

analysis showed a general decrease. Nevertheless, there was also a notable resurgence period, aligning with results from a separate study (*3*). Considering the stated incidence rates of various VH forms, we propose that this resurgence could be due to an escalating prevalence of HCV and HEV, likely influenced by the lack of efficient vaccines (*5*). The observed urban-rural discrepancy may be a result of rural population migration and variations in the standard of medical services. Furthermore, the continuous expansion of the communicable disease surveillance system, established by China in 2004, might have contributed to a rise in the documented number of VH cases.

Several factors, including socioeconomic status, historical events, and exposure to environmental hazards, have contributed to variations in VH mortality risks among different birth cohorts. For urban cohorts, earlier groups experienced a higher risk of VH mortality, with the 1931 cohort demonstrating the highest risk. This heightened risk could potentially be attributed to exposure to war, social unrest, low hygiene standards, contaminated syringes, and other

factors influencing the epidemic of communicable diseases (*9*). However, following the establishment of the People's Republic of China in 1949 and the enactment of the patriotic health campaign (*10*), VH mortality risks began to progressively decrease. In rural cohorts, the peak of VH mortality risk occurred slightly later, in 1966, which might be explained by the relatively lower levels of social activities in rural areas. It is particularly notable that, following the implementation of the universal HBV vaccination program for newborns in 1992, VH mortality risk reached an impressively low level (*11*).

This study has some limitations. First, due to the absence of mortality data for different VH types, we cannot further analyze the changing patterns of different subtypes. Second, the data used was from the statistical reports, not the individual data, and we cannot conduct individual-level analysis. Third, the APC model analysis employed in this study is an ecological method, which restricts our ability to establish causal inferences. But our study mainly proposed relevant scientific explanations based on the statistical reports data and literature.

Conflicts of interest: No conflicts of interest.

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[#] Corresponding authors: Binbin Su, subinbin@sph.pumc.edu.cn; Wanwei Dai, dai_wanwei@163.com.

[1] Department of Population Health and Aging Science, School of Population Medicine and Public Health, Chinese Academy of Medical Science & Peking Union Medical College, Beijing, China; [2] School of Population Medicine and Public Health, Chinese Academy of Medical Science & Peking Union Medical College, Beijing, China; [3] Department of Health Economics, School of Population Medicine and Public Health, Chinese Academy of Medical Science & Peking Union Medical College, Beijing, China; [4] Office of Academic Research of Peking University Third Hospital, Beijing, China.
[&] Joint first authors.

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