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Can Japan Achieve Zero Transmission of HIV? Time Series Analysis Using Bayesian Local Linear Trend Model

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Background: The number of newly diagnosed human immunodeficiency virus (HIV) infections and acquired immune deficiency syndrome (AIDS) patients in Japan appears to be decreasing. However, whether these new infections cease to occur in the future in Japan, similar to abroad, is unclear. To evaluate the feasibility of this achievement, we conducted a time series analysis using Bayesian local linear trend model to evaluate the possibility of zero new infection of HIV/AIDS in Japan.

Methods: We used quarterly data on HIV/AIDS from the first quarter, 2001 to the second quarter, 2020. Bayesian analyses were conducted using Markov chain Monte Carlo (MCMC) method, and a local linear trend model was constructed for number of newly diagnosed HIV infection without AIDS diagnosis, AIDS cases, and their aggregate. Predictions for the following 60 quarters until the second quarter of 2035 were also made for all models.

Results: The mean aggregate cases of HIV/AIDS patients became 0 by the fourth quarter of 2031 (90% credible interval 0-535). For HIV infections alone, mean cases became 0 by the second quarter of 2030 (90%CrI 0-472). For AIDS alone mean cases were 9 at the second quarter of 2035 (90%CrI 0-231).

Conclusion: Our local linear trend model suggested that number of HIV/AIDS cases in Japan could decrease to zero by the first quarter of 2031, if the trend of the infections followed the local linear trend model, yet with rather wide credible interval. Achieving zero new transmission of HIV in Japan is a realistic goal but measures to make it faster may be needed.

INTRODUCTION

The number of newly diagnosed human immunodeficiency virus (HIV) infections and acquired immune deficiency syndrome (AIDS) patients in Japan appears to be decreasing according to surveillance data. In 2019, 903 newly diagnosed HIV infections without AIDS and 333 AIDS patients were reported, and both declined for 3 consecutive years [1]. For this apparent decline, one might be optimistic to consider that Japan is catching up with other developed nations, which successfully declined number of new infections. However, whether they will continue to decline and to reach zero, like goals measures taken abroad, remains unclear [2,3].

Therefore, we conducted a time series analysis using Bayesian inference to using local linear trend model to evaluate the possibility that the zero new HIV infection in Japan is achievable goal.

Subjects and Methods

We used quarterly data on HIV/AIDS from the first quarter, 2001 (2001Q1) to the second quarter, 2020 (2019Q2), provided by Japan Foundation for AIDS prevention (https://api-net.jfap.or.jp/status/japan/nenpo.html). Bayesian analyses were conducted using Markov chain Monte Carlo (MCMC) method, and local linear trend models were constructed for number of newly diagnosed HIV infection without AIDS diagnosis, AIDS cases, and their aggregate.

The expressions of our model are as follows:

$$\mu_t \sim Normal(\mu_{t-1} + \delta_{t-1}, s_w)$$
$$\delta_t \sim Normal(\delta_{t-1}, s_d)$$
$$Y_t \sim Normal(\mu_t, s_o)$$

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In this model, number of newly diagnosed patients, Y, is assumed to follow a normal distribution with the mean of μ and the standard deviation of s_o. We assumed non-informative uniform distributions as priors. The drift component of the mean, δ, follows random walk as well as μ itself. We denoted the standard deviations of each random walk process as s_w and s_d. Predictions for the following 60 quarters (up until the second quarter, 2035) were also made for models, with 90% credible intervals. If projected cases reached zero, the year of the achievement also was documented.

We set 4 separate sampling sequences, each consisting of 5000 random samples (including 2500 samples discarded for convergence) with thinning every 5 samples. Sampling convergence was evaluated by Gelman-Rubin statistics and by visually inspecting a trace plot. We used the R software program, version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria) with a probabilistic programming language Stan (Stan development team) for all Bayesian analyses.

This study was exempted from approval by the ethics committee of Kobe University Graduate School of Medicine as the study used only data on public domain without having conflicts with individual patient safety, confidentiality, or others.

RESULTS

The mean aggregate cases of HIV/AIDS patients became 0 by the fourth quarter of 2031 (90% credible interval 0-535) (Figure 1A). For HIV infections alone, mean cases became 0 by the second quarter of 2030 (90%CrI 0-472) (Figure 1B). For AIDS alone mean cases became 9 at the second quarter of 2035 (90%CrI 0-231) (Figure 1C). All MCMCs showed convergences of trace plot and Rhat of predicted patients remained less than 1.10.

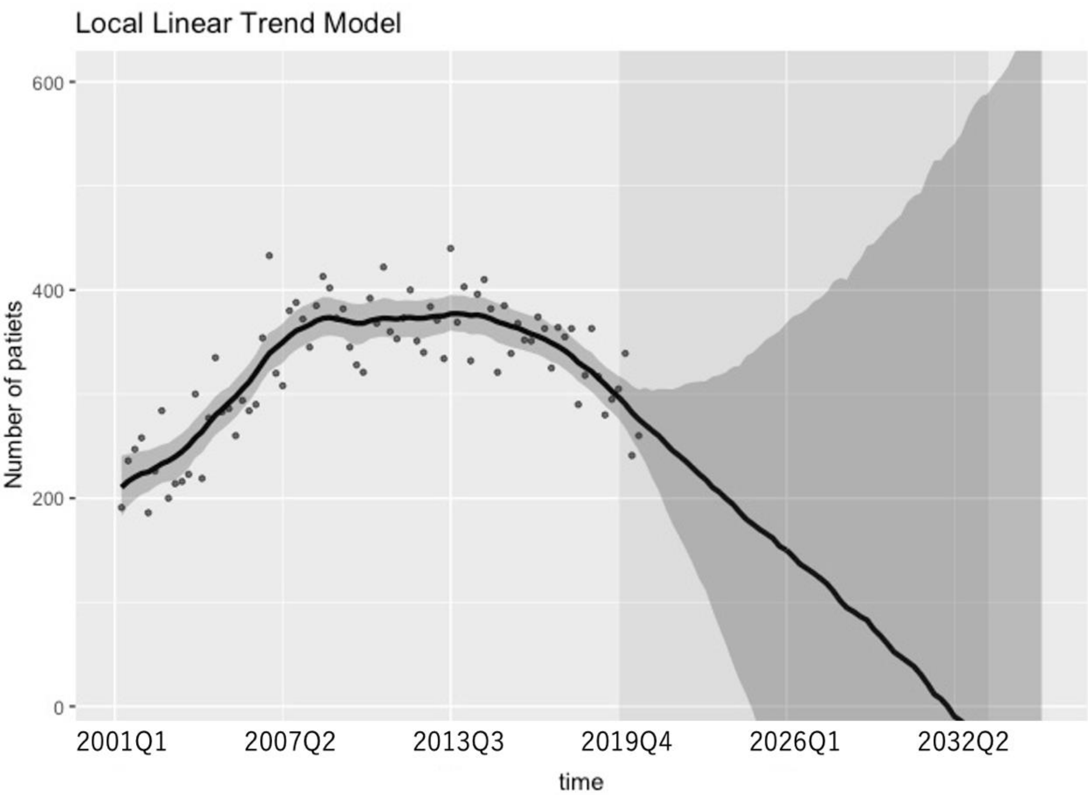

Figure 1A

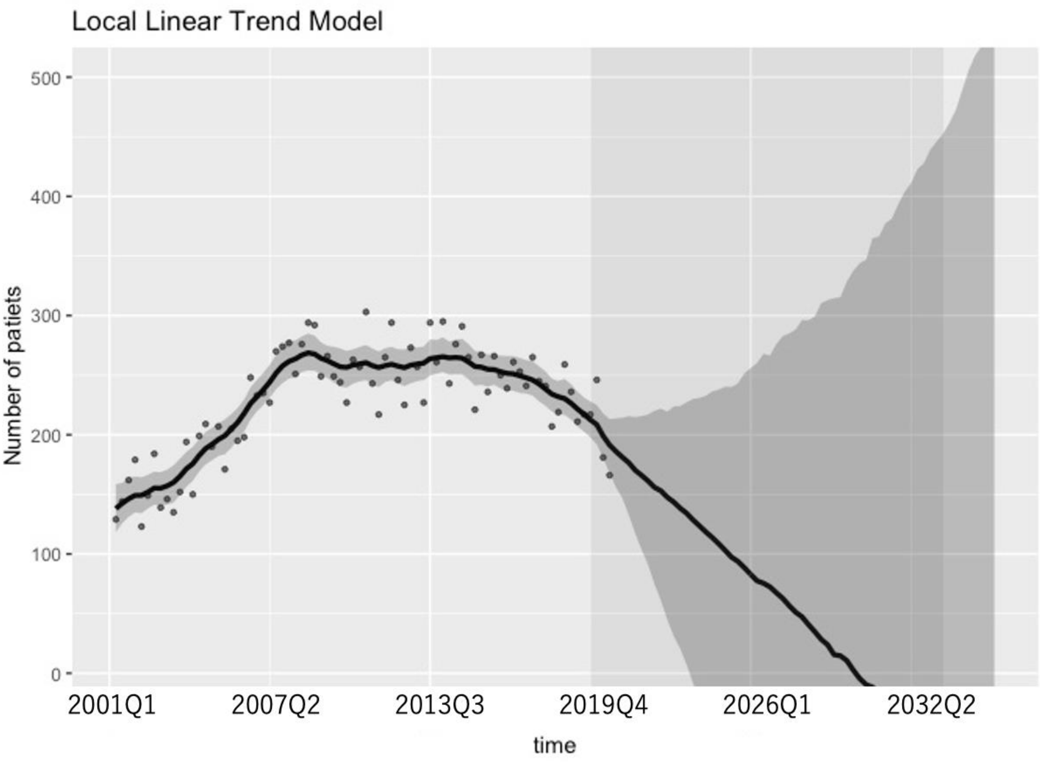

Figure 1B

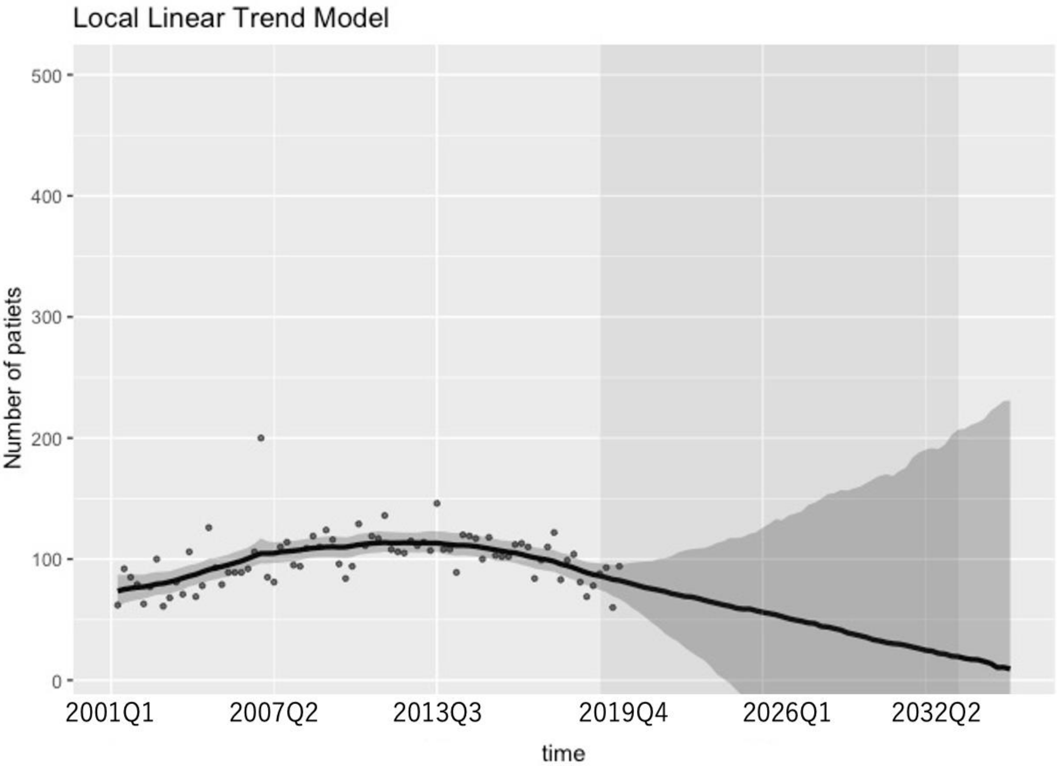

Figure 1C

Fig. 1. Local linear trend model for quarterly reported data on number of A. HIV/AIDS patients, B. HIV patients without AIDS, and C AIDS patients in Japan from 2001 quarter 1 to 2020 quarter 2, with prediction for the following 60 quarters (until 2035 quarter 2). Dot: actual number, solid line: forecasted number, band:90% credible interval, and gray rectangle: predicted numbers. HIV, human immunodeficiency virus. AIDS, acquired immune deficiency syndrome.

DISCUSSION

Our local linear trend model suggested that number of HIV/AIDS cases in Japan could continue to decline if it followed local linear trend model, and could reach zero in 2031, granted there is no significant change in the trend in future, although credible intervals of our analysis were quite wide. These suggest that achieving zero transmission of HIV in Japan is feasible and realistic goal, although it might take for more than 10 years.

The United States aims at ending the spread of HIV in the United States by the year 2030 [2], thanks to early diagnosis and provision of antiretroviral therapy both before and after the infection. The former measure is preexposure prophylaxis (PrEP) and the latter is antiretroviral therapy (ART). The United Kingdom is aiming at the same goal with zero transmission by 2030 [3]. In Japan, PrEP is neither approved nor available as of this writing, and only about 80% of diagnosed HIV infected patients receive ART. Over 10% of HIV infected persons are estimated to remain undiagnosed [4].

Our analysis provides some promise that HIV infection in Japan may continue to decrease thanks to the current measures, and may lead to zero new transmission at the similar time set as a goal by USA and UK. Because of rather dramatic improvement in mortality outcome of HIV/AIDS patients thanks to ART, the cost of outpatient care became very expensive, and increase in cumulative number of infected persons might be quite a burden to Japan's health care system [5]. Therefore, decreasing the number of newly infected persons and achieving zero new transmission is imperative in Japan, as well as in other nations. Effective prevention of HIV transmission is achieved by effective treatment. Suppressing HIV viremia to undetectable level by ART would virtually eliminate the risk of new infection, even without protection during sexual intercourse [6]. Early identification and initiation of ART to those infected by HIV are effective measures in decreasing and even terminating new transmission of HIV.

Our analysis has several inherent limitations. First, we elected to use local linear trend model, but whether the model is accurate to predict the future HIV/AIDS trend in Japan needs to be validated. Second, although we were able to collect enough quarterly data to conduct a time series analysis, it did not lead to prediction with narrower credible intervals. It has been discussed previously that the forecasting of infectious diseases trend for longer period using mathematical models, such as SIR model, has inherent limitation of having rather wide credible intervals, yet the models are useful in demonstrating feasibility of each given scenario [7-9]. This means that the zero transmission might not occur as expected, the number could even increase, but it also means reaching zero new infection might occur even faster, as suggested by both ends of credible intervals shown as shaded area in figures. Third, potential change in the trend due to unexpected events might alter the current trend of decline, unlike our prediction. For example, the pandemic of novel coronavirus disease (COVID-19) might alter sexual behavior of residents in Japan and may increase sexually transmitted diseases, such as HIV infection [10]. Having stated these, we were able to demonstrate that the zero new transmission goal in Japan in the near future similar to other developed nations is indeed realistic and achievable goal. Implementing other measures such as provision of PrEP might even fasten this prediction [11]. The necessity and inevitability of PrEP in achieving zero new infection in Japan is beyond the scope of the current study, but this also needs to be discussed and investigated in future studies.

In conclusion, our local linear trend model suggested that number of HIV/AIDS cases in Japan could potentially lead to zero new transmission in 2031, relatively close to the goal of other nations. One needs to continue and rather try to fasten this trend to achieve this goal to mitigate HIV/AIDS problem in Japan.

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CONFLICTS OF INTEREST

There are no conflicts of interest in this study.

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