Changes of human immunodeficiency virus (HIV) burden globally and in China over three decades: a secondary analysis of global HIV statistics

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Abstract

Background: A more comprehensive understanding of the trends of incidence, prevalence, and mortality in human immunodeficiency virus (HIV), and their complex interrelationships, may provide important evidence for decision-making related to HIV prevention and control. The variances in these indices between different population groups, genders, and ages are critical to decipher evolving patterns of the HIV epidemic in specific populations.

Methods: A secondary analysis of relevant data was conducted using data extracted from the Global Burden of Disease study of 2019. HIV/acquired immune deficiency syndrome (AIDS) incidence, prevalence, AIDS-related mortality, and mortality-to-prevalence ratio (MPR) for annual percentage change, average annual percentage change (AAPC), and corresponding 95% confidence intervals (CIs) were calculated using joinpoint regression statistical analysis.

Results: The AAPC of HIV/AIDS incidence, prevalence, AIDS-related mortality rate, and MPR were –1.4 (95% CI: –1.6, –1.2), 4.1 (95% CI: 4.0, 4.3), 2.0 (95% CI: 1.7, 2.3), and –2.1 (95% CI: –2.3, –1.8) between 1990 and 2019 globally, and were 3.5 (95% CI: 2.2, 4.8), 6.9 (95% CI: 6.8, 7.0), 8.1 (95% CI: 7.1, 9.1), and 1.2 (95% CI: 0.1, 2.3) in China during the same period. In terms of differences in the preceding indicators by gender, we observed a similar pattern of trends for male and female genders both globally and in China during the entire study period. Each specific age group exhibits a distinct pattern in terms of incidence, prevalence, mortality rate, and MPR both globally and in China.

Conclusions: Prevalence and mortality rates of HIV/AIDS have increased between 1990 and 2019 globally and in China. While the incidence rate and MPR have declined globally over the past three decades, these two indicators are observed to present an increasing trend in China. There is a high HIV burden among young and middle-aged adults globally; however, the elderly have a high HIV burden in China. HIV screening at older age should be scaled up, and patients with advanced HIV disease should be provided early with additional care and health resources.

Keywords: Human immunodeficiency virus; Incidence; Mortality; Mortality-to-prevalence ratio; Prevalence

Introduction

The Joint United Nations Programme on human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) (UNAIDS) "90–90–90" strategy has called for 90% of HIV-infected individuals knowing their HIV status, 90% of diagnosed people living with HIV receiving antiretroviral therapy (ART), and 90% of individuals on treatment being virally suppressed by 2020.[1] At the end of 2020, these goals came close to being met globally, with some countries fully achieving the targets. However, there were approximately 37.7 million people living with HIV around the world in 2020,[2] which means that small gaps in the achievement of the "90–90–90" goal might have left a relatively large number of people who were not HIV suppressed. Even with a 47% decline in AIDS-related mortality over the past two decades, there were still 680,000 (480,000–1,000,000) deaths due to AIDS globally in 2020.[2]

Since the Chinese National Free Antiretroviral Therapy Program and other comprehensive HIV response efforts by the Chinese Government have been scaled up in China, the national prevalence of HIV/AIDS in China has stabilized, and the incidence has declined.[3,4] However,

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the HIV/AIDS epidemic in China is not yet fully under control.[5,6] To better understand the enigma of the HIV epidemic in China, the incidence, prevalence, and mortality trends of HIV nationally need to be described, over an extended period. Previously, several studies have described elemental characteristics of the HIV epidemic in China over the long term.[7-9] Recent research indicates that AIDS-related mortality in China has climbed sharply over the past few years, even in the context of the HIV epidemic in China being partially contained.[4] Up till now, AIDS has remained a leading cause of mortality in China, causing the greatest number of deaths among all infectious diseases in China in 2020, according to the Chinese Center for Disease Control and Prevention.[10]

A more comprehensive understanding of the trends of incidence, prevalence, and mortality, and their complex interrelationships, may provide policymakers, sponsors, and medical practitioners with important evidence for decision-making related to HIV prevention and control. To comprehensively assess the burden of disease in populations with different characteristics, the mortality-to-prevalence ratio (MPR) could be an alternative index to utilize for statistical purposes, as it presents mortality data after accounting for prevalence. Moreover, MPR reflects deaths resulting from diseases that the health system ought to cure or prevent.[11] Researchers have recently successfully used this indicator to assess epidemiological differences in hematological malignancies between Europe and China.[12] In addition, Lin *et al*[13] have studied the relationship between mortality and prevalence for coronavirus disease 2019 (COVID-19), and have presented these data as MPR figures to accurately assess the proportion of individuals with undocumented severe acute respiratory syndrome coronavirus 2 infection. Herein, we attempt to use the MPR index as a useful indicator to reflect the changes in HIV/AIDS burden associated with the scale-up of HIV screening, the expansion of ART, and the upgrade to modern antiretroviral drugs in recent decades. In the present study, we describe the trends of HIV/AIDS incidence, prevalence, mortality, and MPR over the past three decades globally and in China. Furthermore, we have analyzed the differences in these indices in the context of different gender and age groups in order to extricate and decipher the varying patterns of the HIV/AIDS pandemic in specific populations.

Methods

Data source

A secondary analysis of existing data was conducted using data extracted from the Global Burden of Disease (GBD) study of 2019, which was conducted by the Institute for Health Metrics and Evaluation (IHME). GBD 2019 systematically, scientifically, and comprehensively estimated 286 causes of death, 369 diseases and injuries, and 87 risk factors in 204 countries and regions based on age, sex, and geography over time.[14] For HIV burden, GBD 2019 groups countries and territories according to the availability of different types of data, and uses unique modeling strategies that take full advantage of the best data available in each country. Group 1 includes countries and territories with HIV prevalence data obtained from antenatal care clinics or serum antibody surveys of representative populations (ie, 48 countries in total, including several in sub-Saharan Africa, and the Dominican Republic, Haiti, India, Papua New Guinea, and Sudan). Group 2 includes the remaining 156 countries, with HIV mortality data gradually becoming available for most countries except 33 that do not have it. These groups are further divided according to the peak prevalence with or without registered data integrity.[14] Details of the GBD 2019 study methods have been fully described elsewhere.[14] All anonymized data are available online at the website of the Institute for Health Metrics and Evaluation (IHME) (http://www.healthdata.org/gbd/2019).

In the present work, the burden of disease indices extracted from the GBD statistics comprised HIV/AIDS incidence, prevalence, and mortality rates in groups stratified by different genders and ages (0–14, 15–49, 50–69, and ≥70 years). A further outcome, that is, MPR, was calculated by dividing the HIV/AIDS mortality (estimated number of deaths) by the corresponding prevalence (estimated number of infections) during the same period.

Data analysis

HIV/AIDS incidence, prevalence, and AIDS-related mortality globally and in China are presented per 100,000 persons and 95% confidence intervals (CIs). MPR are presented as a number and 95% CIs. All of the above rates or ratio are described by gender and age group.

Next, joinpoint regression was used to visualize the change points of indices of HIV burden and to evaluate whether there were significant changes in the observed trend at particular points. HIV/AIDS incidence, AIDS-related mortality, and MPR for annual percentage change (APC), average annual percentage change (AAPC), and corresponding 95% CIs were calculated. All analyses were conducted using the Joinpoint Regression Program (v.4.9.0.1, National Cancer Institute, Bethesda, MD, USA; surveillance.cancer.gov/joinpoint/). Within Joinpoint regression software, we used the Grid Search Method, and selected a model where errors are assumed to have constant variance (homoscedasticity). Joinpoint regression utilized several permutation tests to perform joinpoint regression, and the Monte Carlo permutation method was used for tests of significance.[15] All P values <0.05 were considered statistically significant.

Results

Incidence, prevalence, mortality rate, and MPR comparison with respect to HIV/AIDS globally and in China, 1990–2019

Globally, the temporal trend was an initial increase, and then a subsequent decline of incidence and mortality rates of HIV/AIDS from 1990 to 2019; the peak of the incidence rate and mortality rate was 56.0 (95% CI: 67.2, 47.5) in 1996 and 28.5 (95% CI: 22.3, 35.2) in 2004 per 100,000, respectively. The global AAPC of HIV/AIDS incidence and

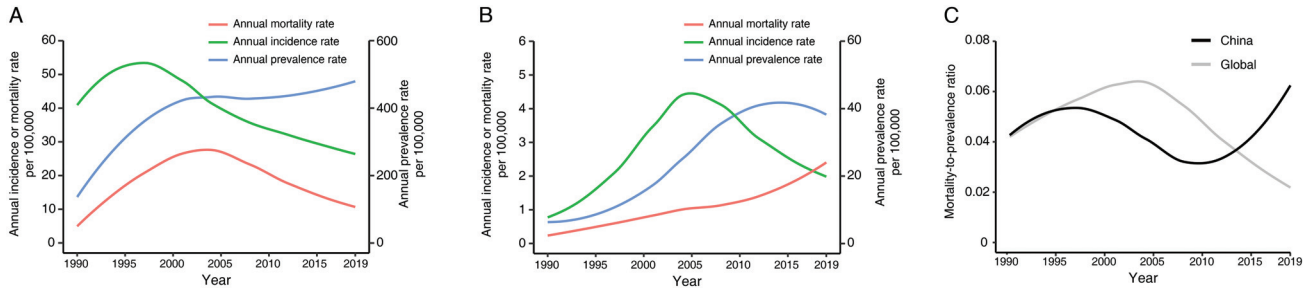

Figure 1: Temporal trends in HIV/AIDS incidence, prevalence, and mortality rate per 100,000 persons (A) globally and (B) in China, 1990 to 2019. (C) MPR was calculated both globally and in China. AIDS: acquired immune deficiency syndrome; HIV: Human immunodeficiency virus; MPR: Mortality-to-prevalence ratio.

AIDS-related mortality rates were –1.4 (95% CI: –1.6, –1.2) and 2.0 (95% CI: 1.7, 2.3) between 1990 and 2019, respectively [Figure 1A]. The global HIV/AIDS prevalence rate increased between 1990 and 2019, and the peak value was observed to be 476.2 (95% CI: 454.3, 502.2) per 100,000 in 2019. Accordingly, the global MPR also rose and subsequently declined, and the peak value was observed to be 0.07 in 2004 [Figure 1C]. In addition, the global AAPC of prevalence rate was 4.1 (95% CI: 4.0, 4.3) and the global AAPC of MPR was –2.1 (95% CI: –2.3, –1.8).

The incidence rate of HIV/AIDS in China initially rose and then subsequently decreased, and the peak value was seen to be 4.8 (95% CI: 3.2, 6.9) per 100,000 in 2005 [Figure 1B]. In contrast to the global trend, the mortality rate in China can be seen to plot an increasing trend as a whole, and the peak value was 2.2 (95% CI: 1.9, 2.5) per 100,000 persons in 2018 [Figure 1B]. Additionally, the AAPC of incidence rate was 3.5 (95% CI: 2.2, 4.8) and the AAPC of mortality rate was 8.1 (95% CI: 7.1, 9.1) in China. The prevalence rate in China initially increased; however, a slight decreasing trend of prevalence rate was observed from its peak (41.9 per 100,000 persons) in 2014. The HIV/AIDS MPR for China initially increased, subsequently decreased, and then has risen again in the three decades between 1990 and 2019; the peak value of the MPR index in China was 0.06 in 2019 [Figure 1C]. Thus, the AAPC of prevalence rate was 6.9 (95% CI: 6.8, 7.0) and the AAPC of MPR was 1.2 (95% CI: 0.1, 2.3) in China. Detailed HIV/AIDS incidence, prevalence, and AIDS-related mortality rates in China and globally from 1990 to 2019 are listed in Table 1.

Different gender and age trends globally and in China between 1990 and 2019

In terms of differences in the aforementioned indicators by gender, we observed a similar pattern of trends in incidence, prevalence, mortality and MRP for male and female people living with HIV/AIDS (PLWH) globally and in China during the entire study period [Figure 2]. Nonetheless, the global incidence, prevalence, and mortality rates of female PLWH were higher than male PLWH from 1990 to 2019, while the preceding observations for China were higher in male PLWH than in female PLWH. Interestingly, the global incidence and mortality rate gaps for HIV/AIDS between men and women have narrowed from the peak. Nevertheless, the gaps for these indices have not narrowed for HIV/AIDS between men and women in China. The MPR trends were observed to be very similar between male and female PLWH, both globally and in China.

The data presented in Figure 3 show that both globally and in China, each age stratum of PLWH has its own unique trend in terms of incidence, prevalence, mortality rate, and MPR. Overall, the main trend seen globally is that incidence, prevalence, and mortality rate in the 15 to 49-year group have always been notably higher than any other age group between 1990 and 2019 [Figure 3A]. In China, these indices in the 0 to 14-year group are appreciably lower and remain relatively stable compared with other age groups. In contrast to the global trend, persons of the older age group (aged >50 years) had a higher incidence rate between 2001 and 2012 and a higher prevalence rate between 2005 and 2019. Moreover, the mortality rate of older age persons was higher in 1990 to 2019 compared to that of individuals aged ≤50, with the difference having become more noticeable since 2014. The MPR seen in the 0 to 14-year group continued to decline both in China and globally from 1990 to 2019 [Figures 3A and 3B].

Joinpoint analysis indicated that persons in the age-range of 0 to 14 years had a significant upward trend of incidence rate among females (2.1, 95% CI: 0.8, 3.4) and males (1.3, 95% CI: 0.1, 2.6) between 1990 and 2019; however, a sharp decline was found from the peak in 2016, where the APC values were observed to be –16.9 (95% CI: –20.8, –12.8) and –16.3 (95% CI: –19.9, –12.5) for females and males, respectively [Figure 4 and Table 2]. Also, the incidence rate in the 15 to 49, 50 to 69, and ≥70 years groups had a significant upward trend, except for the ≥70 years male group between 1990 and 2019 [Table 2]. With respect to the prevalence rate, all age groups were seen to have a significant upward trend [Table 2]. In relation to mortality rate, the 0–14-year group had an almost identical significant upward trend both in male and female PLWH. Additionally, the 15 to 49, 50 to 69, and ≥70 year groups also had significant upward trends for both male and female PLWH, although men had a higher AAPC than women. Figure 4D and Table 2 summarize the results of joinpoint regression analyses of the age and gender-stratified burden of HIV/AIDS in China. The AAPC of calculated MPR indices demonstrated a significant declining trend in all age groups in both genders in the period between 1990 and 2019 [Table 2].

Table 1: HIV/AIDS incidence, prevalence, and AIDS-related mortality rate in China and globally, 1990 to 2019.

	Prevalence rate per 100,000 (95% CI)		Incidence rate per 100,000 (95% CI)		Mortality rate per 100,000 (95% CI)	
Year	China	Globally	China	Globally	China	Globally
1990	5.6 (4.2, 7.3)	146.3 (128.5, 165.4)	0.8 (0.5, 1.5)	38.5 (31.9, 45.4)	0.2 (0.1, 0.3)	6.3 (4.8, 8.5)
1991	6.2 (4.9, 8.0)	177.9 (156.6, 198.7)	1.0 (0.7, 1.6)	43.6 (36.0, 51.5)	0.3 (0.1, 0.4)	7.9 (6.0, 10.7)
1992	6.9 (5.5, 9.0)	210.6 (185.8, 233.6)	1.1 (0.8, 1.8)	47.6 (39.2, 56.8)	0.3 (0.2, 0.4)	9.8 (7.3, 13.2)
1993	7.6 (6.0, 10.2)	243.3 (215.1, 268.5)	1.2 (0.8, 1.8)	50.7 (41.8, 61.0)	0.4 (0.3, 0.4)	11.9 (8.9, 16.0)
1994	8.4 (6.4, 11.6)	275.3 (245.3, 302.0)	1.5 (1.0, 2.4)	53.0 (44.1, 63.7)	0.4 (0.3, 0.5)	14.1 (10.5, 19.0)
1995	9.3 (6.9, 13.2)	306.1 (275.4, 334.0)	1.5 (1.0, 2.4)	54.8 (46.0, 65.8)	0.5 (0.4, 0.5)	16.3 (12.0, 21.9)
1996	10.0 (7.3, 14.4)	335.5 (304.6, 364.3)	1.5 (0.9, 2.4)	56.0 (47.5, 67.2)	0.5 (0.5, 0.6)	18.2 (13.3, 24.4)
1997	10.8 (7.8, 16.2)	362.6 (331.6, 390.4)	1.7 (1.0, 2.9)	56.0 (47.4, 67.5)	0.6 (0.5, 0.6)	19.9 (14.4, 26.6)
1998	11.9 (8.2, 18.2)	385.8 (355.4, 412.4)	2.0 (1.2, 3.4)	54.5 (46.2, 66.0)	0.6 (0.6, 0.7)	21.8 (15.9, 28.9)
1999	13.1 (8.8, 20.5)	404.3 (376.4, 429.5)	2.4 (1.4, 4.0)	52.5 (44.7, 63.6)	0.7 (0.6, 0.8)	23.7 (17.4, 31.2)
2000	14.8 (9.5, 23.4)	418.2 (394.2, 442.0)	2.9 (1.7, 4.8)	50.0 (42.7, 60.6)	0.8 (0.7, 0.8)	25.4 (18.8, 32.8)
2001	16.9 (10.4, 27.1)	427.5 (405.9, 449.3)	3.5 (2.0, 5.5)	47.3 (40.4, 57.2)	0.8 (0.8, 0.9)	26.7 (20.0, 34.2)
2002	19.3 (11.6, 31.3)	432.8 (414.0, 452.2)	4.0 (2.4, 6.2)	44.9 (38.6, 53.9)	0.9 (0.8, 1.0)	27.7 (21.0, 35.1)
2003	21.9 (13.1, 36.2)	434.5 (417.6, 451.4)	4.5 (2.8, 6.6)	42.7 (37.0, 51.0)	0.9 (0.8, 1.0)	28.3 (21.7, 35.5)
2004	25.0 (14.7, 40.9)	433.6 (417.3, 450.2)	4.7 (3.1, 6.8)	40.8 (35.7, 48.2)	1.0 (0.9, 1.1)	28.5 (22.3, 35.2)
2005	28.0 (16.3, 46.0)	430.9 (414.5, 447.9)	4.8 (3.2, 6.9)	39.3 (34.5, 46.0)	1.1 (1.1, 1.2)	27.9 (22.4, 34.2)
2006	30.8 (17.4, 50.4)	427.7 (410.2, 446.8)	4.6 (3.2, 6.6)	38.0 (33.6, 44.1)	1.1 (1.0, 1.2)	26.6 (21.9, 32.2)
2007	33.5 (18.5, 54.9)	425.0 (406.4, 446.8)	4.4 (3.2, 6.2)	36.8 (32.7, 42.5)	1.1 (1.0, 1.2)	24.8 (20.9, 29.7)
2008	35.8 (19.6, 59.1)	424.1 (404.8, 447.8)	4.1 (3.0, 5.8)	35.7 (31.9, 41.1)	1.2 (1.1, 1.3)	22.9 (19.7, 27.3)
2009	37.8 (20.8, 62.7)	425.1 (405.8, 449.6)	3.8 (2.8, 5.5)	34.8 (31.5, 39.9)	1.2 (1.1, 1.3)	21.1 (18.4, 25.0)
2010	39.4 (21.8, 65.6)	427.8 (408.5, 452.9)	3.5 (2.6, 5.2)	33.9 (30.9, 38.7)	1.2 (1.1, 1.4)	19.5 (17.2, 23.3)
2011	40.6 (22.6, 67.8)	431.7 (411.8, 456.6)	3.1 (2.3, 4.8)	33.1 (30.2, 37.6)	1.2 (1.2, 1.4)	18.2 (16.0, 21.7)
2012	41.4 (22.9, 69.3)	436.4 (416.6, 461.4)	2.8 (1.9, 4.4)	32.3 (29.4, 36.7)	1.2 (1.1, 1.3)	16.8 (14.8, 20.0)
2013	41.8 (23.1, 70.5)	441.8 (421.9, 467.0)	2.6 (1.6, 4.0)	31.6 (28.6, 35.8)	1.3 (1.2, 1.4)	15.6 (13.8, 18.6)
2014	41.9 (23.1, 71.6)	447.7 (427.9, 473.2)	2.4 (1.3, 3.8)	30.9 (28.0, 35.0)	1.6 (1.4, 1.7)	14.7 (13.0, 17.5)
2015	41.5 (22.6, 72.4)	453.8 (433.7, 479.6)	2.3 (1.0, 3.6)	30.3 (27.3, 34.2)	1.9 (1.7, 2.0)	13.9 (12.3, 16.5)
2016	40.9 (21.9, 72.8)	459.8 (439.0, 485.5)	2.3 (1.1, 3.7)	29.3 (26.3, 33.0)	2.1 (1.9, 2.2)	13.3 (11.8, 15.7)
2017	40.2 (21.1, 72.5)	465.6 (444.5, 491.2)	2.3 (1.1, 3.7)	28.1 (25.1, 31.8)	2.2 (1.9, 2.4)	12.5 (11.2, 14.6)
2018	39.5 (20.5, 72.4)	471.2 (449.8, 497.0)	2.3 (1.1, 3.7)	26.7 (23.7, 30.2)	2.2 (1.9, 2.5)	11.7 (10.6, 13.5)
2019	38.8 (20.1, 72.2)	476.2 (454.3, 502.2)	2.2 (1.1, 3.6)	25.7 (22.8, 29.2)	2.2 (1.8, 2.6)	11.2 (10.2, 12.9)

AIDS: acquired immune deficiency syndrome; CI: Confidence interval; HIV: Human immunodeficiency virus.

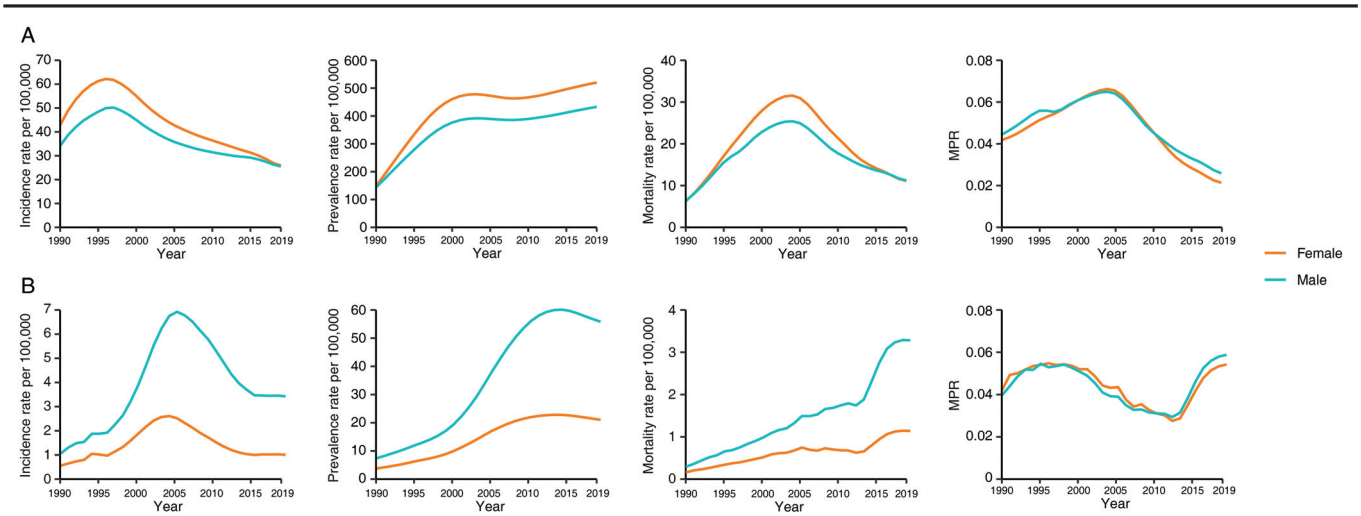

Figure 2: Temporal trends in HIV/AIDS incidence, prevalence, mortality rate, and MPR per 100,000 persons according to gender globally (A, upper four graphs) and in China (B, lower four graphs), 1990–2019. AIDS: acquired immune deficiency syndrome; HIV: Human immunodeficiency virus; MPR: Mortality-to-prevalence ratio.

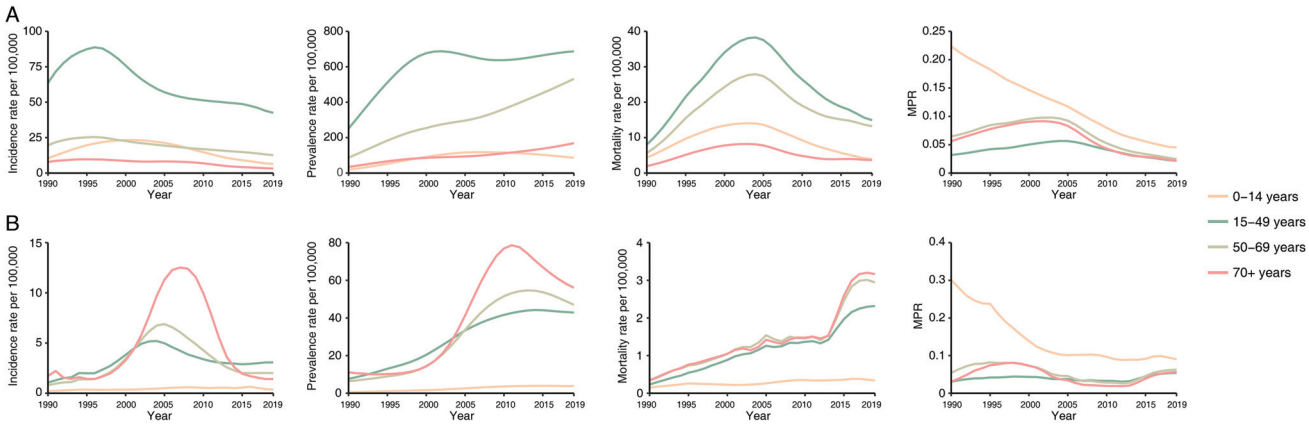

Figure 3: Temporal trends in HIV/AIDS incidence, prevalence, mortality rate, and MPR per 100,000 persons, by age, globally (A, upper four graphs) and in China (B, lower four graphs), 1990 to 2019. Age was stratified into four groups (0–14, 15–49, 50–69, and ≥70 years). AIDS: acquired immune deficiency syndrome; HIV: Human immunodeficiency virus; MPR: Mortality-to-prevalence ratio.

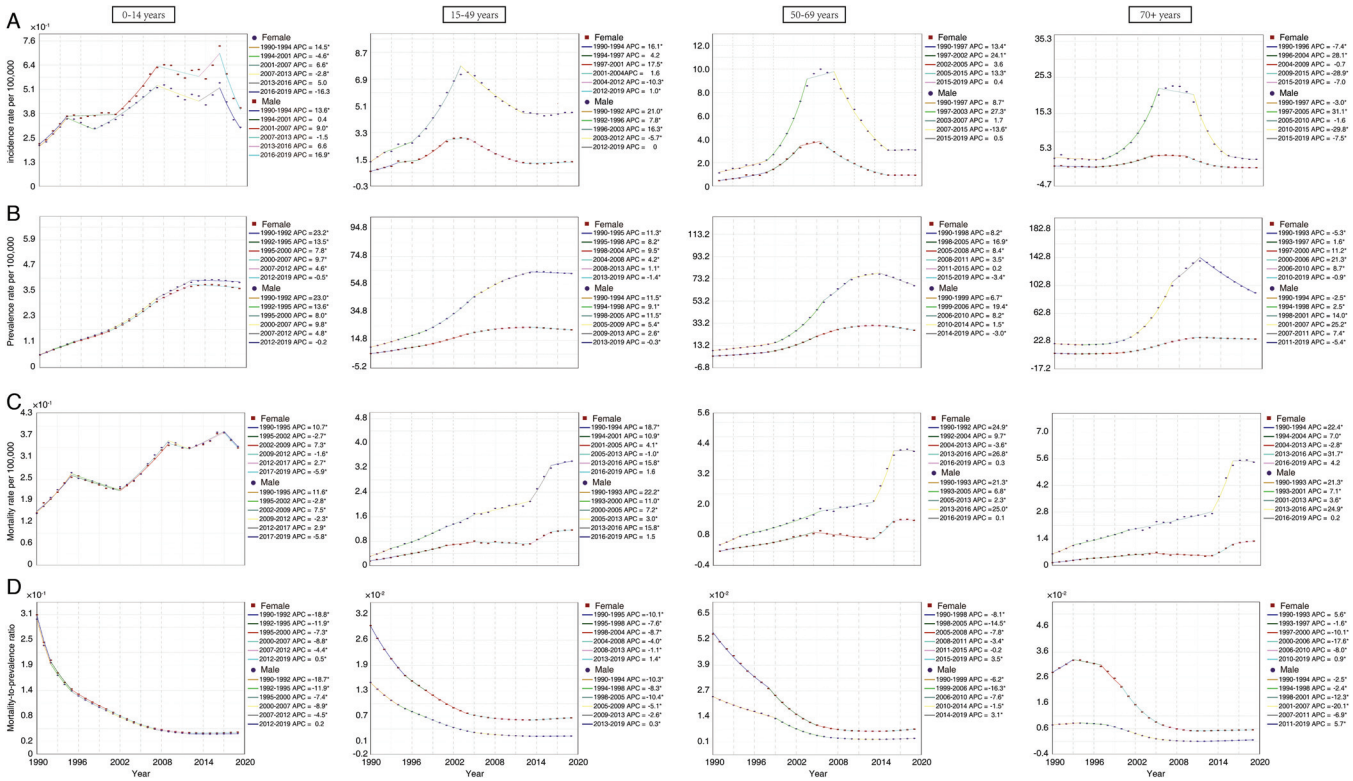

Figure 4: Joinpoint regression analyses of trends in HIV/AIDS incidence rate (A, four graphs in the first row), prevalence rate (B, four graphs in the second row), mortality rate (C, four graphs in the third row), and MPR per 100,000 persons in China (D, four graphs in the fourth row), while considering gender differences in each age group, 1990 to 2019. AIDS: acquired immune deficiency syndrome; APC: Annual percentage change; HIV: Human immunodeficiency virus; MPR: Mortality-to-prevalence ratio.

Discussion

According to the data from the GBD, the global incidence of HIV has decreased since 1996, and the AIDS-related mortality rate has decreased since 2004. Global HIV incidence, prevalence, and mortality rates are dissimilar to prevailing trends in China. The HIV epidemic began relatively late in China, initially spreading among people who injected drugs (PWID), then breaking out in the general population in the mid-1990 s due to contamination of community plasma collections, and subsequently evolving into a sexually transmitted epidemic over recent years.[6] Since the "Four Frees and One Care" policy was promulgated by the Chinese government in 2003,[16] screening for HIV has expanded significantly, and the overall care for people living with HIV has improved correspondingly. Thus, HIV incidence in China was observed to decrease 2 years after the implementation of the policy. However, it is particularly worrying that the AIDS-related mortality rate continued rising even after the peak incidence rate, which is consistent with the observations of Liu *et al*[4] In the present study, we used

Table 2: Joinpoint trend analysis of HIV/AIDS incidence, prevalence, mortality rate, and MPR per 100,000 in China, 1990 to 2019.

Measure	Gender	Trend	0–14 years Year	APC (95% CI)	15–49 years Year	APC (95% CI)	50–69 years Year	APC (95% CI)	≥70 years Year	APC (95% CI)
Incidence	Female	Trend1	1990–1994	13.6* (10.2, 17.1)	1990–1994	16.1* (14.0,18.3)	1990–1997	13.4* (11.0, 15.9)	1990–1996	−7.4* (−11.1, −3.5)
		Trend2	1994–2001	0.4 (−1.3, 2.0)	1994–1997	4.2 (−1.8, 10.6)	1997–2002	24.1* (17.9, 30.7)	1996–2004	28.1* (24.0, 32.3)
		Trend3	2001–2007	9.0* (6.7, 11.3)	1997–2001	17.5* (14.0, 21.0)	2002–2005	3.63 (−12.0, 22.0)	2004–2009	−0.7 (−7.9, 7.2)
		Trend4	2007–2013	−1.5 (−3.6,0.6)	2001–2004	1.6 (−4.3, 7.8)	2005–2015	−13.3* (−14.6, −12.0)	2009–2015	−28.9* (−32.6, −25.0)
		Trend5	2013–2016	6.6 (−3.2, 17.4)	2004–2012	−10.3 (−11.0, −9.6)	2015–2019	0.4 (−4.7, 5.7)	2015–2019	−7.0 (−13.8, 0.3)
		Trend6	2016–2019	−16.9* (−20.8, −12.8)	2012–2019	1.0* (0.2, 1.9)				
		AAPC	1990–2019	2.1* (0.8, 3.4)	1990–2019	2.2* (1.2, 3.1)	1990–2019	2.3* (0.3, 4.4)	1990–2019	−2.9* (−5.0, −0.7)
	Male	Trend1	1990–1994	14.5* (11.3, 17.7)	1990–1992	21.0* (11.7, 31.2)	1990–1997	8.7* (7.1, 10.4)	1990–1997	−3.0* (−6.0, 0)
		Trend2	1994–1998	−4.6* (−8.7, −0.3)	1992–1996	7.7* (3.5, 12.2)	1997–2003	27.3* (24.1, 30.5)	1997–2005	31.1* (27.2, 35.2)
		Trend3	1998–2007	6.6* (5.6, 7.6)	1996–2003	16.3* (14.7, 17.9)	2003–2007	1.7 (−3.9, 7.5)	2005–2010	−1.6 (−8.4, 5.8)
		Trend4	2007–2013	−2.8* (−4.7, −0.8)	2003–2012	−5.7* (−6.5, −4.9)	2007–2015	−13.6* (−14.8, −12.3)	2010–2015	−29.8* (−34.7, −24.6)
		Trend5	2013–2016	5.0 (−3.9, 14.8)	2012–2019	0 (−1.1, 1.1)	2015–2019	0.5 (−3.0, 4.1)	2015–2019	−7.5* (−14.0, −0.6)
		Trend6	2016–2019	−16.3* (−19.9, −12.5)						
		AAPC	1990–2019	1.3* (0.1, 2.6)	1990–2019	4.2* (3.4, 5.1)	1990–2019	3.3* (2.2, 4.5)	1990–2019	−0.72 (−2.8, 1.4)
Prevalence	Female	Trend1	1990–1992	23.2* (20.5, 26.0)	1990–1995	11.2 (10.9, 11.6)	1990–1998	8.8* (8.5, 9.1)	1990–1993	−5.3* (−6.1, −4.5)
		Trend2	1992–1995	13.5* (11.0, 16.1)	1995–1998	8.2 (6.9, 9.6)	1998–2005	16.9* (16.4, 17.4)	1993–1997	1.6* (0.7, 2.5)
		Trend3	1995–2000	7.8* (7.1, 8.6)	1998–2004	9.5 (9.2, 9.8)	2005–2008	8.4* (5.9, 11.0)	1997–2000	11.2* (9.3, 13.1)
		Trend4	2000–2007	9.7* (9.3, 10.1)	2004–2008	4.2 (3.5, 4.8)	2008–2011	3.5* (1.1, 6.0)	2000–2006	21.3* (20.9, 21.8)
		Trend5	2007–2012	4.6* (3.9, 5.4)	2008–2013	1.1 (0.7, 1.5)	2011–2015	0.2 (−1.0, 1.4)	2006–2010	8.7* (7.8, 9.7)
		Trend6	2012–2019	−0.5* (−0.8, −0.2)	2013–2019	−1.4 (−1.6, −1.2)	2015–2019	−3.4* (−4.1, −2.6)	2010–2019	−0.9* (−1.1, −0.8)
		AAPC	1990–2019	7.2* (6.8, 7.5)	1990–2019	5.1* (4.9, 5.3)	1990–2019	7.1* (6.7, 7.5)	1990–2019	5.8* (5.5, 6.0)
	Male	Trend1	1990–1992	23.0* (20.3, 25.7)	1990–1994	11.5* (11.2, 11.9)	1990–1999	6.7* (6.5, 6.9)	1990–1994	−2.5* (−3.4, −1.6)
		Trend2	1992–1995	13.6* (11.1, 16.1)	1994–1998	9.1* (8.5, 9.7)	1999–2006	19.4* (19.0, 19.8)	1994–1998	2.5* (1.0, 3.9)
		Trend3	1995–2000	8.0* (7.3, 8.8)	1998–2005	11.5* (11.3, 11.7)	2006–2010	8.2* (7.1, 9.3)	1998–2001	14.0* (10.8, 17.3)
		Trend4	2000–2007	9.8* (9.4, 10.2)	2005–2009	5.4* (4.8, 5.9)	2010–2014	1.5* (0.5, 2.6)	2001–2007	25.2* (24.4, 26.0)
		Trend5	2007–2012	4.8* (4.0, 5.5)	2009–2013	2.6* (2.1, 3.2)	2014–2019	−3.0* (−3.4, −2.5)	2007–2011	7.4* (5.8, 8.9)
		Trend6	2012–2019	−0.2 (−0.5, 0.1)	2013–2019	−0.3* (−0.5, −0.1)			2011–2019	−5.4* (−5.7, −5.1)
		AAPC	1990–2019	7.3* (7.0, 7.7)	1990–2019	6.6* (6.4, 6.7)	1990–2019	7.3* (7.1, 7.5)	1990–2019	5.6* (5.2, 6.0)
Mortality	Female	Trend1	1990–1995	10.7* (9.4, 12.1)	1990–1994	18.7* (14.8, 22.8)	1990–1992	24.9* (11.1, 40.5)	1990–1994	22.4* (17.3, 27.8)
		Trend2	1995–2002	−2.7* (−3.6, −1.7)	1994–2001	10.9* (8.9, 12.9)	1992–2004	9.7* (8.9, 10.6)	1994–2004	7.0* (5.7, 8.3)
		Trend3	2002–2009	7.3* (6.3, 8.3)	2001–2005	4.1 (−1.3, 9.8)	2004–2013	−3.4* (−4.6, −2.1)	2004–2013	−2.7* (−4.2, −1.3)
		Trend4	2009–2012	−1.6 (−6.8, 4.0)	2005–2013	−1.0 (−2.4, 0.4)	2013–2016	26.7* (12.7, 42.6	2013–2016	31.7* (14.9, 50.9)
		Trend5	2012–2017	2.7* (0.9, 4.5)	2013–2016	15.8* (4.1, 28.9)	2016–2019	0.3 (−5.4, 6.4)	2016–2019	4.2 (−2.6, 11.6)
		Trend6	2017–2019	−5.9* (−10.9, −0.6)	2016–2019	1.6 (−3.6, 7.2)				
		AAPC	1990–2019	2.7* (1.9, 3.5)	1990–2019	7.1* (5.5, 8.7)	1990–2019	7.0* (5.4, 8.7)	1990–2019	7.8* (6.0, 9.6)
	Male	Trend1	1990–1995	11.6* (10.3, 12.9)	1990–1993	22.2* (18.2, 26.3)	1990–1993	21.3* (16.7, 26.0)	1990–1993	21.3* (14.9, 28.1)
		Trend2	1995–2002	−2.7* (−3.6, −1.9)	1993–2000	11.0* (9.8, 12.3)	1993–2005	6.8* (6.3, 74)	1993–2001	7.1* (5.5, 8.6)
		Trend3	2002–2009	7.5* (6.5, 8.4)	2000–2005	7.2* (4.9, 9.4)	2005–2013	2.3* (1.3, 3.4)	2001–2013	3.6* (2.8, 4.3)
		Trend4	2009–2012	−2.3 (−7.3, 2.9)	2005–2013	3.0* (2.1, 3.9)	2013–2016	25.0* (15.7, 35.0)	2013–2016	24.9* (12.0, 39.2)
		Trend5	2012–2017	2.9* (1.2, 4.6)	2013–2016	15.8* (8.3, 23.7)	2016–2019	0.1 (−3.7, 4.0)	2016–2019	−0.2 (−5.4, 5.4)
		Trend6	2017–2019	−5.8* (−10.6, −0.8)	2016–2019	1.5 (−1.9, 4.9)				
		AAPC	1990–2019	2.8* (2.1, 3.6)	1990–2019	8.6* (7.7, 9.6)	1990–2019	8.0* (6.9, 9.0)	1990–2019	7.91* (6.5, 9.4)
MPR	Female	Trend1	1990–1992	−18.8* (−20.7, −17.0)	1990–1995	−10.1* (−10.4, −9.9)	1990–1998	−8.1* (−8.3, −7.9)	1990–1993	5.6* (4.7, 6.5)
		Trend2	1992–1995	−11.9* (−13.9, −9.9)	1995–1998	−7.6* (−8.7, −6.5)	1998–2005	−14.5* (−14.8, −14.1)	1993–1997	−1.5* (−2.4, −0.7)
		Trend3	1995–2000	−7.3* (−7.9, −6.6)	1998–2004	−8.7 (−8.9, −8.4)	2005–2008	−7.8* (−9.9, −5.5)	1997–2000	−10.1* (−11.6, −8.5)
		Trend4	2000–2007	−8.8* (−9.2, −8.5)	2004–2008	−4.0* (−4.6, −3.4)	2008–2011	−3.4* (−5.7, −1.0)	2000–2006	−17.6* (−17.9, −17.3)
		Trend5	2007–2012	−4.4* (−5.1, −3.7)	2008–2013	−1.0* (−1.4, −0.7)	2011–2015	−0.2 (−1.3, 1.0)	2006–2010	−8.0* (−8.8, −7.2)
		Trend6	2012–2019	0.5* (0.2, 0.8)	2013–2019	1.4* (1.2, 1.6)	2015–2019	3.5* (2.7, 4.3)	2010–2019	0.9* (0.8, 1.1)
		AAPC	1990–2019	−6.7* (−7.0, −6.4)	1990–2019	−4.9* (−5.0, −4.7)	1990–2019	−6.6* (−7.0, −6.3)	1990–2019	−5.5* (−5.7, −5.2)
	Male	Trend1	1990–1992	−18.7* (−20.4, −16.9)	1990–1994	−10.3* (−10.6, −10.0)	1990–1999	−6.2* (−6.4, −6.1)	1990–1994	2.5* (1.6, 3.5)
		Trend2	1992–1995	−11.9* (−13.8, −10.0)	1994–1998	−8.3* (−8.8, −7.8)	1999–2006	−16.3* (−16.5, −16.0)	1994–1998	−2.4* (−3.8, −1.0)
		Trend3	1995–2000	−7.4* (−8.0, −6.8)	1998–2005	−10.3* (−10.5, −10.2)	2006–2010	−7.6* (−8.5, −6.7)	1998–2001	−12.3* (−14.8, −9.7)
		Trend4	2000–2007	−8.9* (−9.2, −8.6)	2005–2009	−5.1* (−5.6, −4.6)	2010–2014	−1.5* (−2.5, −0.5)	2001–2007	−20.1* (−20.6, −19.6)
		Trend5	2007–2012	−4.5* (−5.2, −3.9)	2009–2013	−2.6* (−3.1, −2.0)	2014–2019	3.1* (2.6, 3.6)	2007–2011	−6.8* (−8.2, −5.5)
		Trend6	2012–2019	0.2 (−0.1, 0.5)	2013–2019	0.3* (0.1, 0.5)			2011–2019	5.7* (5.4, 6.0)
		AAPC	1990–2019	−6.8* (−7.1, −6.5)	1990–2019	−6.2* (−6.3, −6.0)	1990–2019	−6.8* (−7.0, −6.6)	1990–2019	−5.3* (−5.7, −4.9)

AAPC: Average annual percent change; AIDS: acquired immune deficiency syndrome; APC: Annual percent change; CI: Confidence interval; HIV: Human immunodeficiency virus; MPR: Mortality-to-prevalence ratio. * Statistically significant at alpha = 0.05 ($P < 0.05$).

the MPR as a surrogate index of deaths in HIV-infected individuals to reflect the degree of epidemic control and efficacy of medical care. Between 1990 and 2019, the graphical representation of the MPR index in China has evolved in a "sine wave" manner (first increasing, then decreasing, and then increasing again), and this clearly illustrates that the increasing proportion of advanced AIDS patients is the primary reason for the rising mortality in China of late. It has been reported that the mean duration of HIV infection at diagnosis among new HIV cases in China is 6.3 years.[17] Furthermore, although the duration of HIV infection at the time of diagnosis has decreased in recent years, this decrease has not been adequate to have a meaningful impact on HIV outcomes at the individual, public-health, and epidemic levels.[17]

Global HIV incidence and mortality in females have been observed to be higher than those in males; however, these gender gaps have reduced in the past 20 years.[14] Females are more susceptible to HIV-1 acquisition than males as a result of differences in viral load, levels of sex hormones, and dissimilar immune responses between females and males.[18] In addition, inherent inequities in society, culture, economy, and legislation increases the vulnerability to HIV/AIDS among females.[19] Bold management and control efforts undertaken by many global health programs have resulted in a decrease in incidence and mortality for HIV/AIDS, driving gender parity with respect to these indices.[14] Unlike the trend globally, HIV transmission and deaths in China tend to be male-dominated, and the incidence, prevalence, and mortality gaps for HIV/AIDS between men and women have widened over the past three decades. This tendency might well be inseparable from the increase in numbers of men who have sex with men (MSM) in China. The proportion of newly diagnosed HIV-infected MSM cases has increased exponentially, peaking at 28.2% in 2015, and subsequently falling to 23.3% in 2018.[6] However, the trend in MPR for both genders is approximately identical globally and in China. This tends imply that the levels of HIV care and services available to HIV-infected males and females are largely similar both globally and in China.

The young and middle-aged group (15–49-year-olds) has the highest HIV incidence, prevalence, and mortality rates globally, while the MPR in this population is lower than that in other age groups. Conversely, we found that HIV incidence in China in the older age group (aged >50 years) surged in the 2000 s, and subsequently decreased. The increased HIV incidence in the elderly population in China is likely to be attributable to a variety of factors. Lack of awareness of HIV risk and the low exposure and coverage of HIV prevention campaigns, may be some of the reasons for the high incidence of HIV in this population. Low-cost commercial sex establishments are the primary sites for HIV acquisition in the elderly, and the risk of HIV infection in males aged >50 years who have commercial sex significantly increased due to a certain preference for aphrodisiac use by older men, and the presumed consequent increased bodily fluid exchange with commercial sex workers.[20] Also, condom usage among older men is known to be lower compared to younger age groups.[21,22] It has been observed that around 68.75% of elderly men who admitted high-risk sexual behaviors in rural China had never used a condom.[23] Highly influenced by traditional culture and the underlying threat of stigma, the elderly have limited access to HIV education and HIV testing,[23,24] which leads to delayed diagnosis, delayed treatment, and a higher mortality in these individuals. Other than the mortality rate for children, the mortality rates for the other age groups, especially the older age groups, have increased significantly over the past 30 years. In the absence of ART, >50% of HIV-infected infants progress to AIDS and mortality by 2 years of age.[25] In 2006, the WHO guidelines for ART for HIV infection in infants and children recommended that all HIV-infected infants should be commenced on ART soon after diagnosis, irrespective of their clinical status and/or immunological severity.[26] Initiating ART immediately can reduce morbidity and mortality in HIV-infected children and may improve neurodevelopmental outcomes.[27] Sustained declines in MPR in children suggest an increase in the effectiveness of ART in children. Conversely, therapeutic outcomes in the elderly may appear to be relatively unsatisfactory possibly secondary to the ravages of age-related cognitive impairment, poor overall psychological status in the elderly, and intolerable ART adverse effects.[28-30]

Over the past 30 years, the Chinese government has made continuous and sustained efforts to prevent and control HIV/AIDS in China. Between 1995 and 2015, fiscal spending allocated to HIV prevention and treatment in China increased by 10.1% annually, which equates to thrice the global financial commitment to HIV/AIDS-related causes.[31] In the present study, we have observed discrete trends of the MPR index for HIV in China. We have seen that the prevalence of HIV in China has decreased, and that the mortality rate has increased significantly since the 2010 s. Correspondingly, the MPR began to increase sharply from approximately this time. The possible reason for this phenomenon is likely to be related to the fact that the CRF01_AE sub-type has now become the most prevalent strain in China among individuals infected with HIV through sexual transmission, especially among MSM, since 2006.[32] The CRF01_AE subtype has been associated with a more rapid progression to AIDS compared with the C or the BC subtypes (4.8 *vs*. 8–10 years, respectively).[33] Therefore, after the peak HIV incidence rate observed in 2005, the proportion of patients with advanced disease may be even higher than previously seen. Hu *et al*[34] have reported that a late presentation rate of 70% and an advanced HIV disease presentation rate of 45% were seen among newly diagnosed HIV-infected individuals during 2012 to 2016. Furthermore, the proportion of individuals with a longer HIV infection duration tends to be higher when the overall prevalence is declining, and a longer duration of HIV infection is associated with increasing mortality in HIV-infected individuals.[35-37]

Several limitations exist in the present study. This is an ecological study based on aggregate data extracted from a large cohort; hence the ecological fallacy should not be ignored when making inferences at the individual level. A male–female gender binary was used in this work due to

insufficiency in availability of data pertaining to special gender populations, such as transgender individuals. Sexual orientation was not analyzed in this work; thus, we could not accurately estimate the impact of homosexuality and bisexuality on the HIV/AIDS burden. Sexual transmission has now become the major mode of HIV transmission in China, and therefore the detailed epidemiology of gender characteristics and sexual behaviors relating to HIV/AIDS warrants further investigation.

In conclusion, the prevalence and mortality rate for HIV globally and in China increased during 1990 to 2019. The incidence rate and MPR globally have declined over the past three decades, while those in China present a rising trend. In terms of HIV burden in different genders, the HIV burden in females globally is higher than that in males; however, this gap has reduced over the past 20 years. While there has been a male-dominated HIV burden pattern in China, the gender gap has not narrowed between males and females. In contrast to the high HIV burden among young and middle-aged adults globally, the elderly are much more at risk in China. HIV screening in older age groups should be scaled up, and patients with advanced HIV disease should be provided with early additional care and health resources.

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Conflicts of interest

None.

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