Mathematical Biosciences and Engineering

MBE, 21 (4): 4874–4885.
DOI: 10.3934/mbe.2024215
Received: 25 November 2023
Revised: 16 February 2024
Accepted: 28 February 2024
Published: 29 February 2024

http://www.aimspress.com/journal/MBE

Research article

HIV incidence before and during the COVID-19 pandemic in Japan

Hiroshi Nishiura[1,*], Seiko Fujiwara[1], Akifumi Imamura[2] and Takuma Shirasaka[3]

[1] School of Public Health, Kyoto University, Kyoto, Japan
[2] Department of Infectious Diseases, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, Tokyo, Japan
[3] NHO Osaka National Hospital, AIDS Medical Center, Osaka, Japan

* **Correspondence:** Email: nishiura.hiroshi.5r@kyoto-u.ac.jp; Tel: +81-075-753-4456.

Abstract: At the end of 2022, a total of 20,003 diagnoses of human immunodeficiency virus (HIV) infection and 8,983 cases of acquired immunodeficiency syndrome (AIDS) among Japanese nationals, and 3,860 HIV diagnoses and 1,575 AIDS cases among foreign residents, had been notified to the government in Japan. This study updates the estimate of HIV incidence, including during the COVID-19 pandemic. It aimed to reconstruct the incidence of HIV and understand how the disruption caused by COVID-19 affected the epidemiology of HIV. Using a median incubation period of 10.0 years, the number of undiagnosed HIV infections was estimated to be 3,209 (95% confidence interval (CI): 2,642, 3,710) at the end of 2022. This figure has declined steadily over the past 10 years. Assuming that the median incubation period was 10.0 years, the proportion of diagnosed HIV infections, including surviving AIDS cases, was 89.3% (95% CI: 87.8%, 91.0%). When AIDS cases were excluded, the proportion was 86.2% (95% CI: 84.3%, 88.3%). During the COVID-19 pandemic, the estimated annual diagnosis rate was slightly lower than during earlier time intervals, at around 16.5% (95% CI: 14.9%, 18.1%). Japan may already have achieved diagnostic coverage of 90%, given its 9% increment in the diagnosed proportion during the past 5 years. The incidence of HIV infection continued to decrease even during the COVID-19 pandemic from 2020 to 2022, and the annual rate of diagnosis decreased slightly to 16.5%. Monitoring the recovery of diagnosis along with the effective reproduction number is vital in the future.

Keyword: Incidence; statistical estimation; mathematical model; pandemic; severe acute respiratory syndrome coronavirus-2; AIDS

1. Introduction

Acquired immunodeficiency syndrome (AIDS) is caused by an infection with human immunodeficiency virus (HIV), and is characterized by opportunistic infections. At the end of 2022, a total of 20,003 HIV diagnoses and 8,983 AIDS cases among Japanese nationals, and 3,860 HIV diagnoses and 1,575 AIDS cases among foreign residents had been notified to the government in Japan [1]. The main intervention is a test-and-treat strategy in both low and high income nations. This expands the level of early diagnosis and provides infected individuals with antiretroviral therapy for an extended time period [2,3]. By maintaining good adherence to therapy, it is possible to suppress the viral load below 200 copies/ml for more than 6 months. Infected individuals with undetectable viral levels such as these do not have a chance to cause secondary transmission. The disease is therefore untransmissible, and this status, referred to as U = U, has become widespread. This suggests that it will be possible to successfully control the HIV/AIDS epidemic [4]. Pre-exposure prophylaxis (PreP) prevents 99% of HIV infections via sexual contact [5]. This is not approved for insurance cover in Japan, but has been used in urban areas via clinics that receive subsidy via research program group of the Grant-in-Aid from the Ministry of Health, Labour and Welfare of Japan.

The benefits of diagnosis among HIV-infected individuals are therefore widely recognized. The joint United Nations program on HIV/AIDS (UNAIDS) has thus promoted a global initiative for "90–90–90" by 2020. This sets out goals in care cascades to ensure that 90% of people living with HIV know their HIV status, 90% of people diagnosed with HIV have access to antiretroviral therapy, and 90% of people receiving this therapy have suppressed viral loads [6]. An expanded goal of 95–95–95 at a global level is being seriously targeted for 2030, with the aim of controlling the HIV/AIDS epidemic via the test-and-treat approach.

Japan has designated 380 hospitals for HIV/AIDS treatment. These offer continuous treatment and follow-up, and have achieved far more than 90% rates for retention and viral suppression [7]. However, the focal host of infection has been men having sex with men, and persuading this group to undergo open or at least casual blood testing has not been easy. By the end of 2017, the proportion of diagnosed HIV infections among Japanese nationals was estimated at 80.3% (95% CI: 78.7%, 82.0%) [8], falling short of the first 90% of the 90–90–90 goal.

The COVID-19 pandemic from 2020 was an additional complication in Japan. Local health centers in charge of HIV/AIDS treatment had to adopt contact tracing practice and arrange hospital beds for people with severe COVID-19. The number of voluntary HIV tests offered by health centers abruptly decreased from spring 2020 [9]. Health centers are only one of the places that offer HIV testing, but delayed diagnosis could affect infected individuals' chances of developing AIDS. Japan adopted a suppression policy for COVID-19 from 2020 to 2021, and the cumulative incidence of confirmed cases was less than 3% of the population. As the Omicron variant (B.1.1.529) emerged, the country gradually shifted to a more open policy, and the universal case reporting system for COVID-19 was eased from the middle of 2022. From May 2023, the legal category of COVID-19 as a notifiable disease was downgraded to fifth, which is the same as seasonal influenza. Since then, health centers have no longer been required to find hospital beds for people with severe cases.

It is critical to update the estimate of HIV incidence under these circumstances. This study aimed to update this estimate and understand how the COVID-19 pandemic affected the epidemiology of HIV.

2. Materials and methods

2.1.Epidemiological data and parameters

HIV and AIDS are a category V notifiable disease and all diagnosing physicians are mandated to report cases to the government. We therefore analyzed the epidemiological surveillance data for HIV and AIDS in Japan, which are publicly reported by the Committee of AIDS Trends [1] at the Ministry of Health, Labour and Welfare. The latest data are up to the end of 2022. HIV diagnoses and AIDS incidence are regularly updated, classified by age group and nationality (i.e., Japanese or non-Japanese). This study focused on Japanese nationals. Among both Japanese and non-Japanese people, a cumulative total of 23,863 HIV infections and 10,558 AIDS cases had been reported by the end of 2022. HIV infection was screened using the antibody screening method (i.e., enzyme-linked immunosorbent assay, particle aggregation, immunochromatography) followed by antibody confirmatory testing (i.e., western blot method or immunofluorescence assay) or antigen detection testing, including virus isolation and polymerase chain reaction. AIDS was diagnosed when individuals met the clinical diagnostic criteria of (i) confirmed HIV infection and (ii) the presence of one of 23 indicator diseases representing opportunistic infections or tumors. We used the yearly incidence of HIV diagnoses and new AIDS cases from 1985 to 2022. We stratified by sex during the statistical estimation.

To permit an explicit estimation, we assumed that the incubation period had a median of 10.0 years and a range of 7.5–12.3 years. These figures are consistent with published estimates among hemophiliac people [10,11], cases in a cohort in San Francisco [12] and a multicenter AIDS cohort study [13]. The corresponding parameter values for the scale parameter η and shape parameter k of a discrete Weibull distribution were $\eta = 11.6$ and $k = 2.5$ for the median of 10 years, $\eta = 10.0$ and $k = 1.3$ for the median of 7.5 years, and $\eta = 14.3$ and $k = 2.5$ for the median of 12.3 years. The probability mass function of the incubation period of the length s is:

$$f_s = \left[1 - \frac{\exp\left(-\left(\frac{s+1}{\eta}\right)^k\right)}{\exp\left(-\left(\frac{s}{\eta}\right)^k\right)}\right]\exp\left(-\left(\frac{s}{\eta}\right)^k\right) \quad (1)$$

Doing this way, the yearly probability of illness onset among undiagnosed HIV infected individuals at infection-age s is modelled as $\rho_s = 1 - \exp\left(-\left(\frac{s+1}{\eta}\right)^k\right)/\exp\left(-\left(\frac{s}{\eta}\right)^k\right)$, and using fixed parameters for ρ_s, HIV incidence and diagnostic rate can be jointly estimated from the empirical data. During an increasing phase of the HIV/AIDS epidemic, assuming a longer incubation period leads to a greater HIV incidence. For the rest of this article, the default estimate of HIV incidence was derived by using the median incubation period at 10 years.

2.2. Extended back-calculation model

We used the McKendrick equation described elsewhere [8] to calculate the incidence of HIV diagnoses $u(t)$ and AIDS cases $a(t)$ at calendar time t as:

$$u(t) = \alpha(t) \int_0^t \lambda(t-s)\, exp\left(-\int_{t-s}^t \alpha(x)dx - \int_0^s \rho(y)dy\right) ds, \tag{2a}$$

$$a(t) = \int_0^t \rho(s)\lambda(t-s)\, exp\left(-\int_{t-s}^t \alpha(x)dx - \int_0^s \rho(y)dy\right) ds \tag{2b}$$

where α(t) is the time-dependent hazard rate of HIV diagnosis, $\rho(\tau)$ is the hazard of illness onset as a function of the time elapsed since infection τ, and $\lambda(t)$ is the HIV incidence at calendar time t. Both equations (2a) and (2b) are in continuous time, but we analyzed the yearly incidence data, and therefore discretized it as:

$$u_t = \alpha_t \sum_{s=1}^{t} \lambda_{t-s} \prod_{x=t-s-1}^{t-1} (1-\alpha_x) \prod_{y=1}^{s-1} (1-\rho_y) \tag{3a}$$

$$a_t = \sum_{s=1}^{t} \lambda_{t-s}\rho_s \prod_{x=t-s-1}^{t-1} (1-\alpha_x) \prod_{y=1}^{s-1} (1-\rho_y) \tag{3b}$$

As described above, we used fixed parameters for ρ_s. Doing so, we wanted to estimate λ_t to back-calculate the HIV infection dynamics, and α_t to reconstruct the epidemiologic trend of diagnosis. Both of these were dealt with using a step function, as a piecewise constant model with value changing for every 4 years. However, the COVID-19 pandemic was from 2020, and the last time interval focused on the pandemic period. The corresponding time interval was therefore for 3 years only.

We assumed that both HIV diagnoses and AIDS cases were sufficiently captured by a Poisson distribution. The likelihood function to estimate λ_t and α_t was therefore:

$$L_1 = constant \times \prod_{t=1985}^{2022} E(u_t)^{r_t} exp(-E(u_t)) \prod_{t=1985}^{2022} E(a_t)^{w_t} exp(-E(a_t)). \tag{4}$$

where r_t and w_t are the observed number of HIV diagnoses and AIDS cases in year t. Maximum likelihood estimates of parameters were obtained by minimizing the negative logarithm of equation (4). The 95% confidence interval (CI) of parameters was derived from the profile likelihood. The 95% CI of model estimates (e.g., the number of undiagnosed HIV infections and the proportion diagnosed) were derived using a parametric bootstrap method.

Finally, the proportion of HIV infections that have been diagnosed was calculated as $\sum(a+u) / \sum(x+a+u)$ where x is undiagnosed HIV infections and is calculated as:

$$x_t = \sum_{s=1}^{t} \lambda_{t-s} \prod_{x=t-s-1}^{t-1} (1-\alpha_x) \prod_{y=1}^{s-1} (1-\rho_y). \tag{5}$$

In Japan, the total number of AIDS cases has not been fully counted, especially when the infected case was diagnosed as HIV infected prior to the illness onset of AIDS. Considering that the diagnosed proportion has not been theoretically defined in relation to the prognosis of infection, the present study used $\sum(a+u) / \sum(x+a+u)$ as the default metric. At least, we alternatively calculated $\sum u / \sum(x+u)$, because some people with AIDS have already passed away. But it should be noted that removed a contains only those who were notified to the government (and must have missed a lot of progression to AIDS with preceding HIV diagnosis).

2.3. Ethical considerations

We analyzed publicly available data [1]. The open dataset analyzed was deidentified before analysis. This study therefore did not require ethical approval.

3. Results

Figure 1 shows the comparison between the empirical and predicted numbers of HIV diagnoses and AIDS incidence. The models, characterized by three different median incubation periods, showed a comparable level of agreement with the observed data (Figure 1A), indicating that λ and α were effectively modified to refine the models. The number of newly diagnosed HIV infections and AIDS cases in women was relatively small, but the proposed model was nonetheless precise in capturing the sex-stratified patterns (Figure 1B).

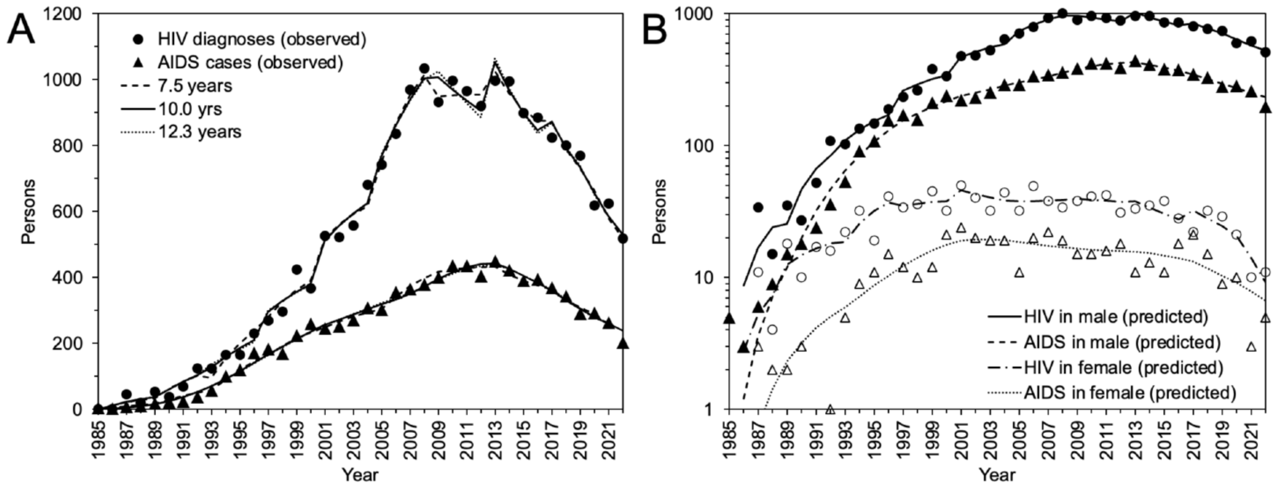

Figure 1. Yearly HIV diagnoses and AIDS incidence in Japan, 1985–2022. (A) Comparisons between observed and predicted yearly numbers of HIV diagnoses and AIDS incidence among Japanese people. Different median incubation periods (i.e., 7.5, 10.0, and 12.3 years) were assumed, but predicted values mostly overlapped. (B) Comparisons between observed and predicted values by sex. Circles represent the observed number of HIV diagnoses and triangles AIDS cases. Solid marks are men and empty marks women. A common logarithmic scale was used on the vertical axis.

Figure 2 shows the estimated yearly incidence λ and yearly probability of diagnosis α. Although our approach relies on crudely modelled step functions, the non-linear pattern of incidence peaked during the time interval from 2006 to 2009, with fewer than 2,500 new infections per year. Because the incidence λ was dealt with as a piecewise constant and not parameterized accounting for non-linear transmission mechanisms, it should be noted that accounting for the possible time-dependent variations in contact may lead to greatly varying incidence, especially during the COVID-19 pandemic from 2020-22. The estimated yearly chance of diagnosis was initially less than 10% with the median incubation periods from 10 to 12.3 years, but the diagnosis rate has steadily increased since then. However, during the pandemic, the latest estimated diagnosis rate from 2020 to 2022 was slightly lower than during the earlier period. It was estimated at 16.5% (95% CI: 14.9%, 18.1%) with the median incubation period of 10 years. The qualitative patterns of HIV incidence and diagnosis did not vary much with different median incubation periods.

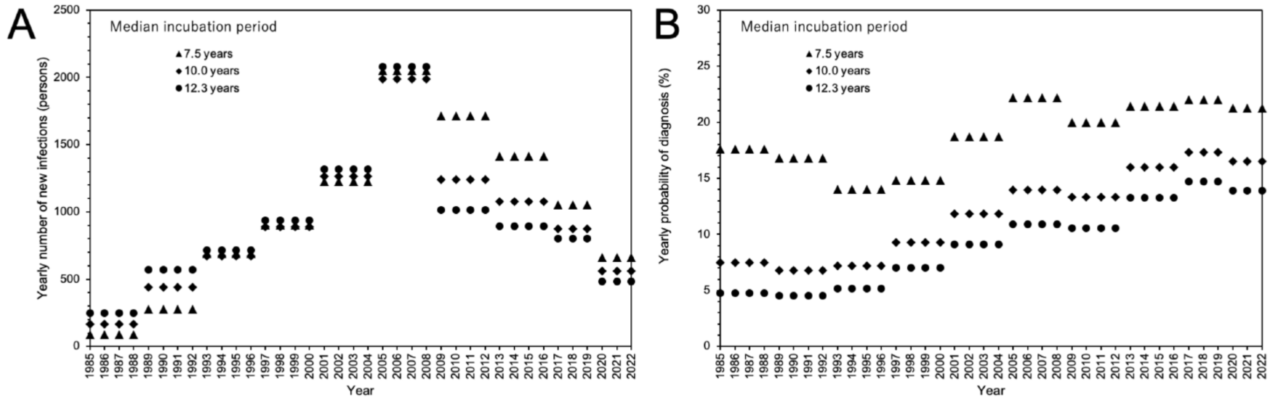

Figure 2. Estimated HIV incidence and diagnosis rates per year in Japan, 1985–2022. (A) Estimates of the yearly incidence based on maximum likelihood, assuming median incubation periods of 7.5, 10.0, and 12.3 years. (B) Estimates of the yearly rate of diagnosis, assuming median incubation periods of 7.5, 10.0, and 12.3 years.

Figure 3 shows the estimated prevalence of undiagnosed HIV-infected individuals over time among Japanese nationals. The apex of undiagnosed HIV infection is believed to have occurred in 2009, with an estimated 7,575 (95% CI: 7,130, 7,991) infections. From 2020 to 2022, approximately 3,209 (95% CI: 2,642, 3,710) infections remained undetected, but the absolute number of undiagnosed cases has shown a decade-long decline. Varying the median incubation period from 7.5 to 12.3 years, the maximum likelihood estimate of undiagnosed HIV infections in the latest time interval ranged from 2,446 to 3,829 infections (Figure 3B). The data in Figures 3C and 3D provide insights into the proportion of diagnosed cases, including those with and without AIDS. By including AIDS cases and ignoring deceased infected individuals, a proportion of diagnosed cases of 90.0% (range 88.6%–91.6%) was obtained for the median incubation period of 10.0 (7.5–12.3) years. Figure 3D shows the estimated diagnosed proportion by sex, excluding AIDS cases. The diagnosed proportion of both men and women increased over time, and women tended to yield higher estimates than men. In the most recent analysis period, excluding AIDS cases, the proportion of diagnosed cases was estimated at 85.7% (range 85.0%–87.9%) among men, and 95.3% (range 90.7%–100.0%) among women.

Figure 4 illustrates the overall undiagnosed number of HIV infections and as a proportion of total infections at the end of 2022. When using a longer median incubation period of 12.3 years, we observed the widest range of uncertainty, with an estimated 3,829 undiagnosed infections (95% CI: 2,952, 4,604). Figure 4B shows the diagnosed proportion, factoring in both the presence and absence of AIDS cases, with 95% confidence intervals. Taking into account AIDS cases and the published number of 2,321 deaths reported by 2022, the prognosis for surviving AIDS cases at the median incubation period stood at 89.3% (95% CI: 87.8%, 91.0%). This rose to 86.2% (95% CI: 84.3%, 88.3%) when AIDS cases were excluded from the denominator.

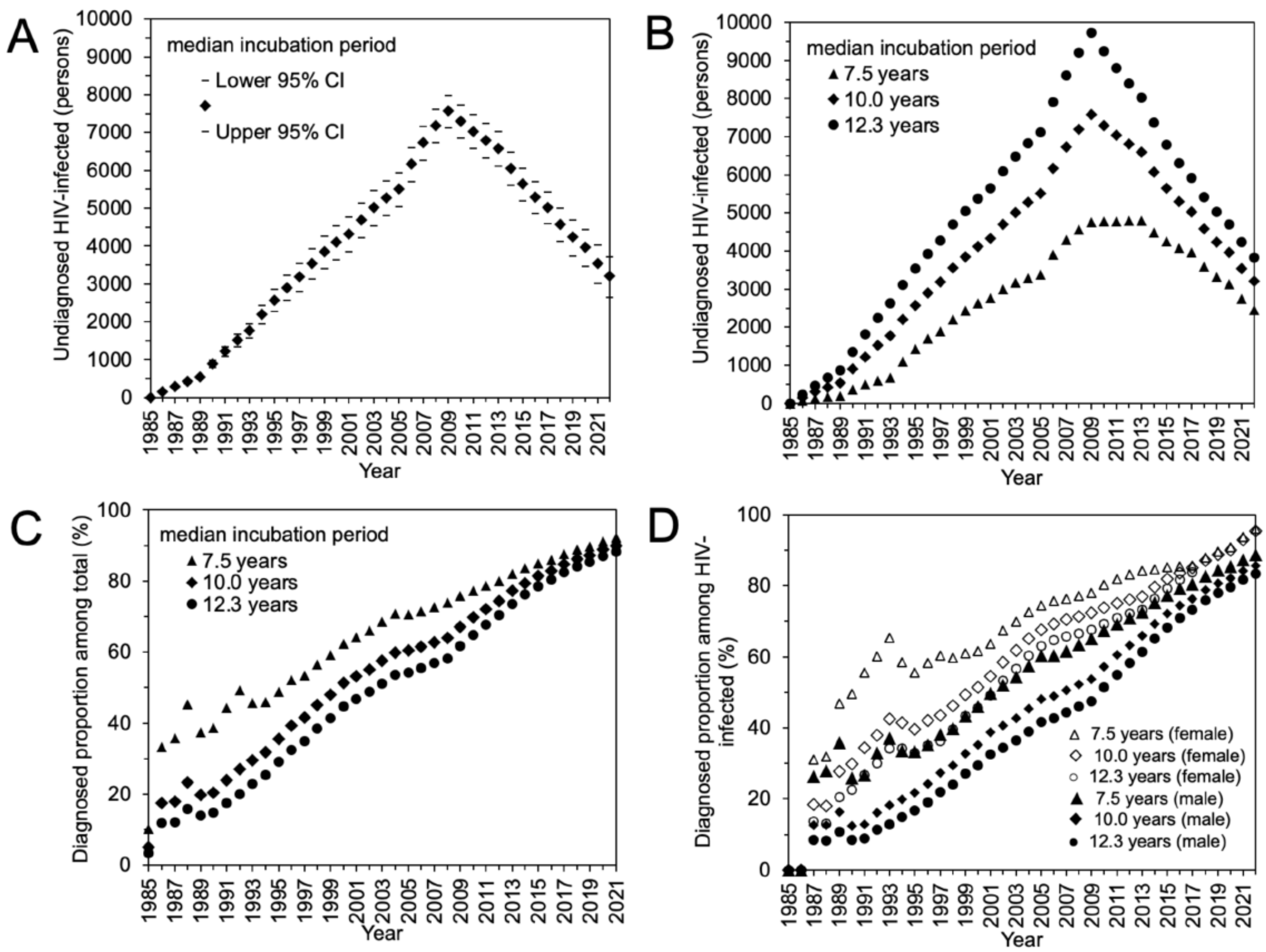

Figure 3. Undiagnosed cases as a proportion of HIV infections in Japan, 1985–2022. (A) Estimates of undiagnosed HIV infections, assuming a median incubation period of 10.0 years. The 95% confidence intervals were determined through the application of profile likelihood. (B) Maximum likelihood estimates of undiagnosed HIV infections for median incubation periods of 7.5, 10.0, and 12.3 years. (C) Diagnosed cases as a proportion of the cumulative number of HIV infections, with AIDS cases also taken into account. (D) Diagnosed cases as a proportion of the cumulative number of HIV infections, without AIDS cases taken into account, by sex.

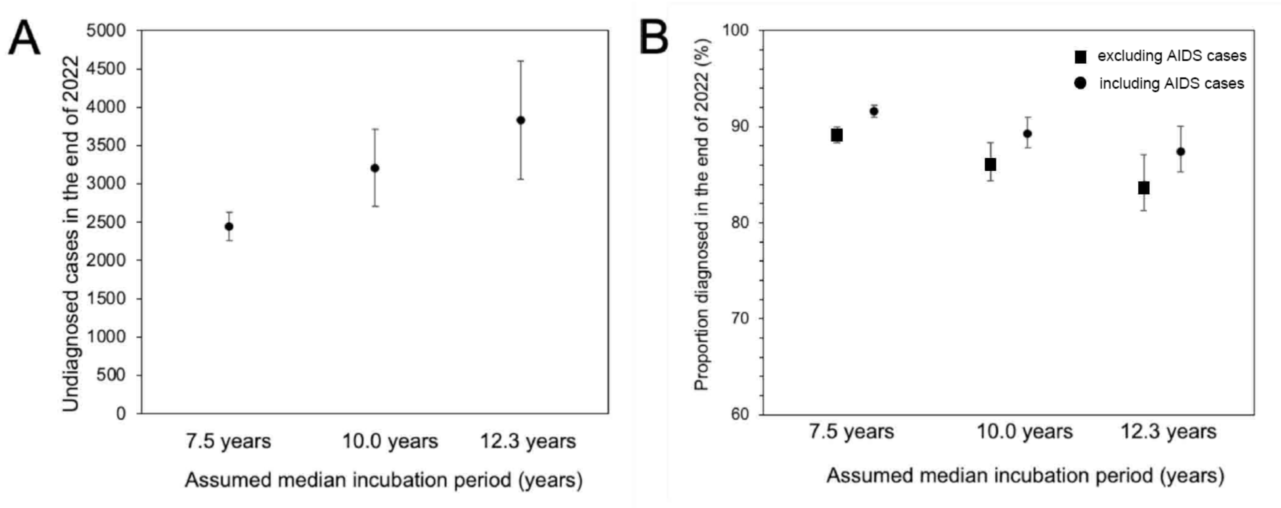

Figure 4. Estimated undiagnosed HIV infections as a proportion of total diagnoses by the end of 2022. (A) Number of undiagnosed infections. (B) Estimates of the diagnosed proportion of HIV infections assuming different incubation periods. For each median incubation period, the estimate on the left (square) is when AIDS cases were excluded, and on the right (circle) when AIDS cases were included. Whiskers extend to lower and upper 95% confidence intervals.

4. Discussion

This study reconstructed the epidemiological dynamics of HIV infection, progression to AIDS and diagnosis of HIV infection before AIDS over the course of time in Japan, during the period from 1985 to 2022. The estimation used epidemiological surveillance data announced by the Committee of AIDS Trends [1], updating incidence and proportion of cases diagnosed 5 years after the last reported estimate in 2017 [8]. An extended back-calculation method that was formulated elsewhere [8] was reused. The updated 5 years contained 2020–2022, the period of the COVID-19 pandemic, during which both healthcare facilities and public health sectors experienced overwhelming pressures on their admission and service capacities. It was estimated that the proportion of undiagnosed HIV infections is decreasing. The proportion of HIV cases that had been diagnosed at the end of 2022 was estimated at 89.3%, and the trend was a steady increase over time.

One of this study's most important contributions to public health is that it shows that Japan has largely achieved diagnostic coverage of 90%, a key element of the UNAIDS strategy of 90–90–90 by 2020. We showed that the proportion was 89.3% (Figure 4B), and that the proportion of diagnosed HIV infections has been steadily increasing over time. The corresponding value in 2017 was 80.3%, and Japan therefore showed a 9% increment in the diagnosed proportion over the past 5 years. The proportion diagnosed was higher among women than men.

Another critical finding of this study was that the incidence of HIV infection continued to decrease even during the COVID-19 pandemic from 2020 to 2022. Approximately 3200 infections have yet to be diagnosed and brought under continued medical care, but it is encouraging that the decreasing trend of undiagnosed infection prevalence was maintained. However, the yearly rate of diagnosis decreased slightly to 16.5% (Figure 2B). The decreased hazard rate of diagnosis is considered to reflect the overwhelming pressure on public health facilities and teams during the pandemic. In local health centers, healthcare professionals who were in charge of prevention and testing of HIV/AIDS were obliged to shift their focus to the control of COVID-19. To improve the capacity of public health activity and testing, it is vital to clarify what type of testing was affected by COVID-19 and what type of cases (e.g., sex, age and place) experienced substantial pandemic impact on their diagnosis.

Is it realistic for Japan to achieve the first 95% of the UNAIDS 95–95–95 goal by 2025? A 9% increase was achieved during the past 5 years, and 95% is therefore theoretically reachable by the end of 2025, provided the current trend continues. Perhaps more important than merely meeting the goal, it is clear that the control of HIV/AIDS has been successful during the past decade. Japan is therefore on its way to adopting a more ambitious goal: to achieve three zeros, i.e., zero HIV-related discrimination, zero HIV incidence and zero AIDS-associated death [14]. To support the monitoring of the epidemiology of these goals, it is essential to continue to estimate the effective reproduction number, possibly stratified by host type and geographic location.

Comparing the proportion of diagnosed HIV infections among high income countries in the Western Pacific region up to the year 2020, the diagnosis rate is higher in Japan than South Korea. The diagnosis rate in 2020 was 62.5% in South Korea and 87.3% in Japan, and this study's findings suggest that the rate in Japan exceeded 90% by 2022 [15]. The number of undiagnosed individuals was 7,809 in South Korea in 2020, compared with just 3,968 in Japan, falling to 3,208 by 2022. Lee et al. [15] suggested that the lower diagnosis rates in South Korea could be due to a shortage of and access to voluntary testing. In Japan, voluntary testing can be undertaken at public health centers, which may contribute to the higher diagnosis rates. The diagnosis rates by gender in 2020 were 69.7% for men and 55.5% for women in South Korea, and 82.2% for men and 90.0% for women in Japan, indicating a smaller gender disparity in diagnosis rates in Japan than in South Korea. Similarly, when comparing with Australia, the diagnosis rate among gay and bisexual men born in Australia shows a reasonably consistent increase from 92.9% in 2010 to 97.2% in 2018 [16,17]. However, the diagnosed proportion among overseas-born gay and bisexual men in Australia has decreased steadily from 84.7% in 2010 to 83.1% in 2018. Overall, the proportion of HIV-positive gay and bisexual men in Australia was 61.7% in 2018 [18], with men constituting 90.0% of HIV infections. In Japan, the proportion of HIV infections arising from men-to-men contact was documented as 73.1% [19] at the end of 2022, with men comprising 97.7% of HIV infections.

Despite reduced testing volume at public health centers during the course of COVID-19 pandemic, why was the rate of HIV diagnosis mostly maintained similar to the level prior to the pandemic? Although not causally demonstrated, there are several possible explanations. First, whereas low risk group was perhaps vulnerable to reduced testing volume (influenced by abrupt decrease in the number of testing at health centers), the observed data imply that people at high risk of infection tended to remain tested. In fact, individual clinics that offer rapid testing service did not experience reduced numbers of testing and positives compared with pre-pandemic period [20]. Second, even during the intense pandemic period, public health centers did make an effort to maintain testing service, even by reducing the number of testing opportunities or limiting the assigned number of people. A specialized testing center (e.g. Higashi Shinjuku testing consultation center in Tokyo) ran regular testing service even during the course of pandemic, meticulously corresponding to people at high risk. Third, HIV testing at public health centers is coupled with testing for syphilis at free of charge. The high-risk groups of syphilis (e.g. female commercial sex workers and heterosexual men) are not necessarily overlapped with that of HIV/AIDS, but syphilis epidemic has been expanding during the later period of COVID-19 pandemic, indirectly leading to increased testing volume of HIV. In addition to maintained testing volume, it should be noted that HIV incidence continued to decline. As an important explanation for the continued reduction of new infections, it should be noted that PrEP has been widespread among a portion of men having sex with men, and the reduced risk due to PrEP must be epidemiologically evaluated in the future.

This study had five technical limitations. First, the extended back-calculation method that was used relied on an assumption of known incubation period distribution. We addressed the uncertainty by using three different distributions for the incubation period, but additional estimates using biomarkers including CD4 count are called for. Second, surveillance data of cases are subject to misclassification bias. For instance, a small number of HIV infections may have already satisfied the definition of AIDS before diagnosis (e.g., esophageal candidiasis among HIV-infected individuals). Third, mobility of humans was not explicitly taken into account, and people who have left Japan may have been included in our model. Fourth, Japan has not managed to maintain a registration system of HIV-infected individuals, and the natural history (e.g., elevated risk of suicide) has not been closely monitored even among samples of those who have been infected and are yet to be diagnosed. The third and fourth limitations mean that this study has potentially underestimated the proportion of diagnosed HIV infections. Fifth, the HIV incidence and yearly rate of diagnosis were estimated using a piecewise constant model, and the precision of step function (i.e. every 4 years) was limited. During the course of COVID-19 pandemic, the diagnostic capacity must have changed over the course of time, but such changes during the latest three years was not explicitly estimated.

Despite these limitations, we believe that we have shown that the number of undiagnosed HIV infections has been decreasing over time. The proportion of HIV infections diagnosed was estimated at 89.3% at the end of 2022, and this proportion has steadily increased over time. The yearly rate of diagnosis decreased during the COVID-19 pandemic. In the future, the recovery of diagnosis rates, along with the effective reproduction number, should be monitored.

5. Conclusions

This study updated the estimate of HIV incidence over a time period that included the COVID-19 pandemic. It aimed to reconstruct the incidence of HIV and understand how the COVID-19 pandemic affected the epidemiology of HIV. Japan appears to have achieved a diagnostic coverage of 90%, with a 9% increment in the diagnosed proportion over the past 5 years. The incidence of HIV infection continued to decrease even during the COVID-19 pandemic, but the yearly rate of diagnosis decreased to 16.5%. Monitoring the recovery of diagnosis along with the effective reproduction number is vital in the future.

Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

Acknowledgments

This study was supported by Health and Labour Sciences Research Grants (21HB1002 and 22HB1002). TS received financial support from Yuai Welfare Foundation in Japan. HN received funding from Health and Labour Sciences Research Grants (20CA2024, 20HA2007, 21HB1002, 21HA2016, and 23HA2005); the Japan Agency for Medical Research and Development

(JP23fk0108685 and JP23fk0108612); JSPS KAKENHI (21H03198 and 22K19670); the Environment Research and Technology Development Fund (JPMEERF20S11804) of the Environmental Restoration and Conservation Agency of Japan, Kao Health Science Research, the Daikin GAP Fund of Kyoto University, and the Japan Science and Technology Agency SICORP program (JPMJSC20U3 and JPMJSC2105); and the RISTEX program for Science of Science, Technology and Innovation Policy (JPMJRS22B4). The funders had no role in the study design, data collection, and analysis, decision to publish, or preparation of the manuscript. We thank the local governments, public health centers, and institutes for surveillance for their assistance with laboratory testing, epidemiological investigations, and data collection. We also thank Melissa Leffler, MBA, from Edanz (https://jp.edanz.com/ac) for editing a draft of the manuscript.

Conflict of interest

The authors declare no conflicts of interest.

References

1. The Committee of AIDS Trends, Ministry of Health, Labour and Welfare. HIV/AIDS in Japan. Tokyo, Ministry of Health, Labour and Welfare. https://api-net.jfap.or.jp/status/japan/nenpo.html
2. R. M. Granich, C. F. Gilks, C. Dye, K. M. De Cock, B. G. Williams, Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: A mathematical model, *Lancet (London, England)*, **373** (2009), 48–57. https://doi.org/10.1016/S0140-6736(08)61697-9
3. R. Granich, B. Williams, J. Montaner, J. M. Zuniga, 90-90-90 and ending AIDS: Necessary and feasible. *Lancet (London, England)*, **390** (2017), 341–343. https://doi.org/10.1016/S0140-6736(17)31872-X
4. C. Okoli, N. Van de Velde, B. Richman, B. Allan, E. Castellanos, B. Young, et al., Undetectable equals untransmittable (U = U): Awareness and associations with health outcomes among people living with HIV in 25 countries, *Sexual. Transmit. Infect.*, **97** (2021), 18–26. https://doi.org/10.1136/sextrans-2020-054551
5. G. Nair, C. Celum, D. Szydlo, E. R. Brown, et al., REACH Protocol Team, Adherence, safety, and choice of the monthly dapivirine vaginal ring or oral emtricitabine plus tenofovir disoproxil fumarate for HIV pre-exposure prophylaxis among African adolescent girls and young women: A randomised, open-label, crossover trial, *Lancet. HIV*, (2023), S2352-3018(23)00227-8. Advance online publication. https://doi.org/10.1016/S2352-3018(23)00227-8
6. UNAIDS, An ambitious treatment target to help end the AIDS epidemic. https://www.unaids.org/sites/default/files/media_asset/90-90-90_en.pdf
7. A. Iwamoto, R. Taira, Y. Yokomaku, T. Koibuchi, M. Rahman, Y. Izumi, et al., The HIV care cascade: Japanese perspectives, *PloS One*, **12** (2017), e0174360. https://doi.org/10.1371/journal.pone.0174360
8. H. Nishiura, Estimating the incidence and diagnosed proportion of HIV infections in Japan: A statistical modeling study, *PeerJ*, **7** (2019), e6275. https://doi.org/10.7717/peerj.6275
9. K. Ejima, Y. Koizumi, N. Yamamoto, M. Rosenberg, C. Ludema, A. I. Bento, et al., HIV testing by public health centers and municipalities and new HIV cases during the COVID-19 pandemic in Japan, *J. Acquir. Immune Deficiency Syndrom.*, **87** (2021), e182–e187.

https://doi.org/10.1097/QAI.0000000000002660

10. R. Brookmeyer, M. H. Gail, Minimum size of the acquired immunodeficiency syndrome (AIDS) epidemic in the United States, *Lancet (London, England)*, **2** (1986), 1320–1322. https://doi.org/10.1016/s0140-6736(86)91444-3
11. R. Brookmeyer, J. J. Goedert, Censoring in an epidemic with an application to hemophilia-associated AIDS, *Biometrics*, **45** (1989), 325–335. https://doi.org/10.2307/2532057
12. J. L. Boldsen, J. L. Jensen, J. Sogaard, M. Sorensen, On the incubation time distribution and the Danish AIDS data, *J. Royal Statist. Soc. Series A (Stat. Soc.)*, **151** (1988), 42–43. https://doi.org/10.2307/2982183
13. A. Muñoz, J. Xu, Models for the incubation of AIDS and variations according to age and period, *Stat. Med.*, **15** (1966), 2459–2473. https://doi.org/10.1002/(sici)1097-0258(19961130)15:22<2459::aid-sim464>3.0.co;2-q
14. UNAIDS. Global AIDS strategy 2021-2026. End inequalities. End AIDS. https://www.unaids.org/sites/default/files/media_asset/global-AIDS-strategy-2021-2026-summary_en.pdf
15. E. Lee, J. Kim, J. Y. Lee, J. H. Bang, Estimation of the Number of HIV Infections and Time to Diagnosis in the Korea, *J. Korean Med. Sci.*, **35** (2020), e41. https://doi.org/10.3346/jkms.2020.35.e41
16. P. G. Patel, P. Keen, H. McManus, T. Duck, D. Callander, C. Selvey, et al., NSW HIV Prevention Partnership Project, Increased targeted HIV testing and reduced undiagnosed HIV infections among gay and bisexual men, *HIV Med.*, **22** (2021), 605–616. https://doi.org/10.1111/hiv.13102
17. R. T. Gray, D. P. Wilson, R. J. Guy, M. Stoové, M. E. Hellard, G. P. Prestage, et al., Undiagnosed HIV infections among gay and bisexual men increasingly contribute to new infections in Australia, *J. Int. AIDS Soc.*, **21** (2018), e25104. https://doi.org/10.1002/jia2.25104
18. J. King, H. McManus, A. Kwon, R. Gray, S. McGregor, HIV, viral hepatitis and sexually transmissible infections in Australia: Annual surveillance report 2022, The Kirby Institute, UNSW Sydney, Sydney, Australia. http://doi.org/10.26190/sx44-5366
19. AIDS Prevention Information Network. (n.d.). Annual Report on the Status of Deaf in Japan. Retrieved November 13, 2023, from https://api-net.jfap.or.jp/status/japan/nenpo.html
20. I. Itoda, T. Sano, M. Kondo, M. Imai, Implementing effective HIV testing at private clinics and improvement of the quality, Annual Research Report of the Health and Labour Research Grant, Ministry of Health, Labour and Welfare: Tokyo, 2022 (written in Japanese)