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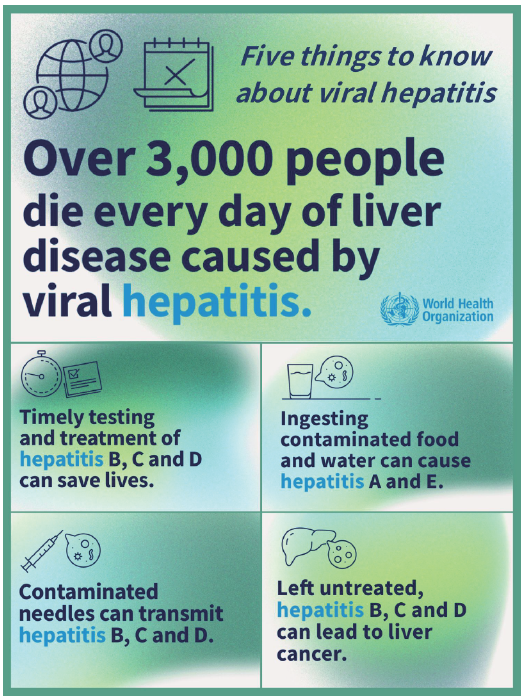

EPIDEMIOLOGICAL TRANSITION IN INFECTIOUS DISEASES ISSUE

Preplanned Studies

Perspectives

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Cover Image: adapted from the World Health Organization, https://www.who.int/multi-media/details/5-things-to-know-about-viral-hepatitis.
This week's issue was organized by Guest Editor Xiaoying Zheng.

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.

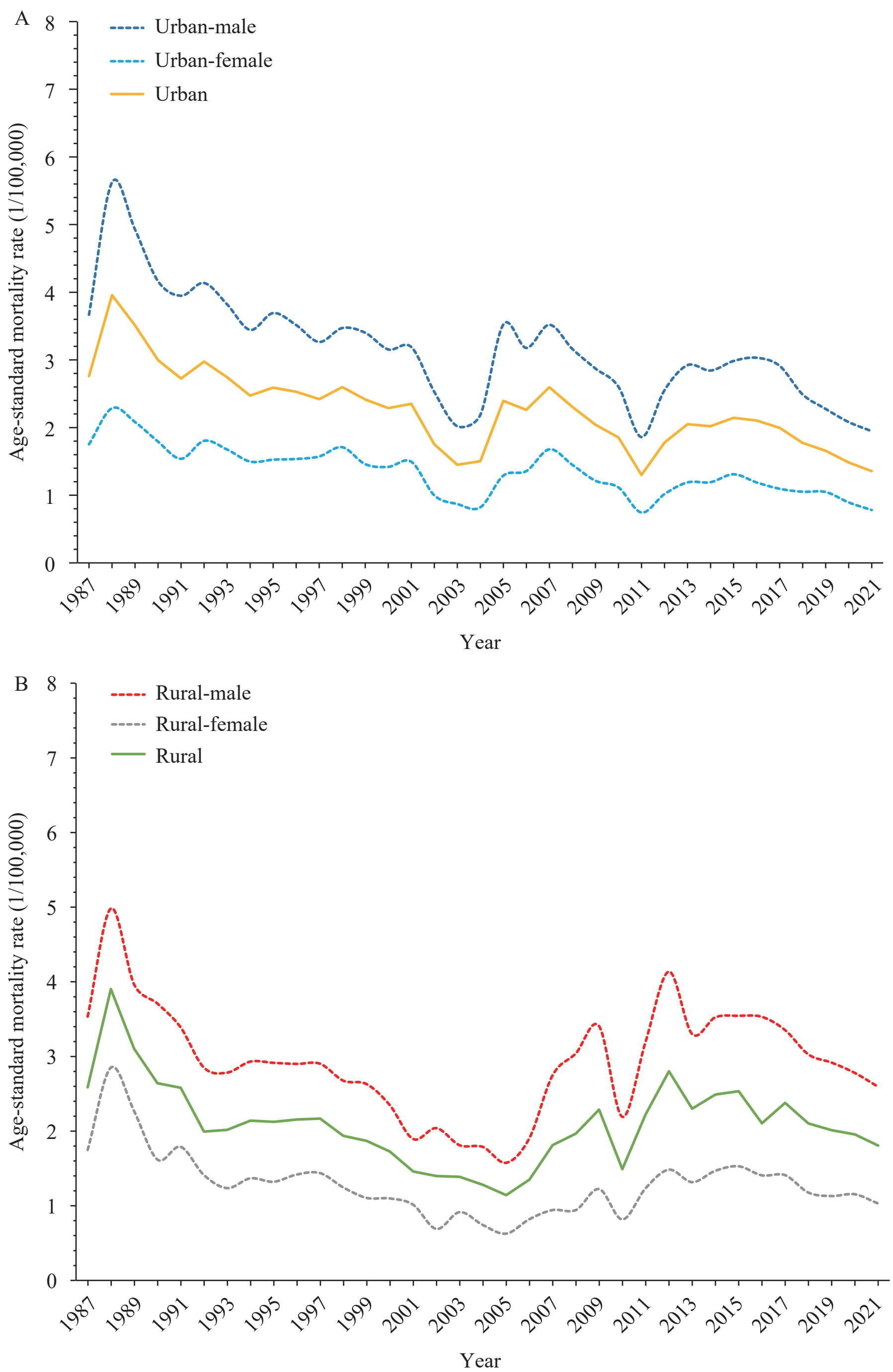

FIGURE 1. Temporal trend of age-standardized mortality of viral hepatitis in (A) urban and (B) rural China from 1987 to 2021.

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

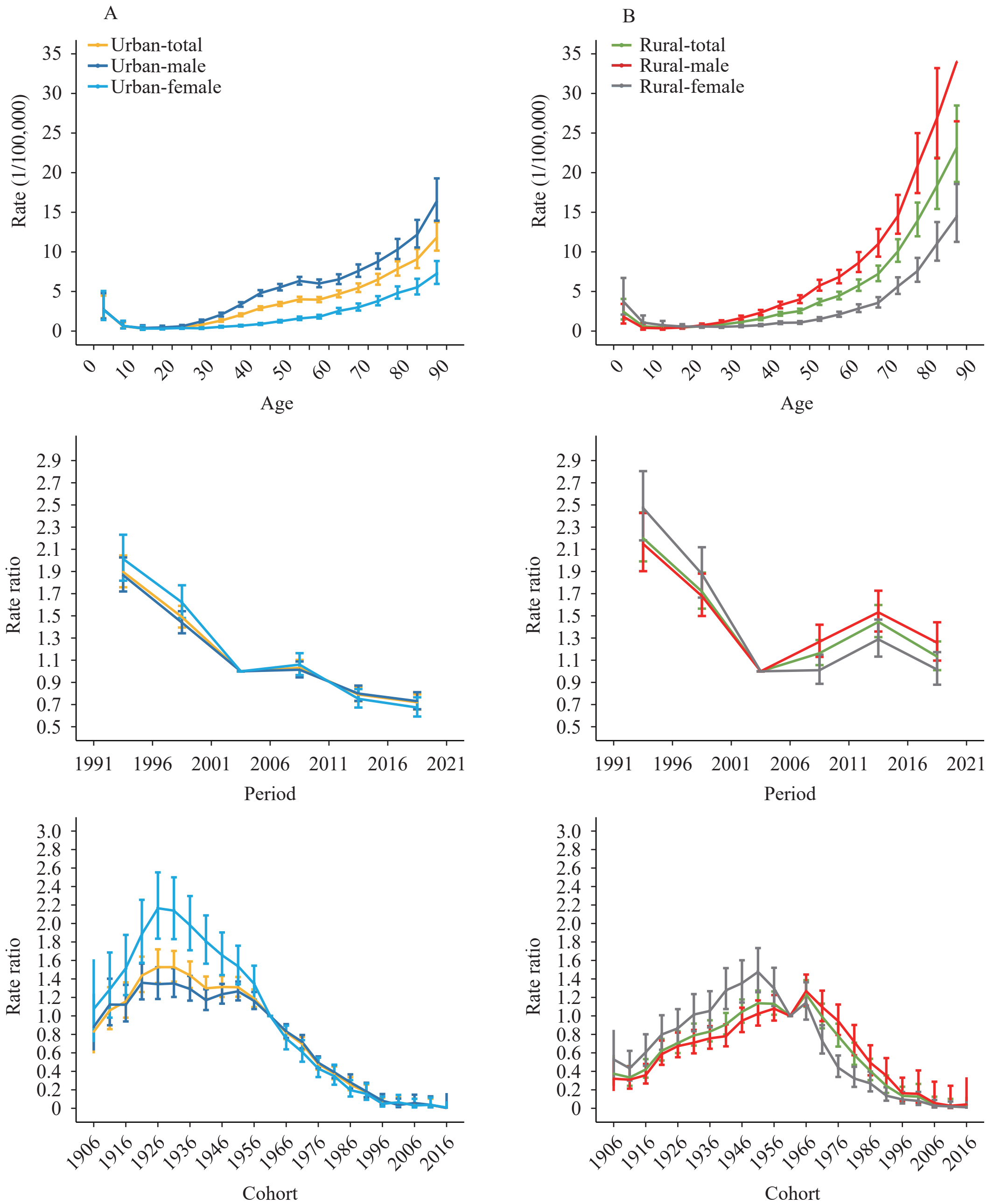

FIGURE 2. The effects of age, period, and cohort on age-standardized mortality rate of viral hepatitis in (A) urban and (B) rural China from 1987 to 2021.

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.

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Preplanned Studies

Trends and Patterns of Respiratory Tuberculosis Mortality in Rural and Urban — China, 1987–2021

Yihao Zhao[1,&]; Binbin Su[2,&]; Yaohua Tian[3,#]; Ruitai Shao[1,#]

Summary

What is already known about this topic?

In China, an estimated 780,000 individuals contract tuberculosis (TB) every year. With TB ranked as the second most prevalent disease in terms of the morbidity and mortality rates for legally infectious diseases, it imparts a substantial disease burden on families and society.

What is added by this report?

This study identifies specific periods and cohort effects related to trends in respiratory TB mortality in both rural and urban regions of China. The mortality rates have been found to decrease at an annual rate of 5.5% in urban regions and 6.6% in rural ones, with a more marked decline evident in rural areas. These findings represent a significant milestone in the prevention and treatment of respiratory TB in China, especially in its rural locales.

What are the implications for public health practice?

This research contributes to policymakers' comprehension, assisting in the early formulation of cogent optimization policies, thereby further supporting the United Nations Sustainable Development Goals (SDGs) and the Endeavor to End Respiratory TB Strategy. It is recommended that policymakers prioritize key groups such as children, young adults aged 20–30 in rural areas, and older men (60 years and over) in urban areas when developing these astute optimization policies.

Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (*1*), globally has a mean incidence rate of approximately 106.7 per 100,000 (*2*). It also emerges as one of the primary causes of death across the world (*3*). Despite longstanding preventive and control measures for TB in China (*4*), the nation ranks third-highest in TB incidence among the 30 countries with the highest TB burden (*2*). The urgent necessity to explore the disease's epidemiology and trajectory caters to shortcomings in the breadth of studies assessing long-range trends of respiratory TB mortality in China across geographical areas and genders. Our study seeks to furnish an all-encompassing scrutiny of temporal patterns to aid policymakers in responsibly devising optimization strategies. Data were derived from the National Health Commission (1954–2013, Ministry of Health; 2013–2018, National Health and Family Planning Commission), categorizing deaths in line with the International Classification of Disease 9th revision (ICD-9) and ICD-10 standard — the former being applied until 2002, followed by ICD-10. Utilizing National Health Commission data, via Joinpoint regression analysis and age-period-cohort (APC) models, we investigated the respiratory TB annual mortality rate estimates spanning 1987 to 2021. The Joinpoint regression model, endorsing a timeline trend evaluation method, facilitates a segmented regression formulation based on disease distribution time characteristics — thereby facilitating a more detailed appraisal of varying time spans within the aggregate respiratory TB mortality trend. To tackle the linear functional interrelationship problem between age effects, period effects, and cohort effects, APC models were deployed. Our outcomes indicate a persistent decline in mortality rates over time, particularly in rural zones. However, the gender divide has expanded over the years. For further abatement of respiratory TB mortality rates and to align with global control objectives, focused interventions should strategically prioritize key clusters like men and the elderly.

Table 1 illustrates the longitudinal trends of respiratory TB in China, disaggregated by region and gender. The data spans from 1987 to 2021 and reveals a compelling decrease in both crude and age-specific mortality rates across all specific populations. Higher mortality rates were observed in males versus females and in rural regions as compared to metropolitan ones. However, the disparity between urban and rural areas progressively lessened over time. In 1987, the age-specific mortality rate (ASMR) associated with respiratory TB in urban areas was 12.22 per 100,000,

TABLE 1. Joinpoint analysis of crude and age-standardized mortality rates from tuberculosis in urban and rural areas.

Tuberculosis	Mortality rate (per 100,000)		Total study period[§]		Period 1		Period 2		Period 3		Period 4	
	1987	2021	AAPC (%)	95% *CI*	Years	APC (%)	Years	APC (%)	Years	APC (%)	Years	APC (%)
Crude mortality												
Urban areas												
Total	9.83	1.25	−5.5*	(−8.5, −2.4)	1987–2000	−9.0*	2000–2003	12.8	2003–2006	−19.2	2006–2021	−2.7*
Male	12.88	1.93	−5.3*	(−6.4, −4.2)	1987–1997	−8.5*	1997–2021	−3.9*	–	–	–	–
Female	6.58	0.56	−6.8*	(−10.4, −3.0)	1987–2000	−11.1*	2000–2003	18.6	2003–2006	−25.5	2006–2021	−3.3*
Rural areas												
Total	20.21	1.65	−6.6*	(−8.4, −4.8)	1987–2001	−6.9*	2001–2005	−21.1*	2005–2021	−2.4*	–	–
Male	25.07	2.52	−6.1*	(−7.6, −4.6)	1987–2001	−6.9*	2001–2005	−18.6*	2005–2021	−1.9*	–	–
Female	15.17	0.74	−8.2*	(−10.2, −6.2)	1987–2001	−7.4*	2001–2008	−19.9*	2008–2016	2.9	2016–2021	−9.7*
Age-standardized mortality[†]												
Urban areas												
Total	12.22	0.78	−7.2*	(−10.9, −3.3)	1987–2000	−10.9*	2000–2003	18.5	2003–2006	−26.6	2006–2021	−4.1*
Male	16.27	1.29	−6.8*	(−10.4, −3.2)	1987–2000	−10.0*	2000–2003	14.7	2003–2006	−23.9	2006–2021	−4.1*
Female	7.69	0.32	−8.3*	(−13.1, −3.3)	1987–2000	−12.6*	2000–2003	24.7	2003–2006	−31.4	2006–2021	−4.8*
Rural areas												
Total	25.16	1.05	−8.3*	(−9.9, −6.6)	1987–2001	−7.7*	2001–2006	−20.1*	2006–2021	−4.6*	–	–
Male	33.06	1.71	−7.9*	(−10.0, −5.7)	1987–2002	−8.0*	2002–2005	−23.9*	2005–2021	−4.4*	–	–
Female	18.41	0.44	−9.9*	(−12.2, −7.4)	1987–2001	−7.8*	2001–2008	−22.0*	2008–2016	0.5	2016–2021	−12.8*

Note: "–" means no joinpoints identified.

Abbreviation: APC=annual percent change; AAPC=average annual percent change; *CI*=confidence interval.

* Significantly different from zero (P<0.05).

† Standardized to the WHO world standard population.

§ Years 1987 to 2021.

with a breakdown of 16.27 for males and 7.69 for females. Up to the year 2021, the rates witnessed a commendable average annual decline of −7.2%, −6.8%, and −8.3% respectively. As for rural regions, the ASMR stood at 25.16 per 100,000 in 1987 with notable rates of 33.06 per 100,000 for males and 18.41 per 100,000 for females. By 2021, the average annual decline had reached −8.3%, −7.9%, and −9.9%, respectively. Strikingly, despite initiating with higher respiratory TB mortality rates than their urban counterparts, rural regions demonstrated a faster rate of decline.

Figure 1 depicts the net-drift and local-drift of respiratory TB. net-drift refers to the average annual trend for the entire population throughout the research period, while local-drift signifies the average trend within specific age groups. The Net-drift demonstrated a significant reduction in respiratory TB mortality in both rural and urban areas of China for the time from 1987 to 2021. The mortality rate decreased by 9.21% [95% confidence interval (*CI*): −9.77% to −8.64%] in rural regions and 6.32% (95% *CI*: −6.82% to −5.81%) in urban areas. A more pronounced annual shift in overall respiratory TB mortality was noted among females compared to males. The Net-drifts for urban men and women were −5.81% (95% *CI*: −6.43% to −5.19%) and −7.76% (95% *CI*: −8.33% to −7.18%), respectively. The figures for rural men and women were −8.27% (95% *CI*: −8.83% to −7.70%) and −10.90% (95% *CI*: −11.58% to −10.22%), respectively. The local-drift showed a general enhancement in China's respiratory TB mortality control, particularly noteworthy among women aged 30–60. However, progression in reducing respiratory TB fatalities was relatively slight for the age groups 10–20 and those 70 years and over, although it remained generally below the 0 lines.

Figure 2 illustrates the influence of age, period, and cohort on the mortality rate of respiratory TB. The age-related effect revealed significant disparities between urban and rural areas. Mortality amongst urban males increased before declining with age, peaking at 75. Conversely, the mortality rate for women steadily decreased after reaching its apex at

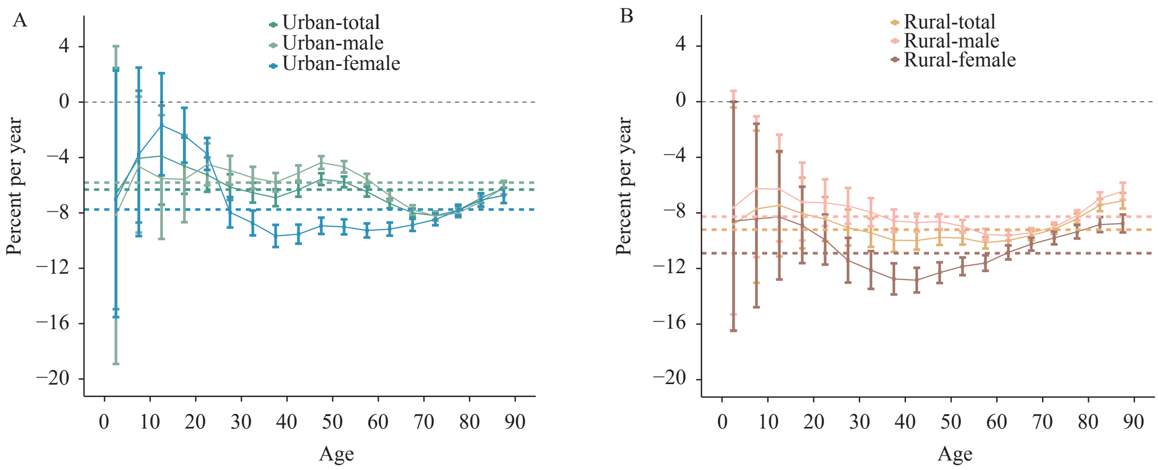

FIGURE 1. Local-drift and net-drift for tuberculosis mortality and urban-rural difference by sex in China from 1987 to 2021. (A) Urban area; (B) Rural area.

approximately age 20. For rural men and women, a consistent decline in the rates became apparent from age 25 onwards. Period effects demonstrated similar trends between rural and urban populations but showed a quicker decrease in rural areas than in metropolitan ones. Furthermore, the situation improved remarkably for females. Prior to 2003, females had higher rates than males, however, this pattern inverted post-2003, indicative of the significant success of respiratory TB control, particularly amongst rural females. The cohort effect exhibited similar patterns across both genders and locations. From 1900 to 1955, the mortality rate ratio of Chinese birth cohorts saw a significant reduction, especially in rural regions. As for the post-1960 birth cohorts, this decline has somewhat decelerated, yet continues to trend downward. The rural female birth cohort experienced the most substantial improvement.

DISCUSSION

This study revealed a continuous decline in tuberculosis (respiratory TB) mortality rates within China from 1987 to 2021, albeit at different rates between genders and geographical areas. Data from 1987 showed that the mortality rate due to respiratory TB in rural populations was 2.05 times higher than in urban areas. However, by 2021, the disparity had reportedly decreased to 1.32 times. The decline in mortality rates was documented at a rate of 5.5% and 6.6% per annum in urban and rural areas, respectively. Additionally, this study identified that the fastest trajectory of decreased respiratory TB mortality occurred from 1987 to 2000 in urban areas and from 2001 to 2008 in rural areas. Intriguingly, the rate of decline was more pronounced in rural areas compared to urban ones.

Significant gender disparities were observed in tuberculosis mortality rates. In the years 1987 and 2021, the male-to-female sex ratio for tuberculosis deaths stood at 1.96 and 3.44 in urban areas, compared to 1.65 and 3.45 in rural settings. This suggests a potential variation in TB risk factors according to gender, potentially linked to differing lifestyle behaviors, metabolic capabilities, and nutritional status (*5*). Another factor increasing the likelihood of TB infection is diminished immunity caused by chronic diseases (*6*).

The APC model revealed inconsistent variations in the age effects within urban and rural locales. In urban regions, the peak mortality rate for respiratory TB was observed among individuals aged between 70 and 80 years, while in rural areas, it reached its zenith among individuals in the 20–30 years age group. Up until the age of 25, women experienced a higher mortality rate in both urban and rural locations, but after the age of 30, the rate was higher among men. As age increased, this gender gap became particularly noticeable within urban areas (*7*). An analysis conducted in Jiangsu Province demonstrated that TB morbidity and mortality did not increase cumulatively with age. In fact, in women, mortality showed a downward trend post the age of 25 (*8*). Additional research is required to ascertain if age-related variables associated with TB risk could account for gender-specific and regional differences in these age effects. Throughout a 35-year observation period, we noted the cohort effect on

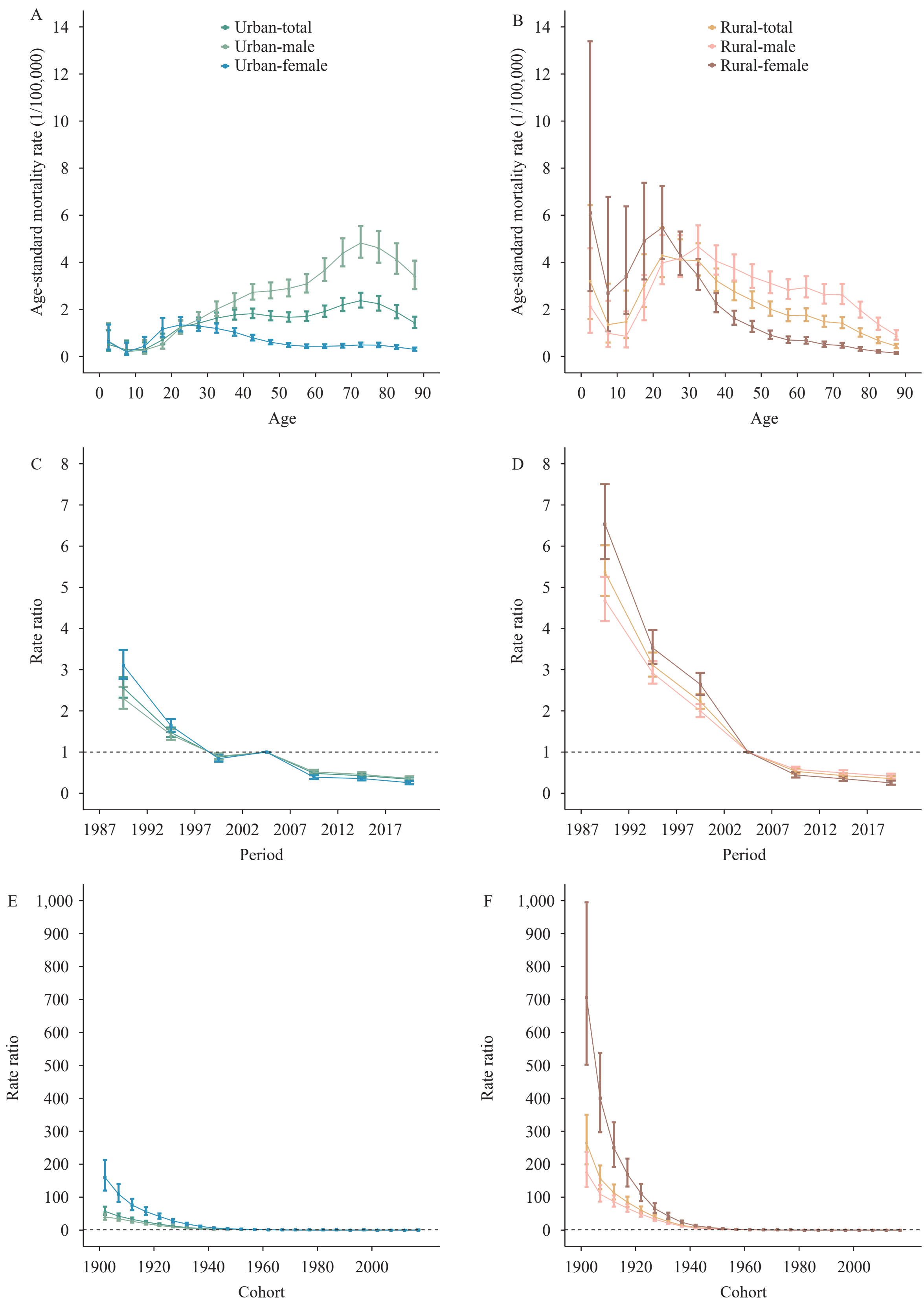

FIGURE 2. Parameter estimates of age, period, and cohort effects on tuberculosis mortality rate in urban-rural China from 1987 to 2021. (A) Age effects in urban areas; (B) Age effects in rural areas; (C) Period effects in urban areas; (D) Period effects in rural areas; (E) Cohort effects in urban areas; (F) Cohort effects in rural areas.

respiratory TB mortality declining in both rural and urban locations. This suggests individuals in more recent birth cohorts have a lower likelihood of TB-related mortality. This can be attributed to fast-paced economic growth, enhanced healthcare coverage (especially in rural areas), and rigorous respiratory TB control policies. For instance, China incorporated the WHO's TB control strategy in 1991, providing complimentary diagnostics for individuals exhibiting TB symptoms as well as free treatment for patients diagnosed with sputum smear-positive disease (*9*).

In conclusion, respiratory TB mortality trends exhibit significant variability across different regions, genders, and age groups. Priority groups for the prevention and control of respiratory TB are identified as children, rural young adults aged 20–30, and urban men aged 60 or older. According to the United Nations SDGs, global epidemics of tuberculosis must be extinguished by 2030 (*10*). To meet these targets, there is an urgent need for comprehensive strategies, such as tobacco control, promotion of healthy diets and nutrition security, the continued promotion of bacillus Calmette-Guérin vaccination, development of new TB vaccines, and improved diagnosis and treatment of drug-resistant tuberculosis. As specified in Healthy China 2030, there is also a need for an integrated service model for tuberculosis, aimed at curtailing the TB epidemic.

This study does have certain limitations. First, the effect quantified by the APC was derived from cross-sectional data, not data from cohorts. Second, the APC model does not include mortality data for respiratory TB in individuals under 20 years of age due to the exceptionally low incidence rate. Third, mortality data need to be further evaluated taking into consideration factors such as geographical divisions and significant socioeconomic disparities between local regions. Third, variances in the surveillance locations, populations under surveillance, and the determination of TB as the cause of death could potentially influence the results, given the extensive period over which the surveillance was conducted.

Conflicts of interest: No conflicts of interest.

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Preplanned Studies

Trends in Mortality and Prevalence of Reported HIV/AIDS Cases — China, 2002–2021

Zhihui Dou[1,&]; Yanan Luo[2,&]; Yan Zhao[1]; Xiaoying Zheng[3,#]; Mengjie Han[1,#]

Summary

What is already known about this topic?

Annually, only the incidence and mortality for Acquired Immune Deficiency Syndrome (AIDS) patients are officially disclosed.

What is added by this report?

For the first time, information detailing the reported rate, mortality rate, and prevalence rate trends of HIV, AIDS, and HIV/AIDS in China's entire population over the past two decades has been provided.

What are the implications for public health practice?

Our research overcomes the longstanding limitation of HIV/AIDS analysis as the sole denominator. Rather, it incorporates a comprehensive examination of the overall population, utilizing indicators and analytic methods from chronic disease analyses.

China has experienced rapid shifts in its population structure, which have notably influenced the prevalence rate of various diseases, including both infectious diseases and chronic conditions (*1*). The implementation of China's policy of free antiretroviral therapy (HAART) for Acquired Immune Deficiency Syndrome (AIDS) patients in 2004 has substantially lengthened the survival timeline of those affected, transforming AIDS from a deadly infectious disease to a manageable chronic condition (*2*–*3*). Therefore, significant changes have been observed in the epidemiological characteristics and mortality rate trends of AIDS. Our study investigates the trends in HIV/AIDS case reported rate, mortality rate, and prevalence rate in an attempt to understand the evolving epidemiological patterns and overarching changes in HIV/AIDS across China's entire population. This investigation provides valuable insights that could inform and enhance HIV/AIDS prevention and control strategies.

The data for this study was from the "China Comprehensive HIV/AIDS Prevention and Control Data Information System" downloaded on June 30, 2023, which included a historical database of HIV-infected individuals/AIDS patients reported before 2022 (infectious disease report cards). It also utilized historical population data from the China Disease Prevention and Control Information System, covering the years 2004 to 2021, which includes nationwide population data categorized by sex and age groups (year), as well as regional code data for different years and counties.

This study applied a multi cross-sectional analytical design, stratified by sex, age groups (year), and geographical regions (Eastern, Central, and Western regions). Annual reported rate, mortality rate, and prevalence rate related to reported HIV/AIDS cases were calculated. The reported rate (RR) was computed by dividing the number of reports in a given year by the population for that year, then multiplying it by 100,000, using the date of onset. Mortality rate for reported cases (MR) was determined using the date of all-cause death, calculated similarly to RR. The prevalence rate of reported cases (PR) was calculated using the combined total of surviving individuals at the start of the year, newly reported cases in that year, and subtracting annual reported deaths, all divided by the population for that year and multiplied by 100,000. The rates were age-standardized (ASR) based on the "2010 China Age-Standardized Population" for the above-mentioned crude rates (CR), consequently yielding SRR, SMR, and SPR. Classification of regions was determined using the "National Regional Code Table" (2023), dividing China into three regions: eastern provincial-level administrative divisions (PLADs) (Beijing, Tianjin, Hebei, Liaoning, Shanghai, Jiangsu, Zhejiang, Fujian, Shandong, Guangdong, Hainan), central PLADs (Shanxi, Inner Mongolia, Jilin, Heilongjiang, Anhui, Jiangxi, Henan, Hubei, Hunan), and western PLADs (Sichuan, Guizhou, Yunnan, Xizang, Shaanxi, Guangxi, Gansu, Ningxia, Qinghai, Xinjiang). The calculation of age (year) at onset (or death) required dividing the difference between the date of onset (or death) and the date of birth by 365.25. All data analysis was performed using

SAS software (version 9.4, NC, USA).

This study found that at the national level in China, the reported rate and mortality rate of HIV/AIDS have shown a long-term slow upward trend, but they started to decline in 2018. However, it was observed that the prevalence rate in the population has continued to slowly increase (Figure 1).

Nationally, the reported rate of HIV/AIDS escalated from 0.37 per 100,000 population in 2002 to 10.27 per 100,000 in 2018 [95% confidence interval (*CI*): 10.22–10.32], before receding to 8.41 per 100,000 in 2021 (95% *CI*: 8.36–8.46). A parallel trend was observed in the standardized reported rate of HIV/AIDS. HIV/AIDS associated mortality rate grew from 0.11 per 100,000 in 2002 to 2.59 per 100,000 in 2018 (95% *CI*: 2.40–2.45), subsequently decreasing to 2.43 per 100,000 in 2021 (95% *CI*: 2.40–2.45). The standardized mortality rate fell from 2.46 per 100,000 in 2018 to 2.08 per 100,000 in 2021. The prevalence rate of reported HIV/AIDS cases rose from 1.09 per 100,000 in 2002 to 60.21 per 100,000 in 2018, and further to 79.62 per 100,000 in 2021 (95% *CI*: 79.47–79.77). The standardized prevalence rate of reported HIV/AIDS cases increased from 62.02 per 100,000 in 2018 to 85.36 per 100,000 in 2021.

The reported rates of AIDS cases saw an increase from 0.26 per 100,000 population in 2002 to peak at 4.06 per 100,000 population in 2018, followed by a decline to 2.78 per 100,000 population in 2021. The standardized reported rate of AIDS showed a reduction

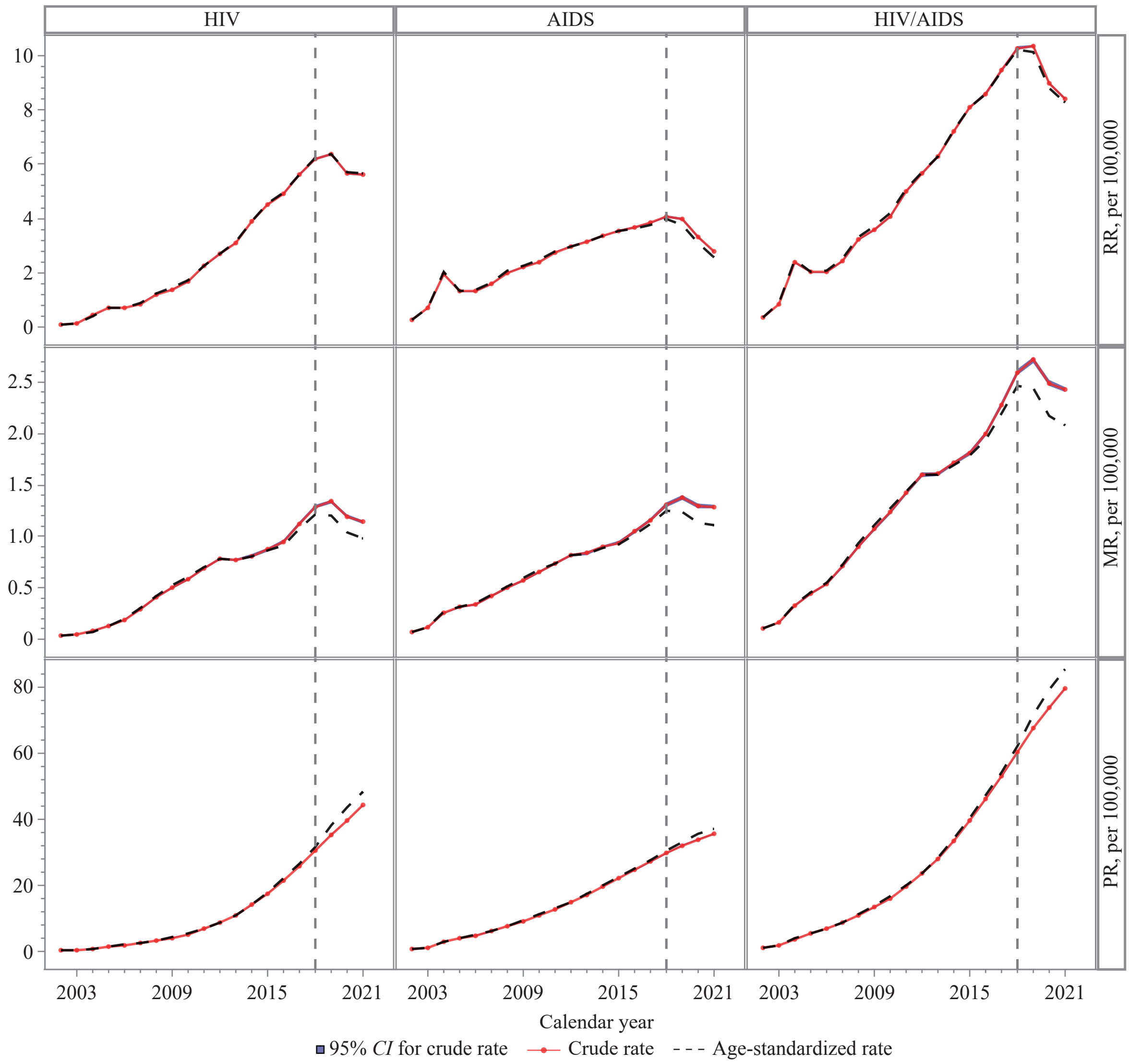

FIGURE 1. The trends of reported rate, mortality rate, and prevalence rate of reported HIV/AIDS cases in China, 2002–2021.
Abbreviation: RR=reported rate; MR=mortality rate; PR=prevalence rate; *CI*=confidence interval.

from 3.99 per 100,000 population in 2018 to 2.58 per 100,000 population in 2021. The mortality rate of reported cases saw a rise from 0.07 per 100,000 population in 2002 to 1.31 per 100,000 population in 2018, which then slightly decreased to 1.28 per 100,000 population in 2021 (95% *CI*: 1.27–1.31). The adjusted mortality rate showed a decrease from 1.25 per 100,000 population in 2018 to 1.11 per 100,000 population in 2021. The prevalence rate of reported cases increased from 0.64 per 100,000 population in 2002 to 29.66 per 100,000 population in 2018 and further to 35.46 per 100,000 population in 2021 (95% *CI*: 35.36–35.56). The standardized prevalence rate increased from 30.51 per 100,000 population in 2018 to 37.01 per 100,000 population in 2021.

The standardized reported rate of HIV saw an elevation from 0.10 per 100,000 in 2002 to 6.21 per 100,000 in 2018, before undergoing a subsequent decrease to 5.67 per 100,000 in 2021. The standardized mortality rate of these reported HIV cases experienced a similar growth, increasing from 0.13 per 100,000 in 2002 to 1.22 per 100,000 in 2018, followed by a drop to 0.98 per 100,000 in 2021. The standardized prevalence rate of HIV reported cases mounted from 0.43 per 100,000 in 2002, reaching 31.51 per 100,000 in 2018, and escalating further to 48.34 per 100,000 in 2021.

Sex-specific analysis indicates that peak values for reported rate, mortality rate, and prevalence rate of HIV/AIDS cases in males are 4.0, 3.5, and 2.86 times higher, respectively, compared to females (Figure 2A). Age-specific data demonstrate peak reported rates for HIV/AIDS cases in the following age groups: 0–14 years (0.71/100,000), 15–29 years (9.80/100,000), 30–44 years (12.73/100,000), 45–59 years (13.00/100,000), 60–74 years (15.90/100,000), and ≥ 75 years (8.41/100,000) respectively (Figure 2B). Region-specific analysis indicates similar reported rate, mortality rate, and prevalence rate of reported HIV/AIDS cases in the eastern and central regions. However, in the western region, peak values are, respectively, 3.56, 4.74, and 3.05 times higher than those reported in the central region (Figure 2C).

Our study reveals that at a national scale in China, there was a measured, consistent escalation in the reported rate, mortality rate, and prevalence rate of reported HIV/AIDS cases through 2018. Following this period, these trends partially inverted, indicating a decline in reported rate and mortality rate, which may be due to the effects of China's comprehensive HIV/AIDS prevention and control strategy and its overlapping impact of pandemic control efforts. Yet, the prevalence rate within the population maintained a slow upward trajectory. Two primary factors are likely contributors to the consistent escalation trends before 2018 as follows:

First, sustained efforts by the Chinese government in preventing, controlling, and actively treating HIV/AIDS have expanded the scope of HIV screening among the population, thereby contributing to an annual increase in the reported rate for HIV/AIDS cases, with HIV reported cases being the predominant contributor (*4*). Second, significant advancements in the therapeutic landscape for HIV/AIDS played a key role. The extensive application of the "Four Frees and One Care" policy initiated in 2004 proved to be a pivotal juncture in China's preventative and treatment initiatives for HIV/AIDS. Recently, over 90% treatment coverage has been achieved for HIV/AIDS patients in China, along with a treatment success rate surpassing 90% (*4*–*5*). The mortality rate among individuals receiving antiretroviral therapy for HIV/AIDS has now declined to less than 4 per 100 person-years (*6*), resulting in a marked enhanced life expectancy for patients. This extended life expectancy has led to a sustained accumulation of reported living HIV/AIDS cases, which in turn, drives the steadily ascending rate of prevalence. Collectively, these findings underscore the significant progress China has made in the prevention and control of HIV/AIDS.

Our findings indicate notable differences in the reported rate, mortality rate, and prevalence rate of reported HIV/AIDS cases across sex, age (year), and geographical regions. Males demonstrated a higher rate, mortality rate, and prevalence rate of reported HIV/AIDS cases than females. This difference may be attributed to variations in sex disparities in the mode of HIV/AIDS transmission (such as male-to-male transmission being predominant). Furthermore, the reported rate of HIV/AIDS varies with age, with a higher reported rate among older individuals, potentially because older individuals have more opportunities for HIV screening, and there is a greater accumulation of infected individuals in the elderly population.

Additionally, there is a significantly lower reported rate of HIV/AIDS in the central and eastern regions of China compared to its western regions. This could be attributed to the western regions of China (e.g., Yunnan, Sichuan, and Xinjiang) serving as the focal points of the HIV/AIDS epidemic. In the western

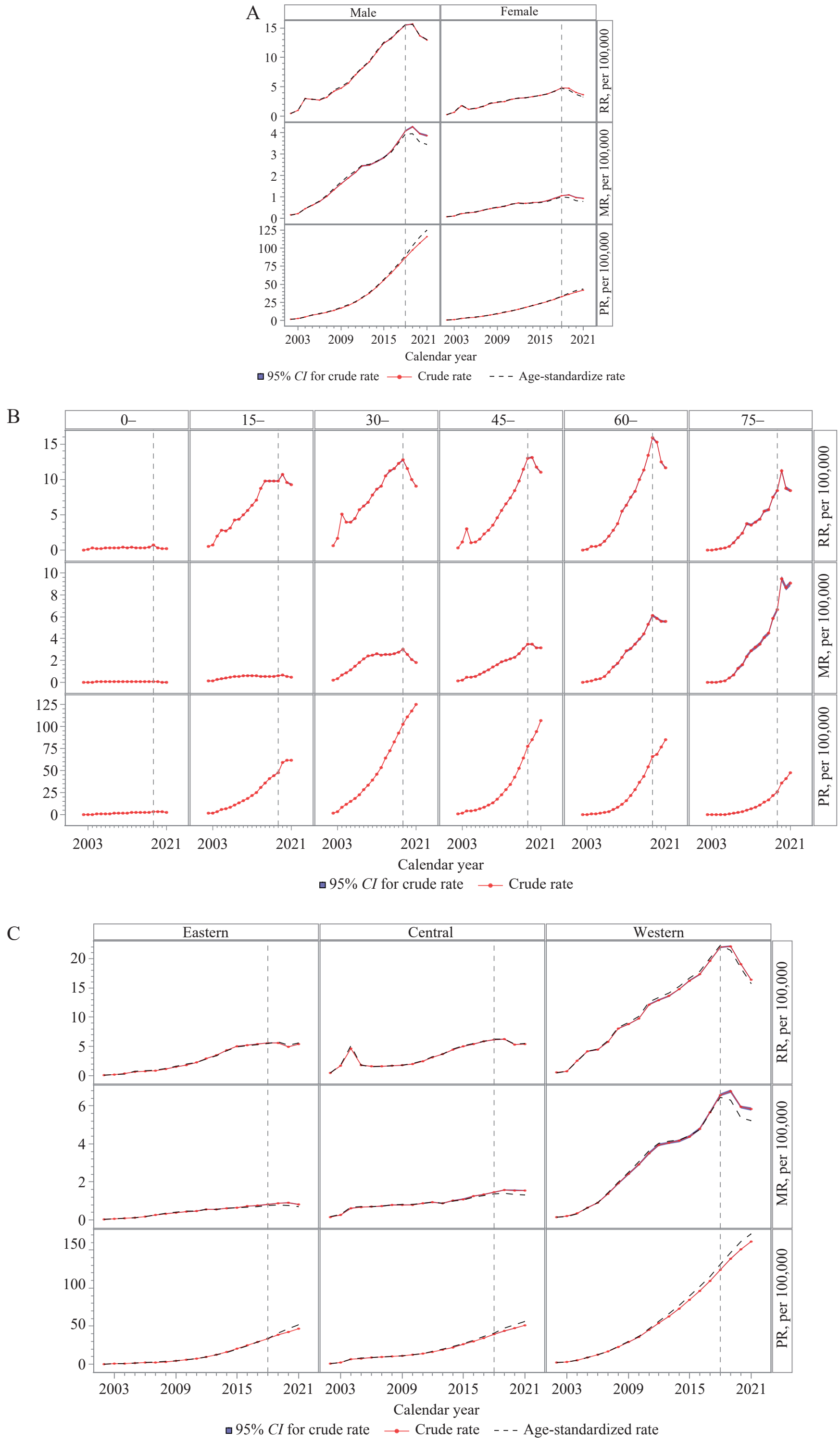

FIGURE 2. The trends of reported rate, mortality rate, and prevalence rate of reported HIV/AIDS cases in China, by (A) sex, (B) age groups (year), and (C) region, 2002–2021.
Abbreviation: RR=reported rate; MR=mortality rate; PR=prevalence rate; *CI*=confidence interval.

areas, the HIV/AIDS outbreak initially stemmed from intravenous drug use as the primary mode of transmission, with heterosexual transmission being predominant, which stood in contrast to the primary transmission routes in the eastern areas. And these disparities may contribute to the comparatively elevated reported rate, mortality rate, and prevalence rate of reported HIV/AIDS cases in the western regions.

Our manuscript is subject to several limitations. First, our analyses are largely dependent on case-reported data, which chiefly represents reported cases of HIV/AIDS, as opposed to actual case numbers. Further investigation into this aspect is required. Second, this research adopts a descriptive study approach, omitting inferential analyses concerning trend alterations, tipping points, or contributing factors related to HIV/AIDS.

To summarize, data from China indicates a steady, the incremental increase in the reported rate, mortality rate, and prevalence rate of reported HIV/AIDS cases through 2018. Subsequent reversal trends suggest a decline, yet the cumulative prevalence rate among the population continued its slow incline. These increasing trends can be largely accredited to the relentless efforts made by the Chinese government in HIV prevention, control and effective treatment strategies. These efforts, coupled with a significant reduction in AIDS-related mortality rate and marked improvements in patient life expectancy, play a pivotal role in the continued rise in the number of people living with HIV/AIDS. The findings of our research could provide valuable insights to support the future monitoring and prevention efforts for HIV/AIDS.

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Perspectives

Epidemiological Shifts in Infectious Diseases in China: Implications and Policy Recommendations

Binbin Su[1,&]; Zuliyaer Talifu[2,&]; Luzhao Feng[1,3,4,#]

ABSTRACT

In recent decades, China has experienced significant alterations in its landscape of infectious diseases, with noteworthy reductions in historically prevalent illnesses such as tuberculosis and viral hepatitis. At the same time, emerging pathogens like severe acute respiratory syndrome (SARS), Influenza A virus subtype H7N9 (H7N9), and SARS coronavirus 2 (SARS-CoV-2) pose new challenges. These epidemiological shifts, fueled by fast economic development, urbanization, modifications in the healthcare system, and an aging population, present considerable obstacles to the country's public health infrastructure and policy frameworks. This article provides a comprehensive review of these changes, underscoring the driving forces behind them and the resultant impact on health policy and infrastructure. It stresses the challenges and calls for an intensification of surveillance efforts, the establishment of collaborative partnerships both nationally and internationally, the encouragement of worldwide cooperation, and the reinforcement of public health education as pivotal strategies for managing China's changing spectrum of infectious diseases.

Since the founding of the People's Republic of China, the initiation of national immunization programs, infectious disease surveillance and early warning systems, along with public health education campaigns, has substantially diminished the spread and outbreak of infectious diseases. Consequently, morbidity and mortality rates from major infectious diseases have significantly declined over the past decades (*1*).

Historically, infectious diseases were the primary cause of mortality in the early days of China. Today, however, the epidemiological profile has drastically evolved. Presently, nine of the top ten causes of death in China are attributed to chronic non-communicable diseases, with road traffic injuries being the lone exception (*2*). The risk once associated with numerous infectious diseases has waned, making them rare incidents in contemporary times. These shifts in public health have considerably enhanced the average life expectancy, providing benefits not only to the Chinese population, but also having a positive global impact (*3*).

The National Health Commission's 2021 report revealed a total of 2,711,785 reported instances of 27 Class A and B notifiable infectious diseases in China. This equates to an incidence rate of 192.58 per 100,000. Among these, bloodborne and sexually transmitted diseases accounted for a rate of 131.03 per 100,000, with intestinal infectious diseases at a markedly low 7.42 per 100,000. In spite of the overall decline in conventional infectious diseases, China continues to be susceptible to the outbreak of new and unpredictable forms of infection. The severe acute respiratory syndrome (SARS) epidemic of 2003, recurring mutations in zoonotic diseases, and the ongoing SARS coronavirus 2 (SARS-CoV-2) pandemic highlight this susceptibility. Such incidents serve as potent reminders of the continuing fight against infectious diseases and emphasize the pressing need for more stringent control measures.

ISSUES AND CHALLENGES

Emerging Infectious Diseases: Uncertainty and Complexity

Emerging infectious diseases present a significant degree of uncertainty and complexity, both in their inherent characteristics and management strategies (*4*). Determining the origins and transmission pathways of these diseases is an intricate task, necessitating an integration of various methodologies. These include field epidemiological investigations, sample procurement and pathogen identification, as well as molecular or sero-testing, and transmission dynamics modeling studies. Definitive conclusions typically demand extensive and time-consuming research initiatives.

The acceleration of population mobility has further propagated the dissemination of emerging infectious diseases (*5*). These novel strains, unrecognizable to the human immune system, can rapidly proliferate within brief periods. Some of these diseases may not immediately produce apparent symptoms in patients, thus posing challenges in monitoring their propagation. Additionally, certain diseases have the potential to disperse through various modes, including airborne, contact, or droplet transmission, thereby complicating containment operations.

The recent surge in zoonotic and respiratory infections underscores the unpredictable character of emerging diseases. The early dissemination of respiratory ailments, taking SARS-CoV-2 for example, posed substantial challenges. Simultaneously, zoonotic diseases like avian influenza and monkeypox, notable for their frequent strain variations, emphasize the importance of vigilance and underscore the value of addressing environmental risks in disease prevention.

Delays in Vaccine and Drug Development

Vaccines and pharmaceuticals serve as crucial tools in the control of infectious diseases, with several such diseases being significantly impaired or effectively managed through large-scale immunization initiatives (*6*). Nonetheless, the development of these countermeasures is inherently sluggish due to the complex characteristics of infectious agents, rigorous regulatory criteria, protracted research phases, substantial financial commitments, and intrinsic risks. For novel pathogens, an in-depth understanding is essential in crafting specific vaccines or drug regimens. Moreover, exhaustive evaluations ensure safety and effectiveness. However, mutations in pathogens can diminish the efficacy of newly developed vaccines or pharmaceuticals, thereby posing substantial challenges in disease management.

The Deficiency in Global Collaboration and Information Sharing

The worldwide proliferation of emerging infectious diseases has escalated given the amplification in global interconnectivity. Despite this, there remains a lack of robust global systems for cooperation and data dissemination. The SARS-CoV-2 crisis underscored the essentiality of global concordance, yet it also unveiled multiple challenges such as media controversies, technological barriers, and disparities in resource allocation (*7*). The divergence in cultural norms, political ideologies, and commercial interests often pose considerable barriers to international unity, subsequently sabotaging cooperative efforts to combat diseases. The global response efforts are further strained by challenges such as inconsistent data sharing, disparate technological capabilities, and issues associated with intellectual property rights.

The Dilemma of Talent Cultivation

Addressing infectious diseases requires persistent commitment, broad-ranging policies, and unwavering governmental backing. The extensive costs associated could dissuade investment, leading to a shortage of specialized professionals. The multidisciplinary and societal-wide strategies needed to combat infectious diseases pose obstacles in training versatile experts. Current public health education may be lacking in areas central to these efforts, including infectious disease control, epidemiology, health policy, and health system management. Deficiencies in curriculum and practical training may limit professionals' preparedness. Further, the absence of interdisciplinary and inter-sectoral collaboration in education impedes the development of professionals equipped for effective, multifaceted cooperation. A reconsideration and revision of the public health education curriculum and training programs to enhance practical experience, encourage academia-practice collaboration, and bolster multidisciplinary training might better align education with the shifting needs of public health.

The Influence of Public Anxiety on Information Distortion

In today's digital era, the rapid and extensive dissemination of information is possible. Notwithstanding, the emergence of infectious diseases often incites increased public anxiety and the proliferation of distorted information (*8*). A prevalent lack of comprehension among the public can foster misconceptions about the disease, including its transmission, severity, and preventative strategies. Misinformation can swiftly multiply during disease outbreaks, thereby intensifying public fears and impeding disease control efforts.

IMPLICATIONS FOR POLICY

Enhancing the System for Infectious Disease Prevention and Control

Historical outbreaks such as the SARS epidemic of

2003 emphasize the crucial need for an adaptable response framework. China's implementation of a comprehensive disease prevention and control system, encompassing a broad surveillance network and the creation of a sophisticated early warning platform, is laudable. However, to ensure the efficiency of these systems, continuous policy support, financial investment, and talent engagement are necessary. Capitalizing on the capabilities of detection, risk assessment, and early warning, and maintaining preparedness through regular desktop and practical exercises, is crucial. The eradication of information silos across departments can facilitate "early detection, early prevention, and evidence-based control." Clear policies must be established, mandating interdepartmental data sharing and delineating roles.

Improving Technological Responses to Emerging Disease Outbreaks

The merging of modern technology with infectious disease control considerably boosts the alacrity and accuracy of response initiatives. Progressive early outbreak warning paradigms feature intelligent systems with multi-trigger, multi-channel capabilities. Cutting-edge sensing technology, remote data monitoring, and real-time analysis form critical components of these forward-thinking strategies. Leveraging big data, artificial intelligence, and machine learning uncovers crucial outbreak patterns, enabling health authorities to make well-informed decisions. Additionally, advancements in genetic engineering and microbiomics accelerate vaccine development processes, fortifying a more robust public health response (*9*).

Promoting Global Collaboration: An Empirical Study

The global emergence of infectious diseases underscores the essentiality of international collaboration in the quick detection, comprehension, and mitigation of novel infectious threats. This collaborative effort, epitomized by the Global Health Security Agenda (GHSA), encourages the dissemination of critical information and resources such as pathogen specimens, genetic sequences, and transmission vectors, thereby refining containment strategies. The recent SARS-CoV-2 pandemic underlines this scenario, where international cooperation facilitated the urgent sharing of viral sequences and the development of vaccines and therapeutics. Furthermore, the collaborative efforts between the Global Vaccine Alliance (GAVI) and the World Health Organization (WHO) demonstrated how global cooperation can deliver vaccines to low-income nations, thereby mitigating the impact of pandemics on a global scale (*10*).

Formulating Effective Risk Communication and Public Health Education Strategies

The widespread use of social media platforms has largely eradicated geographical limitations in information dissemination. It is crucial to establish authoritative channels for risk communication and public health education. By accurately conveying scientific information, providing accurate preventive guidance, and promoting public involvement in containment measures, we can mitigate potential public anxiety and misinformation.

Enhancing Preventative Measures and Sustaining the Patriotic Health Movement

The recent pandemic has underscored the importance of swift, effective preventative measures. Consistent hygiene practices including mask usage and frequent hand cleaning are crucial in curtailing the spread of disease. China's public health strategy is greatly bolstered by the Patriotic Health Movement, which places a strong emphasis on preventative techniques to maintain and improve societal health. Over the years, this initiative has been a key factor in public health successes. Therefore, it is crucial to continuously revise and adapt its guidelines to align with evolving circumstances, truly embodying the principle of preventative health as a societal responsibility.

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