Letter to the Editor

Estimating the Effects of the COVID-19 Outbreak on the Decreasing Number of Acquired Immune Deficiency Syndrome Cases and Epidemiological Trends in China*

LI Yan Yan[1], DING Wen Hao[1], BAI Yi Chun[1], WANG Lei[2], and WANG Yong Bin[1,#]

Since the first case of acquired immune deficiency syndrome (AIDS) was detected in the United States in 1981, this disease has spread to every corner of the world. Despite the annual incidence of AIDS showing a slight decline since 1997, it remains a major cause of infectious disease-related death worldwide. Unlike global epidemiological trends, the number of notified AIDS cases has increased in recent years in China[1]. Moreover, among the class B notifiable infectious diseases, AIDS was responsible for the highest mortality rate from 2008 to 2019, still failing to be identified as a vaccine-preventable disease[1]. Thus, to provide more unambiguous and quantitative direction for the effective formulation of preventive planning strategies and for the reasonable allocation of limited resources, a forecasting model with high precision and accuracy to understand the future epidemic behaviors of AIDS is required. During the model-building process, accurate statistics are vital to ensure the forecasting accuracy of the model.

Since December 2019, coronavirus disease 2019 (COVID-19) has rapidly evolved into a major global public health issue. Confronted with this unprecedented crisis, countries have taken various measures to stop the continued spread of COVID-19. In China, a series of effective measures were implemented, and these measures played an important role in stopping the spread of COVID-19[2]. However, it is discovered that these rigorous prevention and control strategies and measures also had an effect on the incidence and mortality rates of other diseases; however, further studies are needed to measure the impacts. To date, there are no reports on the effect of such interventions on AIDS case numbers in China.

Time series analysis is frequently used to provide predictions that aid the development of effective prevention and control strategies. The causal impacts of strict counter-virus measures on AIDS case numbers can be assessed with intervention analysis under the Bayesian structural time series (BSTS) model that can generate a counterfactual prediction in a synthetic control series to describe outcomes in the absence of the intervention[3]. Therefore, the current study aims to estimate the effect of counter-COVID-19 measures on the reduction in AIDS case notifications and to predict the epidemic patterns using the BSTS model. Our findings offer insight that will aid the development of effective strategies to control AIDS case numbers in China in the future.

The monthly number of AIDS cases and population data from 31 provinces in mainland China from January 2004 to December 2020 were collected. All cases were checked medically and diagnosed in accordance with the diagnostic criteria for HIV/AIDS before being reported to the Chinese Centre for Disease Control. Considering the effects of COVID-19 on the epidemiological trend of AIDS, the data from January 2004 to December 2019 were only used when exploring the usefulness and flexibility of the BSTS model in forecasting trends in the AIDS epidemics. The average annual percentage change (AAPC) and annual percentage change (APC) were employed to describe the epidemic patterns of AIDS[4]. The BSTS model was used to perform causal inference and time series forecasting. The mean absolute deviation (MAD), root mean square error (RMSE), mean absolute percentage error (MAPE),

doi: 10.3967/bes2022.019

*This work was supported by the Innovation and Entrepreneurship Training Project for University Students of Henan Province and Xinxiang Medical University [S202110472047, S202010472007, and XYXSKYZ201932]; the Key Scientific Research Project of Universities in Henan [21A330004]; and the National Natural Fund Youth Project [31802024].

1. Department of Epidemiology and Health Statistics, School of Public Health, Xinxiang Medical University, Xinxiang, Henan, China; 2. Center for Musculoskeletal Surgery, Charité–Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt–Universität Zu Berlin and Berlin Institute of Health, Berlin, Germany

mean error rate (MER), and root mean square percentage error (RMSPE) were adopted to judge the forecasting performance of the BSTS model[4]. All statistical analyses were performed using R software (Version 3.4.3).

During the study period, there were a total of 643,800 case notifications (2.866 per 100,000 persons). A notable upward trend was observed in case numbers [AAPC = 20.446, 95% confidence interval (*CI*) 16.685 to 24.329; t = 11.493, $P < 0.001$] that comprised two stages: an upsurge from 2004 to 2010 (APC = 41.731, 95% *CI* 31.421 to 52.849; t = 10.062, $P < 0.001$) and then a slow increase from 2011 to 2020 (APC = 6.127, 95% *CI* 3.825 to 8.481; t = 5.907, $P < 0.001$) (Supplementary Figure S1, available in www.besjournal.com). The primary reason for this variation may be China's action planning on the prevention and control of AIDS (2006–2010), which stated that by 2010, the number of people living with HIV in China must be reduced to less than 1.5 million, and therefore a series of AIDS prevention measures were implemented. The incidence of AIDS showed a trough in January/February and a peak in December each year, and this seasonal pattern became more marked since 2010 (Supplementary Figure S2, available in www.besjournal.com). The effect of the spring festival may be closely related to the seasonality of AIDS.

The year 2020 was regarded as a period of intervention when performing intervention analysis using the BSTS method. In estimating the causal effect of interventions on case number reduction by use of the BSTS method, the seasonality, time effects, and the population were deemed as covariates. The predicted expected case notifications are provided in Table 1, suggesting a monthly average decrease in AIDS case notifications of 41% (95% *CI* 24% to 58%) from January–March 2020, 19% (95% *CI* 14% to 46%) from January–June 2020, and 16% (95% *CI* 7.3% to 24%) from January–December 2020 owing to the COVID-19 pandemic. The BSTS model can infer the temporal changing trends of potential effects, incorporate prior empirical information on the parameters, and deal with a complex covariate structure[3]. Considering that the Bayesian confidential interval and posterior probability of a causal effect under the BSTS model rejected the reduction in AIDS case notifications owing to the COVID-19 outbreak as a random event, this confirmed reliable evidence for a true causal impact (Table 1, Supplementary Figures S3 and S4, available in www.besjournal.com). This result suggested that COVID-19 may have resulted in medium- and longer-term impacts for the AIDS epidemic, which corroborated a previous finding that COVID-19 may have medium- and longer-term impacts on disease patterns[5]. There are a number of possible explanations for these effects[5,6]. First, people with chronic conditions or mild symptoms were discouraged from seeking medical help to reduce congestion in hospitals. Second, the stringent prevention and control measures and the mandatory requirement for the negative results of nucleic acid testing may have resulted in reluctance among people infected with HIV to have a medical diagnosis and examination. Third, many hospitals declined non-urgent service requests, especially when the medical system was overburdened during the peak of the COVID-19 outbreak. Fourth, there has been a significant decrease in the number of people administered preventive AIDS treatment, and a decrease in spending on AIDS diagnostic, therapeutic, and prevention services. Fifth, AIDS-specialized medical personnel and molecular diagnostic platforms may have been reallocated to the COVID-19 response. Sixth, the stringent anti-contagion policies restricted the movement of people, and the sudden economic disruption may have made it difficult for people infected with HIV to visit hospitals. Seventh, there are some similarities between the clinical features of AIDS (e.g., influenza-like symptoms, systemic fatigue, loss of appetite, fever, and cough) and COVID-19, resulting in concerns about stigma. Lastly, there have been delays in reporting HIV infections during the COVID-19 pandemic.

The expected figures were forecasted by averaging across the 500 Markov Chain Monte Carlo (MCMC) draws under the BSTS model (Supplementary Tables S1–S6, available in www.besjournal.com). Table 2 lists the values of MAD, RMSE, MAPE, MER, and RMSPE, which measure the predictive ability of the BSTS model. Accurate forecasts for the 12, 24, 36, 48, and 60 holdout periods were obtained because of the low error rates (this can be attributed to the BSTS model accurately showing the stochastic behavior of a time series and generating a projection based on the Bayesian model averages[7]). Whereas, an unacceptable forecast for the 72 holdout period was obtained owing to the large values of the above-mentioned five indices, especially the MAPE value, which was greater than 50% (Supplementary Figure S5, available in www.besjournal.com).

At present, the WHO has proposed an ambitious

Table 1. Causal effects of the COVID-19 pandemic on the reductions in the monthly average and cumulative number of AIDS cases from January–December 2020

Months	Average cases	Predictions (95% *CI*)	Absolute effect (95% *CI*)	Cumulative cases	Predictions (95% *CI*)	Absolute effect (95% *CI*)	Relative effect, % (95% *CI*)	*P*	Prob. of causal effect, %
1	2,759	5,355 (3,797, 6,920)	−2,596 (−4,161, −1,038)	2,759	5,355 (3,797, 6,920)	−2,693 (−4,295, −1,141)	−48 (−78, −19)	0.002	99.80
1−2	2,446	5,437 (4,308, 6,531)	−2,991 (−4,085, −1,862)	4,892	10,874 (8,615, 13,062)	−5,982 (−8,170, −3,723)	−55 (−75, −34)	0.001	99.90
1−3	3,233	5,520 (4,553, 6,425)	−2,286 (−3,191, −1,320)	9,700	16,559 (13,659, 19,274)	−6,859 (−9,574, −3,959)	−41 (−58, −24)	0.001	99.90
1−4	3,915	5,602 (4,708, 6,478)	−1,687 (−2,563, −793)	15,660	22,409 (18,831, 25,911)	−6,749 (−10,251, −3,171)	−30 (−46, −14)	0.001	99.90
1−5	4,229	5,684 (4,919, 6,486)	−1,456 (−2,257, −690)	21,144	28,422 (24,594, 32,431)	−7,278 (−11,287, −3,450)	−26 (−40, −12)	0.001	99.90
1−6	4,676	5,767 (4,963, 6,520)	−1,090 (−1,844, −286)	28,059	34,600 (29,777, 39,120)	−6,541 (−11,061, −1,718)	−19 (−32, −5)	0.004	99.60
1−7	4,883	5,849 (5,185, 6,526)	−966 (−1,642, −301)	34,183	40,943 (36,292, 45,680)	−6,760 (−11,497, −2,109)	−17 (−28, −5.1)	0.003	99.70
1−8	4,919	5,931 (5,627, 6,628)	−1,013 (−1,709, −348)	39,349	47,449 (42,135, 53,025)	−8,100 (−13,676, −2,786)	−17 (−29, −5.9)	0.002	99.80
1−9	5,142	6,013 (5,401, 6,646)	−872 (−1,504, −259)	46,276	54,121 (48,607, 59,813)	−7,845 (−13,537, −2,331)	−14 (−25, −4.3)	0.004	99.60
1−10	5,082	6,096 (5,482, 6,715)	−1,013 (−1,633, −400)	50,822	60,957 (54,822, 67,153)	−10,135 (−16,331, −4,001)	−17 (−27, −6.6)	0.001	99.90
1−11	5,150	6,178 (5,608, 6,790)	−1,028 (−1,640, −458)	56,646	67,958 (61,685, 74,690)	−11,312 (−18,044, −5,039)	−17 (−27, −7.4)	0.002	99.80
1−12	5,263	6,260 (5,719, 6,784)	−997 (−1,521, −457)	63,154	75,124 (68,634, 81,407)	−11,970 (−18,253, −5,480)	−16 (−24, −7.3)	0.002	99.80

Note. *CI*, confidence interval

target for AIDS prevention, with a 75% reduction in new infections, including key populations, from 2010 to 2020, and the end of the AIDS epidemic as a public health threat by 2030[8]. Accordingly, we re-erected the BSTS model based on 17 complete years of data (including the modified 2020 data) to forecast the AIDS epidemic from January 2021 to December 2025. The results showed that the estimated incident rates will continue to surge (APC = 6.374, 95% *CI* 5.541 to 7.213; t = 16.855, $P < 0.001$) reaching a comparatively high level of 94,870 cases (95% *CI* 1,620 to 5,611,911) in 2025, which will be 2.593-fold higher than the 36,594 cases recorded in 2010 (Supplementary Table S7, Figures S6 and S7, available in www.besjournal.com). Currently, an estimated 70% of individuals infected with HIV globally occur in low- and middle-income settings, mainly in eastern and southern Africa, western and central Africa, and the Asian–Pacific region[9], and achieving set objectives will also depend on whether efforts in these settings accelerate or stall. Moreover, China's new AIDS cases accounted for 23% of the total number of new infections in the Asian–Pacific region in 2019[9]. These findings indicate that AIDS will still plague China and achieving the goal of ending the AIDS epidemic by 2030 poses a great challenge[8]. Therefore, to tackle such a major public health problem, intervention strategies need to be strengthened and new effective prophylaxis methods for AIDS need to be proactively explored. In addition, it is estimated that more than 60% of AIDS cases are infected through heterosexual sex, and student infections are increasing in China[10], thus there is an imminent need to implement HIV screening and popularize earlier sex education (from age 9) according to UNESCO guidance.

This study had several limitations. First, the data spanned the period of policy intervention (2010). Though the results stemmed from the preferred model are as good as the expected, the real effects before and after the sudden escalation of AIDS morbidity on the model accuracy remain unknown. Second, an estimated 32.4% of people who have been infected with AIDS are unaware of their infection status in China[1]. Hence, the actual situation may be more serious than that estimated. Third, many complicated influencing factors, some of which may be unpredictable, can be contributors to the transmission of AIDS incidence. Fourth, it is necessary to make timely updates to models as short-term data becomes available to increase the predictive ability of the model. Lastly, the analytical epidemic data merely represent the country-level situation and overall trends in AIDS incidence, our method may be of great benefit to other regions or infectious diseases as well.

In summary, the current findings indicate that COVID-19 may have significant consequences for the AIDS epidemic, as determined by the BSTS model. This model can act as a useful technique to estimate the temporal behaviors of AIDS, and thus assist policymakers in rationally allocating health resources and appropriately formulating prevention and control strategies for this disease. Since new AIDS infections will continue to increase, there is an urgency to adopt appropriate and effective prevention and control policies in China.

#Correspondence should be addressed to WANG Yong Bin, Professor, MD, Tel: 86-373-3831646, E-mail: wybwho@163.com

Biographical note of the first author: LI Yan Yan, female, born in 1996, Master of Medical Science, majoring in infectious disease epidemiology.

Table 2. Comparisons of the predictive performance under the BSTS models

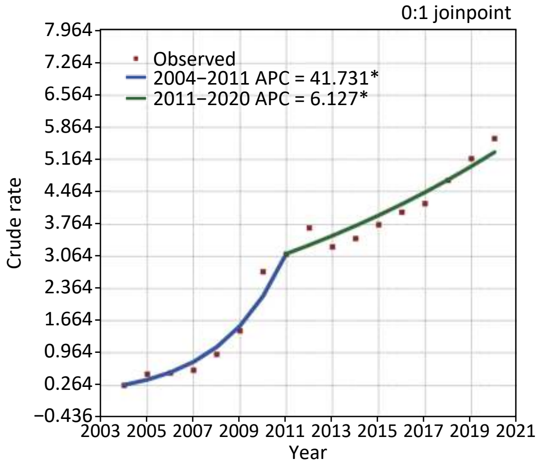
BSTS Models	Testing horizons				
	MAD	MAPE	RMSE	MER	RMSPE
12-step ahead prediction	874.248	13.469	1,110.482	0.144	0.167
24-step ahead prediction	604.931	11.062	723.140	0.105	0.131
36-step ahead prediction	890.655	16.853	1,088.463	0.163	0.202
48-step ahead prediction	2,062.473	37.534	2,541.301	0.392	0.440
60-step ahead prediction	767.230	15.228	1,020.522	0.151	0.199
72-step ahead prediction	3,140.360	59.821	3,889.489	0.644	0.698

Note. BSTS, Bayesian structural time series model; MAD, mean absolute deviation; MAPE, mean absolute percentage error; RMSE, root mean square error; MER, mean error rate; RMSPE, root mean square percentage error.

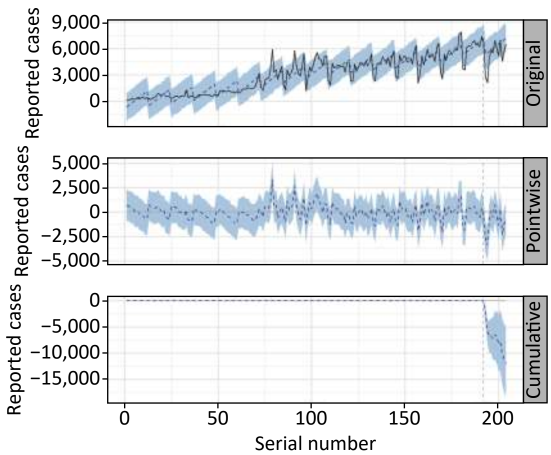
Received: August 24, 2021;
Accepted: November 4, 2021

REFERENCES

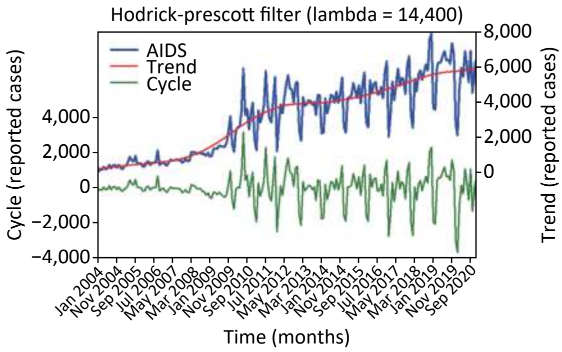
1. Chinese Center for Disease Control and Prevention. Infectious diseases. http://www.chinacdc.cn/mtbd_8067/201610/t20161031_135188.html. [2021-10-21]. (In Chinese)
2. Pan A, Liu L, Wang CL, et al. Association of public health interventions with the epidemiology of the COVID-19 outbreak in Wuhan, China. JAMA, 2020; 323, 1915−23.
3. Brodersen KH, Gallusser F, Koehler J, et al. Inferring causal impact using Bayesian structural time-series models. Ann Appl Stat, 2015; 9, 247−74.
4. Wang YB, Xu CJ, Ren JC, et al. Secular seasonality and trend forecasting of tuberculosis incidence rate in china using the advanced error-trend-seasonal framework. Infect Drug Resist, 2020; 13, 733−47.
5. WHO. Global tuberculosis report 2020. https://apps.who.int/iris/handle/10665/336069. [2021-10-21].
6. Qi JL, Zhang DD, Zhang X, et al. Do lockdowns bring about additional mortality benefits or costs? Evidence based on death records from 300 million Chinese people. medRxiv, 2021.
7. Scott SL, Varian HR. Bayesian variable selection for nowcasting economic time series. National Bureau of Economic Research. Cambridge. 2013.
8. WHO. Global health sector strategy on HIV: 2016-2021. https://www.who.int/publications/i/item/WHO-HIV-2016.05. [2021-10-21].
9. WHO. HIV/AIDS. https://www.who.int/health-topics/hiv-aids#tab=tab_1. [2021-10-21].
10. Xu JJ, Reilly KH, Lu CM, et al. A cross-sectional study of HIV and syphilis infections among male students who have sex with men (MSM) in northeast China: implications for implementing HIV screening and intervention programs. BMC Public Health, 2011; 11, 287.



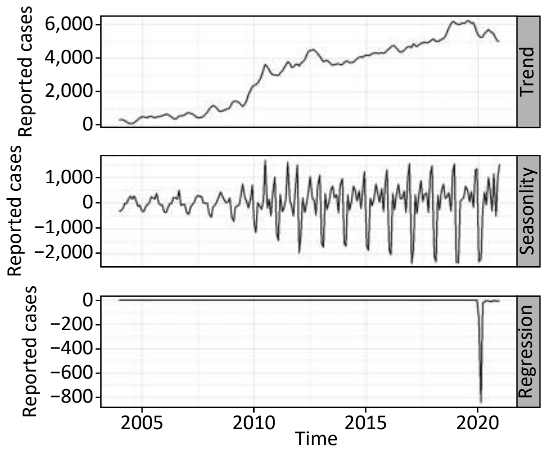
Supplementary Figure S1. Joinpoint regression plot showing the AIDS epidemiological trends during 2004–2020. *Showed that the annual percent change (APC) is statistically significant.



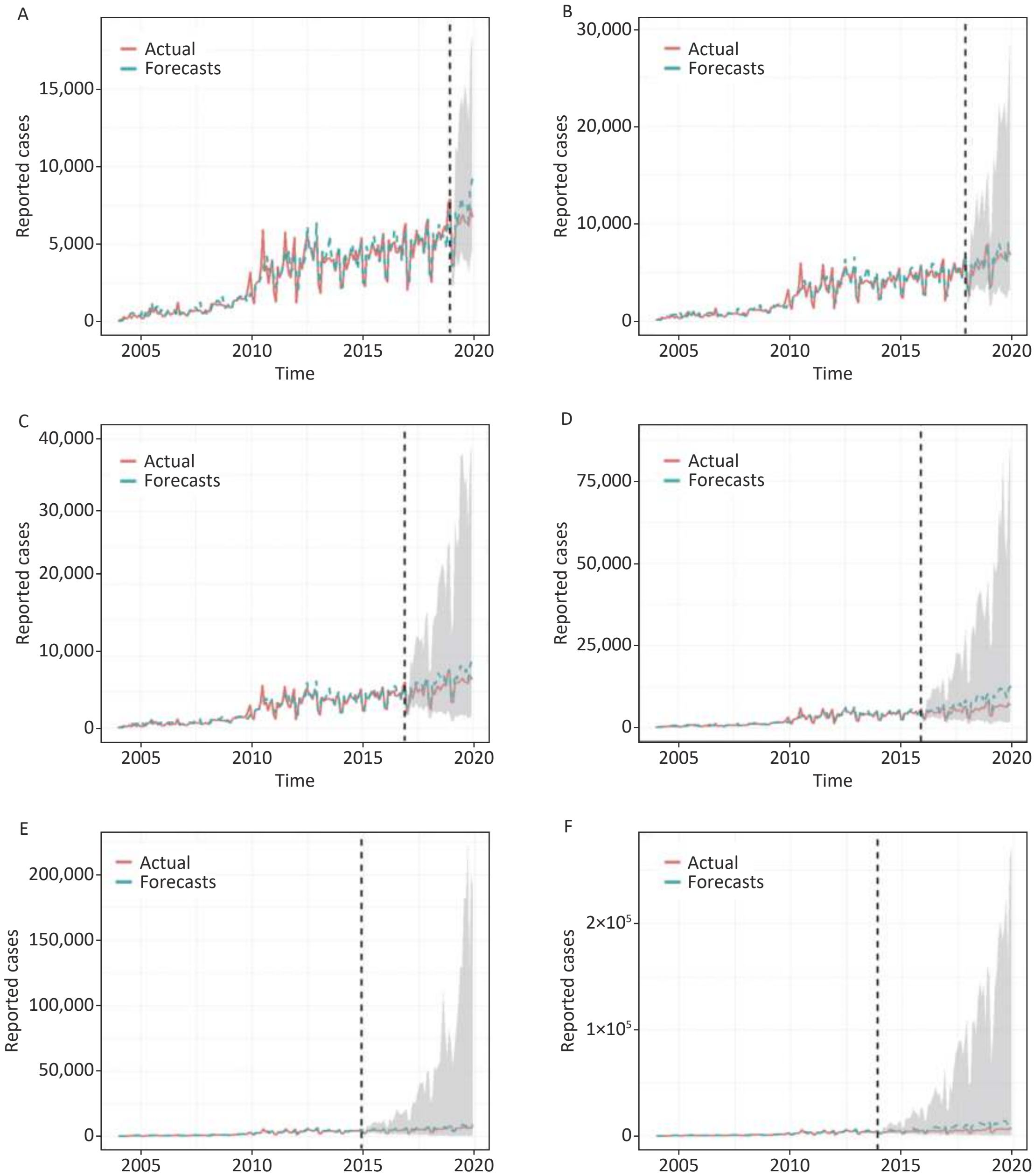
Supplementary Figure S3. Time series plot displaying the causal impacts of the COVID-19 outbreak on the decreases in AIDS cases from January–December 2020. The first panel provides the reported AIDS cases and counterfactual expected figures for the post-outbreak period. The second panel describes the pointwise causal impact that indicates the difference between reported cases and expected figures. The third panel illustrates a cumulative effect of the COVID-19 pandemic on the decreases in AIDS cases via accumulating the pointwise effects from the second panel.



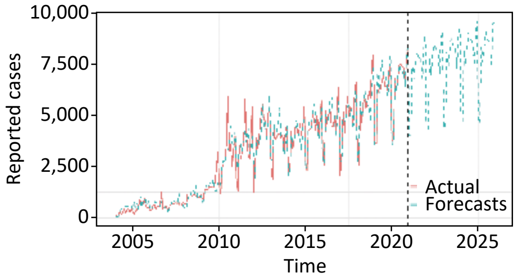
Supplementary Figure S2. Time series plot showing the AIDS incidence and the decomposed tend and cyclicity based on the Hodrick-Prescott filter technique.



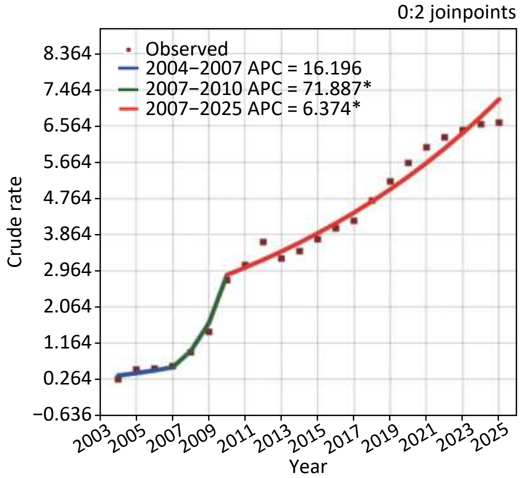
Supplementary Figure S4. Contribution of trend, seasonality, and regression (COVID-19 outbreak) components to the AIDS incidence. As depicted, the AIDS incidence has a noticeable seasonal pattern and the COVID-19 outbreak causes a remarkable decrease in AIDS cases during this period.



Supplementary Figure S5. Time series plot showing the forecasted temporal trends of the AIDS incidence for (A) 12 holdout data, (B) 24 holdout data, (C) 36 holdout data, (D) 48 holdout data, (E) 60 holdout data, and (F) 72 holdout data under BSTS approaches. It can be seen that the BSTS approaches are able to better capture the long-term epidemiological trends of AIDS for the 60-step ahead forecast except for the 72 holdout data.



Supplementary Figure S6. Time series plot showing the forecasting results until 2025. This plot displays the actual series in red, and the fitting and forecasting results as a blue line. It seemed that the BSTS method predicted a rising trend from January 2021 to December 2025.



Supplementary Figure S7. Joinpoint regression plot showing the AIDS epidemiological trends during 2004–2025. *Showed that the annual percent change (APC) is statistically significant.

Supplementary Table S1. Projection into the next 12 months with the best BSTS model

Time	Observed values	Forecasts	Lower 95% *CI*	Upper 95% *CI*
Jan-19	3,688	3,585	2,312	5,456
Feb-19	3,587	3,705	2,392	5,749
Mar-19	6,086	7,096	4,435	11,251
Apr-19	6,277	6,243	3,561	10,956
May-19	6,291	7,160	3,953	13,509
Jun-19	6,642	7,998	4,629	14,462
Jul-19	6,912	7,419	4,017	13,787
Aug-19	6,404	7,495	3,994	15,313
Sep-19	6,435	7,645	3,919	14,208
Oct-19	6,207	6,554	3,210	12,858
Nov-19	7,366	8,685	4,182	17,364
Dec-19	6,735	9,262	4,648	18,713

Note. BSTS, bayesian structural time series; *CI*, confidence interval.

Supplementary Table S2. Projection into the next 24 months with the best BSTS model

Time	Observed values	Forecasts	Lower 95% *CI*	Upper 95% *CI*
Jan-18	3,309	2,706	1,733	4,268
Feb-18	2,559	3,282	2,034	5,223
Mar-18	5,331	5,764	3,453	9,530
Apr-18	4,642	5,084	3,012	8,324
May-18	5,593	5,713	3,337	10,153
Jun-18	5,809	6,589	3,817	13156
Jul-18	5,289	5,947	3,413	10,132
Aug-18	5,750	6,046	2,982	11,945
Sep-18	6,155	6,299	3,339	13,452
Oct-18	5,823	5,156	2,819	10,586
Nov-18	7,622	6,724	3,594	13,686
Dec-18	7,897	7,782	3,960	15,353
Jan-19	3,688	3,270	1,460	8,265
Feb-19	3,587	3,948	1,691	9,199
Mar-19	6,086	6,775	3,091	16,810
Apr-19	6,277	5,947	2,570	15,191
May-19	6,291	7,084	3,006	17,463
Jun-19	6,642	7,916	3,595	22,345
Jul-19	6,912	7,161	2,983	20,196
Aug-19	6,404	7,167	2,806	21,118
Sep-19	6,435	7,223	2,768	22,372
Oct-19	6,207	5,907	2,186	19,169
Nov-19	7,366	8,081	3,164	23,776
Dec-19	6,735	8,696	3,095	29,832

Note. BSTS, bayesian structural time series; *CI*, confidence interval.

Supplementary Table S3. Projection into the next 36 months with the best BSTS model

Time	Observed values	Forecasts	Lower 95% *CI*	Upper 95% *CI*
Jan-17	2,053	2,944	1,868	4,654
Feb-17	3,325	2,815	1,749	4,723
Mar-17	5,179	5,577	3,370	9,258
Apr-17	4,140	4,976	2,788	8,672
May-17	5,025	5,517	2,834	10,287
Jun-17	5,916	6,377	3,482	12,599
Jul-17	4,950	6,269	3,141	12,730
Aug-17	5,400	5,717	2,748	11,901
Sep-17	5,283	6,059	3,008	12,664
Oct-17	4,485	5,100	2,345	10,740
Nov-17	6,136	6,371	3,006	14,836
Dec-17	6,622	7,131	2,986	16,146
Jan-18	3,309	3,441	1,504	7,664
Feb-18	2,559	3,267	1,299	8,142
Mar-18	5,331	6,569	2,303	14,159
Apr-18	4,642	6,023	2,296	15,409
May-18	5,593	6,394	2,034	15,797
Jun-18	5,809	7,606	2,418	19,859
Jul-18	5,289	7,200	2,279	21,236
Aug-18	5,750	6,673	2,307	22,733
Sep-18	6,155	7,243	2,021	21,877
Oct-18	5,823	5,769	1,755	18,021
Nov-18	7,622	7,548	2,445	24,995
Dec-18	7,897	8,122	2,112	25,658
Jan-19	3,688	4,014	1,178	13,043
Feb-19	3,587	3,796	842	14,831
Mar-19	6,086	7,528	1,739	28,360
Apr-19	6,277	6,792	1,596	24,977
May-19	6,291	7,499	1,692	26,202
Jun-19	6,642	8,662	1,901	37,588
Jul-19	6,912	8,251	1,831	37,973
Aug-19	6,404	7,661	1,746	33,448
Sep-19	6,435	8,179	1,764	34,716
Oct-19	6,207	6,671	1,312	27,925
Nov-19	7,366	8,418	1,565	35,771
Dec-19	6,735	9,528	1,606	40,078

Note. BSTS, bayesian structural time series; CI, confidence interval.

Supplementary Table S4. Projection into the next 48 months with the best BSTS model

Time	Observed values	Forecasts	Lower 95% *CI*	Upper 95% *CI*
Jan-16	2,862	2,766	1,781	4,174
Feb-16	2,582	2,751	1,717	4,439
Mar-16	5,255	5,259	3,168	8,292
Apr-16	4,574	4,938	2,831	8,590
May-16	5,041	5,151	2,922	8,973
Jun-16	5159	6106	3454	11682
Jul-16	4,459	6,173	3,197	11,654
Aug-16	4,469	5,745	2,797	11,691
Sep-16	4,877	6,061	3,029	13,069
Oct-16	4,244	4,885	2,295	9,766
Nov-16	5,743	6,146	3,018	12,823
Dec-16	6,335	6,898	3,033	14,758
Jan-17	2,053	3,339	1,592	7,973
Feb-17	3,325	3,362	1,433	8,756
Mar-17	5,179	6,321	2,557	15,687
Apr-17	4,140	5,876	2,221	13,813
May-17	5,025	6,263	2,290	15,660
Jun-17	5,916	7,497	2,779	18,637
Jul-17	4,950	7,643	2,277	22,919
Aug-17	5,400	6,807	2,341	22,403
Sep-17	5,283	7,443	2,333	22,594
Oct-17	4,485	5,853	1,745	16,034
Nov-17	6,136	7,388	2,245	23,326
Dec-17	6,622	8,332	2,706	29,883
Jan-18	3,309	4,021	1,123	13,424
Feb-18	2,559	3,994	1,037	14,080
Mar-18	5,331	7,724	2,011	27,797
Apr-18	4,642	7,050	1,963	31,483
May-18	5,593	7,573	1,900	27,575
Jun-18	5,809	9,408	2,449	37,644
Jul-18	5,289	9,804	2,312	40,557
Aug-18	5,750	8,510	2,014	41,629
Sep-18	6,155	9,478	2,198	36,469
Oct-18	5,823	7,441	1,447	32,547
Nov-18	7,622	9,239	1,979	37,493
Dec-18	7,897	10,527	1,783	44,662
Jan-19	3,688	5,195	1,086	24,229
Feb-19	3,587	5,156	1,042	25,715
Mar-19	6,086	9,818	1,860	50,315
Apr-19	6,277	9,066	1,679	46,861
May-19	6,291	9,884	1,700	50,171
Jun-19	6,642	11,797	2,223	65,983
Jul-19	6,912	12,051	2,034	61,158
Aug-19	6,404	10,416	1,676	81,220
Sep-19	6,435	11,049	1,731	58,159
Oct-19	6,207	8,958	1,486	51,077
Nov-19	7,366	11,484	1,667	74,941
Dec-19	6,735	12,685	1,831	88,125

Note. BSTS, bayesian structural time series; CI, confidence interval.

Supplementary Table S5. Projection into the next 60 months with the best BSTS model

Time	Observed values	Forecasts	Lower 95% *CI*	Upper 95% *CI*
Jan-15	2,597	2,474	1,534	4,413
Feb-15	2,294	2,574	1,436	4,199
Mar-15	4,238	4,854	2,911	8,455
Apr-15	4,299	4,196	2,592	7,072
May-15	4,401	4,612	2,580	8,747
Jun-15	5,089	5,411	3,130	10,218
Jul-15	4,701	5,836	2,930	11,613
Aug-15	4,268	4,749	2,546	9,391
Sep-15	4,967	5,105	2,315	11,255
Oct-15	3,955	4,103	2,018	9,834
Nov-15	5,040	5,004	2,234	10,702
Dec-15	5,707	5,819	2,536	13,160
Jan-16	2,862	2,703	1,067	6,714
Feb-16	2,582	2,776	893	7,598
Mar-16	5,255	5,274	1,924	13,781
Apr-16	4,574	4,288	1,575	10,917
May-16	5,041	4,984	1,554	12,621
Jun-16	5,159	5,793	1,757	16,881
Jul-16	4,459	6,415	1,910	21,076
Aug-16	4,469	5,358	1,465	16,956
Sep-16	4,877	5,619	1,634	17,392
Oct-16	4,244	4,662	1,452	17,245
Nov-16	5,743	5,677	1,804	19,784
Dec-16	6,335	6,425	1,591	20,543
Jan-17	2,053	3,010	732	11,769
Feb-17	3,325	3,051	720	13,038
Mar-17	5,179	5,875	1,364	22,057
Apr-17	4,140	5,123	1,168	26,849
May-17	5,025	5,609	1,159	24,855
Jun-17	5,916	6,616	1,177	32,987
Jul-17	4,950	6,833	1,181	39,226
Aug-17	5,400	6,172	1,115	40,976
Sep-17	5,283	6,263	1,049	41,277
Oct-17	4,485	5,240	931	31,314
Nov-17	6,136	6,396	940	48,099
Dec-17	6,622	7,250	1,060	50,689
Jan-18	3,309	3,367	357	24,691
Feb-18	2,559	3608	418	30,930
Mar-18	5,331	6,746	643	53,437
Apr-18	4,642	5,930	465	50,670
May-18	5,593	6,379	648	53,217
Jun-18	5,809	7,881	737	57,138
Jul-18	5,289	8,078	677	78,031
Aug-18	5,750	7,179	487	111,173
Sep-18	6,155	7,219	540	80,104
Oct-18	5,823	6,078	584	60,510
Nov-18	7,622	7,437	503	82,208
Dec-18	7,897	8,265	533	71,013
Jan-19	3,688	3,820	211	52,724
Feb-19	3,587	4,016	236	68,210
Mar-19	6,086	7,672	460	83,660
Apr-19	6,277	6,665	318	101,159
May-19	6,291	7,481	322	129,623
Jun-19	6,642	8,742	415	128,950

Continued

Time	Observed values	Forecasts	Lower 95% *CI*	Upper 95% *CI*
Jul-19	6,912	8,871	453	182,465
Aug-19	6,404	7,825	323	181,758
Sep-19	6,435	8,215	304	222,292
Oct-19	6,207	6,633	216	130,049
Nov-19	7,366	8,190	337	199,002
Dec-19	6,735	9,085	230	188,134

Note.BSTS, bayesian structural time series; *CI*, confidence interval.

Supplementary Table S6. Projection into the next 72 months with the best BSTS model

Time	Observed values	Forecasts	Lower 95% *CI*	Upper 95% *CI*
Jan-14	2,245	2,248	1,364	3,811
Feb-14	2,289	2,326	1,417	4,103
Mar-14	4,221	4,551	2,796	8,753
Apr-14	3,369	4,071	2,337	7,789
May-14	3,823	4,300	2,242	8,564
Jun-14	4,432	5,176	2,632	11,535
Jul-14	4,354	6,050	3,237	13,252
Aug-14	3,997	5,118	2,518	10,324
Sep-14	4,611	5,095	2,510	11,326
Oct-14	3,999	4,216	2,080	9,447
Nov-14	4,464	5,388	2,334	12,817
Dec-14	5,411	5,983	2,389	14,747
Jan-15	2,597	2,886	1,249	8,076
Feb-15	2,294	2,991	1,121	8,015
Mar-15	4,238	5,855	2,103	16,965
Apr-15	4,299	5,358	1,821	15,957
May-15	4,401	5,732	2,180	17,290
Jun-15	5,089	6,551	2,356	19,142
Jul-15	4,701	7,366	2,031	25,922
Aug-15	4,268	6,224	1,919	22,123
Sep-15	4,967	6,304	1,843	21,615
Oct-15	3,955	5,018	1,325	16,571
Nov-15	5,040	6,926	1,817	25,702
Dec-15	5,707	7,242	1,651	26,487
Jan-16	2,862	3,499	780	14,964
Feb-16	2,582	3,619	773	15,472
Mar-16	5,255	7,045	1,596	29,623
Apr-16	4,574	6,511	1,430	29,495
May-16	5,041	7,017	1,527	34,917
Jun-16	5,159	7,990	1,740	38,840
Jul-16	4,459	8,977	1,779	463,46
Aug-16	4,469	7,771	1,604	38,165
Sep-16	4,877	7,892	1,443	40,796
Oct-16	4,244	6,228	1,004	29,315
Nov-16	5,743	8,205	1,686	38,088
Dec-16	6,335	9,241	1,489	62,837
Jan-17	2,053	4,246	804	24,857
Feb-17	3,325	4,470	826	24,584
Mar-17	5,179	8,495	1,276	49,529
Apr-17	4,140	7,744	1,220	40,241
May-17	5,025	8,628	1,425	61,772
Jun-17	5,916	9,532	1,397	76,932

Continued

Time	Observed values	Forecasts	Lower 95% *CI*	Upper 95% *CI*
Jul-17	4,950	10,786	1,551	82,617
Aug-17	5,400	9137	1237	90,036
Sep-17	5,283	9,181	1,195	89,067
Oct-17	4,485	7,446	862	74,554
Nov-17	6,136	9,671	1,319	91,413
Dec-17	6,622	10,857	1,249	109,528
Jan-18	3,309	5,181	606	48,530
Feb-18	2,559	5,157	582	49,770
Mar-18	5,331	10,082	1,226	105,203
Apr-18	4,642	9,580	925	109,208
May-18	5,593	10,171	1,086	95,111
Jun-18	5,809	11,679	1,260	128,081
Jul-18	5,289	12,890	1,174	144,514
Aug-18	5,750	11,262	935	131,632
Sep-18	6,155	11,565	799	141,919
Oct-18	5,823	9,189	664	102,419
Nov-18	7,622	11,952	1,042	159,851
Dec-18	7,897	12,981	959	151,496
Jan-19	3,688	6,427	538	67,619
Feb-19	3,587	6,515	476	91,573
Mar-19	6,086	12,569	971	138,145
Apr-19	6,277	11,290	724	155,486
May-19	6,291	12,570	814	188,043
Jun-19	6,642	14,170	873	201,496
Jul-19	6,912	16,199	1,331	183,713
Aug-19	6,404	13,710	916	196,102
Sep-19	6,435	13,720	863	222,283
Oct-19	6,207	11,039	589	166,215
Nov-19	7,366	141,95	829	260,006
Dec-19	6,735	16,142	885	272,946

Note.BSTS, bayesian structural time series; *CI*, confidence interval.

Supplementary Table S7. Projection into time windows between January 2021 and December 2025 with the best BSTS model

Time	Forecasts	Lower 95% *CI*	Upper 95% *CI*
Jan-21	3,997	2,570	6,051
Feb-21	4,029	2,744	6,276
Mar-21	7,365	4,578	11,810
Apr-21	6,796	4,239	10,739
May-21	7,340	4,303	12,784
Jun-21	8,096	4,501	13,923
Jul-21	7,905	4,592	14,086
Aug-21	7,717	4,192	15,547
Sep-21	7,780	4,325	15,556
Oct-21	6,792	3,493	13,938
Nov-21	8,348	4,260	16,684
Dec-21	8,923	4,320	19,075
Jan-22	4,205	1,838	10,566
Feb-22	4,331	1,630	10,914
Mar-22	7,804	3,282	18,627
Apr-22	6,971	2,796	19,686
May-22	7,854	2,662	24,626
Jun-22	8,462	2,885	26,701

Continued

Time	Forecasts	Lower 95% *CI*	Upper 95% *CI*
Jul-22	8,349	2,543	29,112
Aug-22	8,113	2,312	29,307
Sep-22	7,987	2,466	28,822
Oct-22	6,987	1,814	27,818
Nov-22	8,734	2,159	36,316
Dec-22	9,077	2,204	41,700
Jan-23	4,383	932	21,373
Feb-23	4,359	824	26,530
Mar-23	8,055	1,700	42,445
Apr-23	7,354	1,399	46,078
May-23	8,076	1,407	54,858
Jun-23	8,753	1,531	69,291
Jul-23	8,451	1,195	68,181
Aug-23	8,417	1,238	92,746
Sep-23	8,258	1,042	68,585
Oct-23	7,251	838	67,220
Nov-23	8,917	975	98,745
Dec-23	9,380	983	99,853
Jan-24	4,436	391	47,999
Feb-24	4,545	364	58,966
Mar-24	8,161	616	123,931
Apr-24	7,552	472	129,781
May-24	8,209	480	142,703
Jun-24	9,008	583	187,843
Jul-24	8,725	426	189,636
Aug-24	8,648	426	224,957
Sep-24	8,502	384	171,097
Oct-24	7,510	307	163,992
Nov-24	9,163	297	267,638
Dec-24	9,575	327	312,094
Jan-25	4,594	141	158,220
Feb-25	4,651	114	182,361
Mar-25	8,332	230	324,672
Apr-25	7,598	157	307,727
May-25	8,367	147	400,556
Jun-25	9,073	190	522,450
Jul-25	8,714	134	535,229
Aug-25	8,604	122	576,059
Sep-25	8,463	104	548,544
Oct-25	7,485	100	525,668
Nov-25	9,453	97	726,947
Dec-25	95,36	84	803,479

Note.BSTS, bayesian structural time series; *CI*, confidence interval.