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Joinpoint regression and age period cohort analysis of global and Chinese HIV incidence trends from 1990 to 2021

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In China and globally, to analyze the temporal trends of HIV incidence and age, period and cohort effects from 1990 to 2021. A Joinpoint regression model was applied to analyze the time-varying trends of standardized HIV incidence rates worldwide and in China from 1990 to 2021, using data from the Global Burden of Disease Study 2021. The study also explored the effects of age, period, and cohort on HIV incidence trends. From 1990 to 2021, the global standardized incidence of AIDS increased initially and then declined, with females experiencing a higher disease burden than males. In China, the burden was greater in males than females. The age–period–cohort model revealed that the global risk of AIDS incidence peaked between ages 60 and 69, while in China, it was highest between ages 75 and 79. From 1990 to 2021, the global and Chinese standardized incidence rates of AIDS generally followed an increasing trend before declining, with notable gender differences and the highest incidence rates observed in older populations. It is important to address the issues related to AIDS among the elderly and develop targeted health policies to reduce societal burdens and improve public health.

Keywords AIDS, Incidence, Joinpoint regression, Age–period–cohort

Acquired immune deficiency syndrome (AIDS), caused by human immunodeficiency virus (HIV), is a deadly infectious disease with high morbidity and mortality rates, posing a significant threat to human health[1]. HIV infection is characterized by a typically long incubation period, with an asymptomatic period of 2–10 years from initial infection to the onset of AIDS[2]. During this period, the virus persists through blood, sexual contact, and vertical transmission from mother to child, and infected individuals may become a hidden source of transmission due to the lack of typical clinical symptoms[3]. Despite being recognized for over 40 years, HIV remains a leading global sexually transmitted disease (STD)[4,5]. Since 1981, nearly 80 million AIDS cases have been reported worldwide, resulting in over 35 million deaths[6]. The Centers for Disease Control and Prevention (CDC) defines individuals aged 50 and above as older adults among those infected with HIV[7]. With the progress of antiretroviral therapy (ART), survival rates for AIDS patients have improved, and the growing number of newly infected older adults has led to a significant increase in AIDS patients aged 50 and above[8]. Emphasized the significant gender differences in HIV incidence, highlighting the importance of studying HIV trends from a demographic perspective at the national level[9]. The current study employed the Joinpoint regression model to analyze the temporal trends in standardized HIV incidence rates globally and in China from 1990 to 2021, investigating the influence of age, period, and cohort on these trends. The goal is to provide a scientific foundation for the development of public health policies aimed at AIDS prevention and control and for optimizing the allocation of health resources.

Methods

Source of information

The data for this study were sourced from the Global Burden of Disease Study 2021 (GBD 2021), which employs the International Classification of Diseases (ICD-10) to classify the diseases analyzed. The GBD 2021 burden of disease and injury analysis utilized 100,983 data sources to estimate metrics such as years of disability life lived (YLDs), years of life lost (YLLs), disability-adjusted life years (DALYs)for 371 diseases and injuries. Counts and age-standardized rates were calculated from 1990 to 2021 for 7 super-regions, 21 regions, 204 countries and

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territories (including 21 countries with subnational locations) and 811 subnational locations worldwide[10]. For data screening of the GBD2021 database, the disease "HIV/AIDS", regions "China" and "Global", and year range "1990–2021" were selected. The gender selection included "all-sex", "male" and "female". 15–79 year olds were selected for this study because of the paucity of data on HIV prevalence among those under 15 and over 79 years of age. Each age group spans 5 years, making a total of 13 age groups. The data on HIV prevalence stratified by sex, age group (15–19, 20–24, , 70–74, 75–79 years) in GBD 2021 were pooled.

Statistical analysis

The joinpoint regression model uses the Monte Carlo permutation test to determine the best-fit model[11]. In this study, standardized incidence, DALY rates, YLD rates and YLL rates were calculated in units per 100,000 person-years by direct standardization method, and their long-term change trends in the world and China from 1990 to 2021 were analyzed by the joinpoint model. Annual rates of change (APC), annual rates of change (AAPC) and 95% confidence intervals were calculated. The Joinpoint regression model can be expressed as E[y│x] = e^(β_0 + β_1 χ + δ_1 (χ−τ_1)^ + + _… + δ_k (χ−τ_k)^ +), in which y is the incidence rates, x refers to the year, β is a constant term, and δ, τ, and k denote regression coefficients of each segmented function, unknown turning points, and turning points, respectively. AAPC > 0, the incidence of the disease is increasing in that time period; conversely, if AAPC < 0, the incidence is decreasing in that time period. Similarly, AAPC > 0 and AAPC < 0 indicate that the incidence rates is increasing and decreasing over time, respectively; AAPC = APC indicates a monotonically increasing or monotonically decreasing trend. The APC model was used to analyze the effects of age, period, and birth cohort on HIV incidence. Age and period were spaced 5 years apart, and cohort was period minus age. The effect coefficients of age, period and cohort were estimated using the endogenous factor method (IE), and then relative risk (RR) was obtained, RR = EXP (effect coefficient). When the effect coefficient < 0, the risk of morbidity is reduced; when the effect coefficient > 0, the risk of morbidity is increased. In this study, we used EXCEL to organize the data, Joinpoint (version 4. 9. 0. 0) to analyze the time trend, and Stata1 software to construct the APC model, with the test level of α = 0. 05.

Results

Trends in the incidence of AIDS

Between 1990 and 2021, the global standardized incidence rates of AIDS generally showed an upward and then a downward trend, with the burden of AIDS disease being higher among women than among men. However, the burden of disease is higher for men than for women in China. The global standardized incidence rates of AIDS declined from 36.54 per 100,000 in 1990 to 20.77 per 100,000 in 2021; among them, the incidence rates of AIDS among men declined from 33.69 per 100,000 in 1990 to 21.16 per 100,000 in 2021; it is worth noting that the trend of change in the incidence rates of AIDS among women is larger, from 39.52 per 100,000 in 1990 to 20.44 per 100,000 in 2021. The global standardized HIV incidence rates has decreased by an average of 1.80% annually (AAPC = − 1.80%, $p < 0.001$). The decline in female incidence has been more pronounced, with a decrease of 2.11% per year (AAPC = − 2.11%, $p < 0.001$). Joinpoint analysis revealed that, while the global HIV incidence rates is declining, China experienced an average annual increase of 3.99% in its standardized HIV incidence rates from 1990 to 2021 (AAPC = 3.99%, $p < 0.001$), and the standardized HIV incidence rates in men increased by an average of 4.26% per year (AAPC = 4.26%, $p < 0.001$), and the standardized incidence rates of AIDS in females increased by an average of 2.98% per year (AAPC = 2.98%, $p < 0.001$) from 1990 to 2021. See Table 1 and Fig. 1. Global AIDS DALY rates began to rise in 1990, peaked and declined in 2002–2005, while China is generally on the rise. Data are as follows: global AIDS DALY rates increased from 346.90/100,000 in 1990 to 496.40/100,000 in 2021, and China increased from 6.75/100,000 in 1990 to 83.47/100,000 in 2021;global AIDS YLD rates increased from 18.23/100,000 in 1990 to 50.76/100,000 in 2021, and China increased from 0.66/100,000 in 1990 to 4.89/100,000 in 2021;global AIDS YLL rates from 328.67/100,000 in 1990 to 445.63/100,000 in 2021, and China from 6.09/100,000 in 1990 to 78.57/100,000 in 2021. See Figs. 2, 3 and 4.

Age–period–cohort modeling of HIV incidence

Age effect

The global risk of HIV incidence tends to increase and then decrease with age, with the highest risk of incidence for males in the age group 60–64 years (with an effect size of 0.93), followed by the age group 65–69 years (with an effect size of 0.88). For women, the risk of AIDS peaked at age 65–69 (with an effect factor of 1.04), followed by age 70–74 (with an effect factor of 0.70). In China, the risk of AIDS also peaks at age 75–79 (with an effect factor of 0.73), as shown in Fig. 5.

Time effect

The global risk of HIV incidence shows an increasing and then decreasing trend over time from 1990 to 2021, reaching a peak in 1995–1999 (with an effect coefficient of 0.25). The risk of HIV incidence in China peaked from 2005 to 2009 (with an effect coefficient of 0.90), and then declined year by year over time. See Fig. 6.

Cohort effects

The global risk of HIV incidence has been generally decreasing over birth cohorts. For males, the risk decreased from 0.24 in 1915–1919 to − 0.82 in 2005–2009, a decrease of 2.89%. For females, the risk decreased from 0.54 in 1930–1934 to − 0.81 in 2010–2014, a decrease of 3.87%. The risk of AIDS incidence in China has generally shown an upward and downward fluctuating trend as the birth cohort has progressed, with the risk of incidence for males decreasing from 0.97 in 1915 to 1919 to − 0.49 in 1925 to 1929, a decrease of 4.30%, and increasing from − 0.57 in 1980 to 1984 to 1.00 in 2000 to 2004, an increase of 5.08%. The risk of morbidity for females decreased

Sex name	Year	APC (95%CL)	T	p	AAPC (95%CL)	Z	p
Global Both	1990–1992	9.04 (7.55 to 10.56)	13.19	< 0.001	− 1.80 (− 1.92 to 1.67)	− 27.70	< 0.001
Global Both	1992–1995	3.18 (2.73 to 3.63)	15.09	< 0.001			
Global Both	1997–2006	− 5.21 (− 5.35 to − 5.07)	− 74.72	< 0.001			
Global Both	2006–2016	− 1.71 (− 1.84 to − 1.59)	− 28.85	< 0.001			
Global Both	2016–2021	− 4.63 (− 4.92 to − 4.33)	− 32.29	< 0.001			
Global male	1990–1992	8.21 (7.10 to 9.33)	16.31	< 0.001	− 1.50 (− 1.61 to 1.38)	− 25.40	< 0.001
Global male	1992–1997	3.24 (2.90 to 3.57)	20.82	< 0.001			
Global male	1997–2006	− 4.51 (− 4.62 to − 4.40)	− 87.43	< 0.001			
Global male	2006–2012	− 2.09 (− 2.32 to − 1.87)	− 19.54	< 0.001			
Global male	2012–2016	− 1.07 (− 1.58 to − 0.56)	− 4.47	< 0.001			
Global male	2016–2021	− 3.92 (− 4.14 to − 3.70)	− 36.94	< 0.001			
Global female	1990–1992	9.28 (7.89 to 10.68)	15.14	< 0.001	− 2.11 (− 2.31 to 1.91)	− 20.40	< 0.001
Global female	1992–1995	3.99 (2.67 to 5.33)	6.68	< 0.001			
Global female	1995–1998	− 0.03 (− 1.30 to 1.25)	− 0.06	0.954			
Global female	1998–2006	− 6.03 (− 6.19 to − 5.87)	− 79.47	< 0.001			
Global female	2006–2014	− 1.40 (− 1.57 to − 1.23)	− 18.04	< 0.001			
Global female	2014–2018	− 3.75 (− 4.36 to − 3.13)	− 13.03	< 0.001			
Global female	2018–2021	− 6.19 (− 6.79 to − 5.59)	− 21.81	< 0.001			
China Both	1990–1992	25.53 (16.13 to 35.7)	6.14	< 0.001	3.99 (3.19 to 4.80)	9.87	< 0.001
China Both	1992–1996	10.88 (6.64 to 15.28)	5.57	< 0.001			
China Both	1996–2003	16.64 (15.12 to 18.19)	24.59	< 0.001			
China Both	2003–2014	− 6.64 (− 7.2 to − 6.07)	− 23.82	< 0.001			
China Both	2014–2021	0.34 (− 0.7 to 1.39)	0.68	0.506			
China female	1990–1994	20.13 (18.02 to 22.28)	22.02	< 0.001	2.98 (2.12 to 3.84)	6.86	< 0.001
China female	1994–1997	6.78 (0.95 to 12.95)	2.49	0.025			
China female	1997–2001	18.51 (15.23 to 21.88)	12.9	< 0.001			
China female	2001–2004	2.35 (− 3.24 to 8.26)	0.88	0.392			
China female	2004–2013	− 8.13 (− 8.69 to − 7.56)	− 29.5	< 0.001			
China female	2013–2021	− 0.09 (− 0.7 to 0.52)	− 0.32	0.751			
China male	1990–1992	26.01 (18.28 to 34.24)	7.79	< 0.001	4.26 (3.36 to 5.16)	9.45	< 0.001
China male	1992–1996	9.71 (6.3 to 13.24)	6.25	< 0.001			
China male	1996–2001	19.15 (16.79 to 21.56)	18.67	< 0.001			
China male	2001–2004	9.42 (2.71 to 16.56)	3.03	0.008			
China male	2004–2014	− 6.74 (− 7.28 to − 6.2)	− 25.76	< 0.001			
China male	2014–2021	0.15 (− 0.69 to 1)	0.38	0.712			

Table 1. APC and AAPC (%) for global and Chinese standardised HIV incidence, 1990–2021.

from 0.75 in 1915–1919 to − 0.59 in 1925–1929, a decrease of 3.81%, and increased from − 0.58 in 1980–1984 to 2.28 in 2005–2009, an increase of 5.26%. See Fig. 7.

Discussion

In this study, we explored the temporal trends of HIV incidence using the APC model with the IE algorithm and joinpoint regression analysis,and systematically assessed the long-term trends of global and Chinese AIDS incidence rates from 1990 to 2021. The results show that AIDS incidence and DALY rates have experienced an "upward and then downward" trend globally, and the burden of AIDS disease is higher among women than men. In China, the incidence of AIDS has been increasing, then decreasing, and then leveling off,DALY rates are on a slow upward trend,especially in the male population and the elderly. The difference in HIV incidence between China and the rest of the world may be due to the following reasons:

In recent years, the gradual decline in the global standardized incidence rates and DALY rates of AIDS is related to the strengthening of global measures for the prevention, testing, and treatment of HIV. The widespread use of ART has not only increased patient survival but also significantly reduced virus transmission rates. In addition, governments and international organizations have dedicated substantial resources to preventing HIV spread, particularly through interventions targeting high-risk groups, such as the use of pre-exposure prophylaxis (PrEP) and promoting safer sex practices[12]. These combined efforts have contributed to the decline in global AIDS incidence over the past three decades, with a more significant reduction observed in women. This may be due to higher adherence to HIV prevention strategsies and better access to treatment for women[13,14]. Women globally have a higher incidence of HIV than men and are more susceptible to HIV-1 infection due to factors such as viral load differences, hormonal levels, and immune response disparities between the sexes[15]. Although

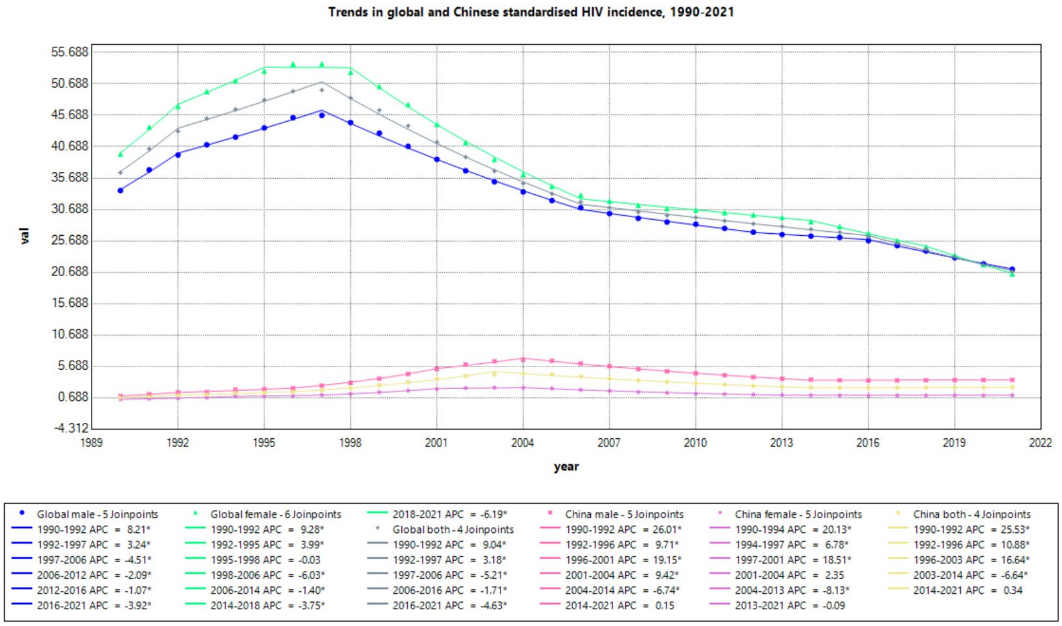

Fig. 1. Trends in global and Chinese standardised HIV incidence, 1990–2021. *Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.

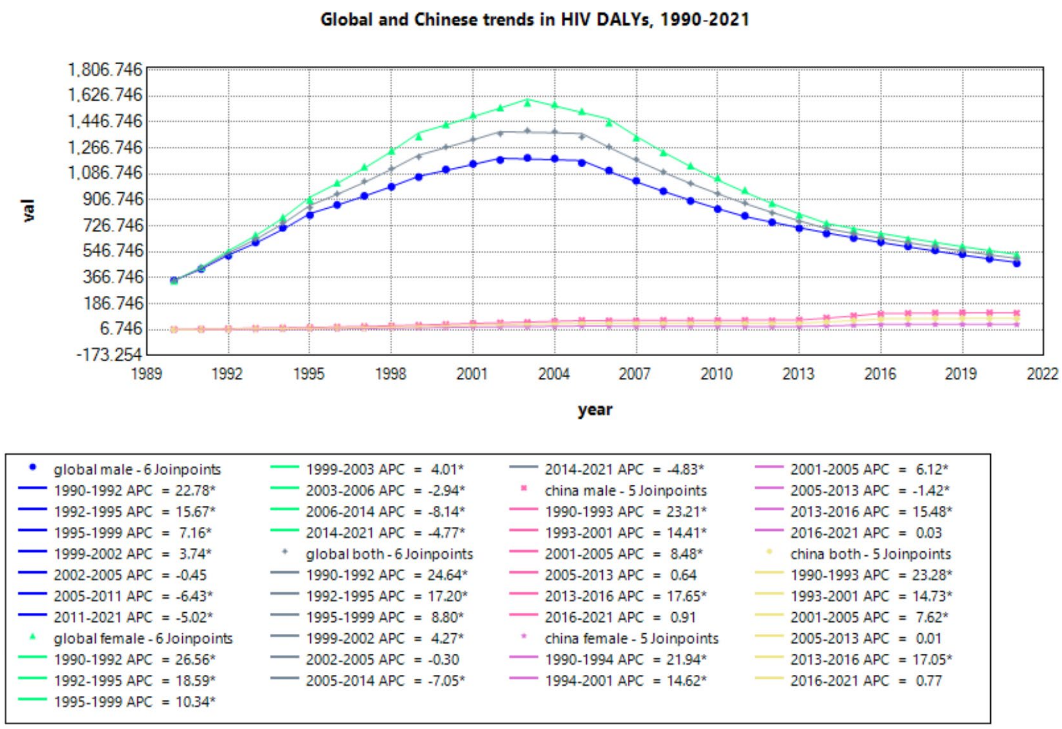

Fig. 2. Global and Chinese trends in HIV DALYs, 1990–2021. *Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.

the global standardized incidence of AIDS has declined, China's standardized incidence of AIDS has increased by an average of 3.99% per year from 1990 to 2021. Possible explanations include the following: China's rapid socio-economic development in recent years has led to significant changes in the lifestyles of the population, especially in the male population, with an increase in the prevalence of high-risk sexual behaviors, including sexual behaviors without condom use and the phenomenon of multiple sexual partners. The size of China's migrant population and men who have sex with men (MSM) groups has been expanding, and these groups often suffer from low HIV testing rates and weak awareness of prevention and treatment, resulting in a higher risk of

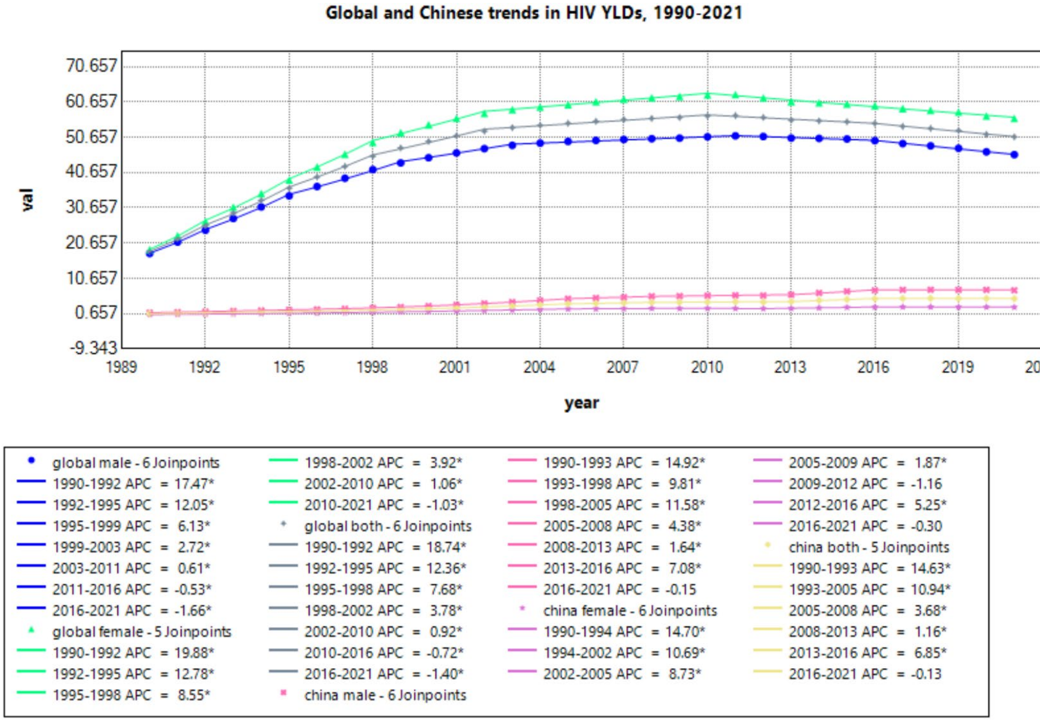

Fig. 3. Global and Chinese trends in HIV YLDs, 1990–2021. *Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.

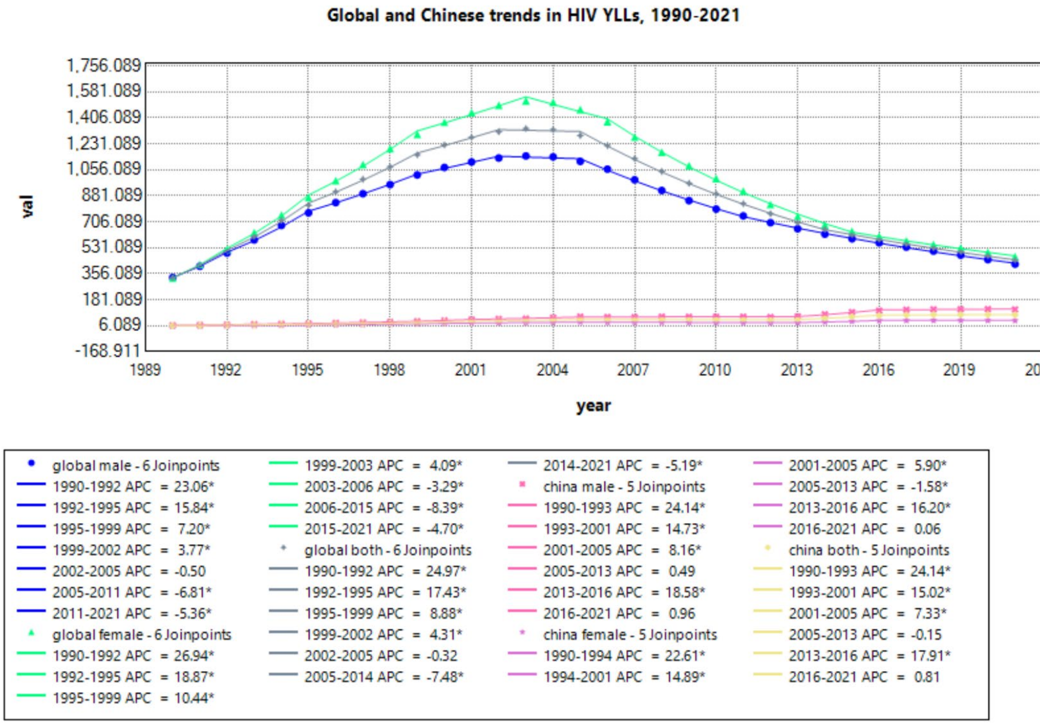

Fig. 4. Global and Chinese trends in HIV YLLs, 1990–2021. *Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.

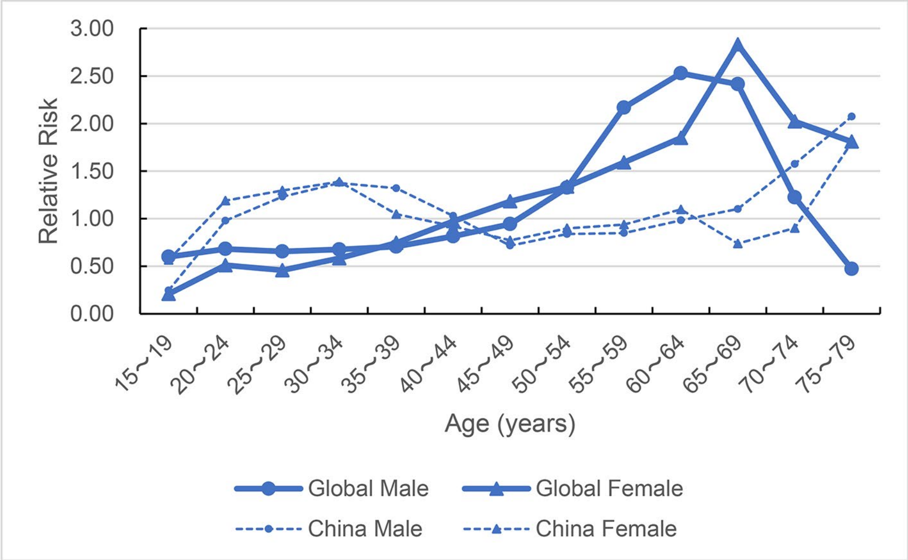

Fig. 5. Age effect on AIDS incidence, 1990–2021.

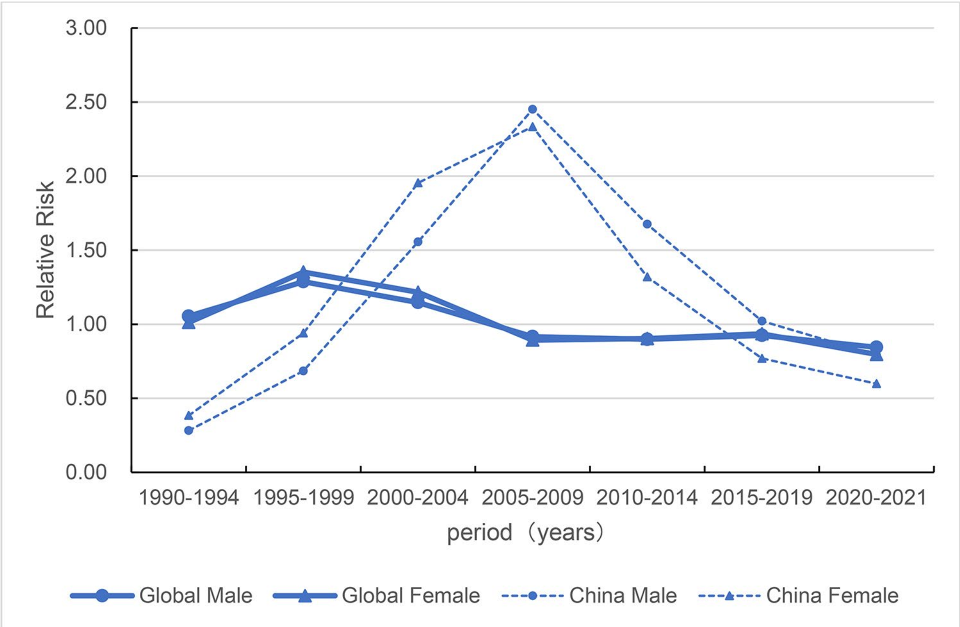

Fig. 6. Period effect of AIDS incidence from 1990 to 2021.

HIV infection[16–18]. With the gradual improvement of China's HIV testing and surveillance system, more cases of HIV infection are being recognized and reported in a timely manner, thus reflecting the rising incidence[19]. The higher global HIV prevalence among women than men may stem from biological differences higher risk of mucosal exposure and social structural factors sexual violence or transactional sex as a result of gender power inequality[20]. In contrast, the significantly higher prevalence of men than women in China is associated with the concentration of high-risk behaviors and high exposure of men in the mobile population, and the higher tolerance of traditional Chinese culture towards male sexuality, which may lead to a weak sense of protection[21].

Age effect analysis: Both global and Chinese AIDS incidence rates show an age effect, the risk is higher in older age groups. Specifically, the risk of AIDS incidence peaks at 60–69 years of age globally and at 75–79 years of age in China. This trend highlights the extended survival of HIV patients due to the wider availability of ART, resulting in a significant increase in the number of older individuals living with HIV[22–24]. Additionally, the proportion of new infections among older adults is rising, likely due to their sexual activity combined with lower awareness of prevention and limited knowledge about HIV risks[25]. Consequently, health policies should

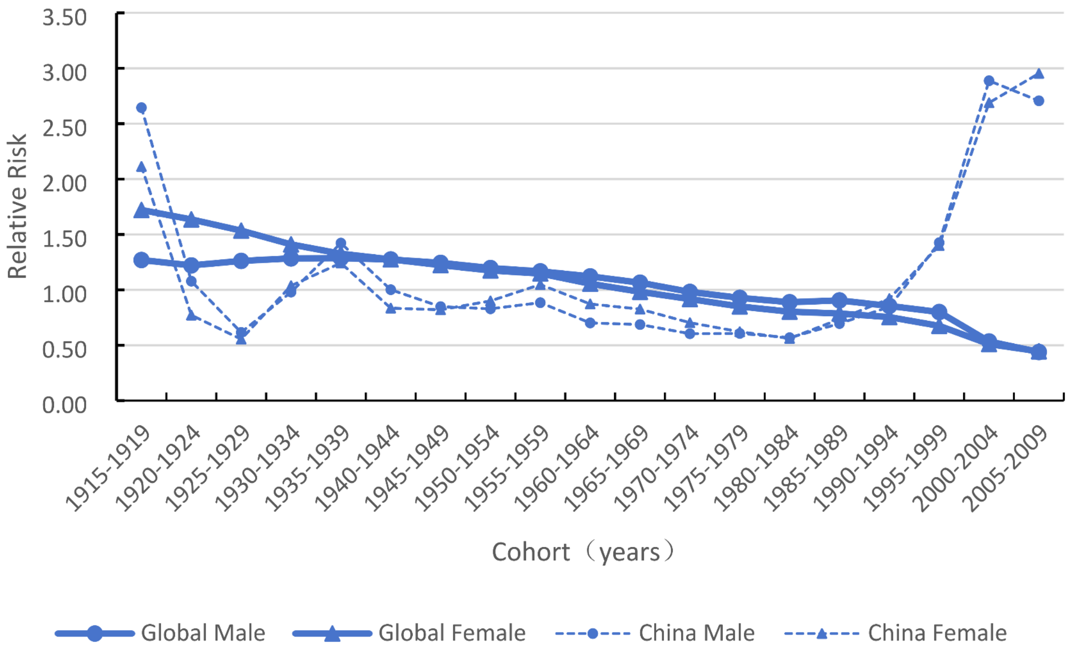

Fig. 7. Period effect of AIDS incidence from 1990 to 2021.

focus more on HIV prevention and treatment for the elderly, promote HIV testing and education, and enhance preventive measures, especially for older age groups.

Regarding period and cohort effects, global AIDS risk peaked between 1995 and 1999 and has since declined. This shift is likely linked to the HIV outbreak peak in the early 1990s, when public awareness was limited and preventive measures were not widespread[26]. As ART and preventive measures gained momentum, incidence risks were effectively controlled in the early 2000s. In China, the period effect peaked between 2005 and 2009 and then gradually decreased, reflecting enhanced HIV prevention strategies post-2005, such as expanded testing, ART promotion, and targeted interventions for high-risk groups[27–29]. Cohort analysis showed that the risk of AIDS onset generally declined with each birth cohort, especially among younger groups, where the risk was notably lower. This suggests that the risk of HIV infection in the younger cohort is gradually decreasing as HIV prevention and education efforts are intensified. However, the relatively small decrease in China suggests that HIV prevention and treatment measures for young people still need to be further strengthened, especially among MSM groups and mobile populations[30].

In summary, although the standardized incidence of AIDS is decreasing year by year, there are still many countries where the infection situation should be paid more attention. It is possible to expand the coverage of ART, improve the health knowledge and quality of treatment of the relevant population, raise public awareness of prevention and treatment, and encourage HIV-related testing and health education among high-risk groups such as MSM, clandestine prostitutes, young people and the elderly to reduce the risk of covert transmission.

Limitations

First, this study used GBD2021 data for analysis, but it is possible that some low-income countries have low testing coverage and high underreporting, and there may be some deviation from the actual situation. Second, this study analyzed only global and Chinese AIDS situation and did not take into account the variability between regions, and finally,The database lacks data on the prevalence of HIV among people under 15 and over 79 years of age.

Further research direction

Future studies consider regional differences in China, strengthen data coverage and validation, supplement data from weak regions, and visualize regional differences. In addition, expanding the age-range analysis to include pediatrics and octogenarians would provide a more comprehensive view of the AIDS epidemiology.

Data availability

The datasets for our study were obtained from the GBD dataset, available at [https://www.healthdata.org/].

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Author contributions
Menghan Wu and Cheng Hong wrote the main manuscript text. Zhengdong Dou conceptualization, writing—review and editing. All authors contributed to the article and approved the submitted version.

Declarations

Competing interests
The authors declare no competing interests.

Ethics approval and consent to participate
This is a database study that reuses data from GBD pooled data set. This study has received ethical approval and consent from all relevant parties.

Additional information
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