Review

Ewha Med J 2024;47(3):e36
https://doi.org/10.12771/emj.2024.e36
eISSN 2234-2591

The epidemiology of HIV/AIDS and the use of antiretroviral therapy in Korea: a narrative review

Nam Su Ku

Division of Infective Diseases, Department of Internal Medicine and AIDS Research Institute, Yonsei University College of Medicine, Seoul, Korea

Received Jun 15, 2024
Revised Jul 17, 2024
Accepted Jul 17, 2024

Corresponding author
Nam Su Ku
Division of Infective Diseases, Department of Internal Medicine and AIDS Research Institute, Yonsei University College of Medicine, 50-1, Yonsei-Ro, Seodaemun-gu, Seoul 03722, Korea
E-mail: smileboy9@yuhs.ac

Keywords
Antiretroviral therapy; HIV; Non-AIDS-defining comorbidities

The availability of combined antiretroviral therapy has significantly reduced the number of new HIV infections and the associated mortality, and HIV infection has become a chronic disease with long-term survival. In Korea, more than 1,000 new HIV infections have been registered annually since 2013. After peaking at 1,223 in 2019, the number of new infections decreased between 2020 and 2023. In 2023, the majority of newly HIV-infected people were men, and the proportions of young people under 40 years, homosexual contacts and foreigners increased. Acquired immunodeficiency syndrome (AIDS)-related deaths from opportunistic infections associated with immunosuppression and AIDS-defining cancers are gradually decreasing, whereas non-AIDS defining comorbidities such as non-AIDS defining cancers, cardiovascular disease and metabolic complications are emerging as major causes of death. Since the introduction of zidovudine, approximately 30 antiretroviral drugs have been approved for the treatment of HIV infection. Early and continuous antiretroviral treatment for all people living with HIV is an effective strategy for maintaining viral suppression and preventing transmission of HIV infection. In conclusion, achieving the 95–95–95 target among those living with HIV in Korea requires multifaceted efforts to improve early diagnosis, early and proper treatment of HIV infection including the management of chronic diseases, and adherence to antiretroviral therapy.

Introduction

Since the first report of acquired immunodeficiency syndrome (AIDS) in 1981, the epidemiology of HIV has changed markedly worldwide [1]. Over the past 40 years, the global HIV epidemic has continued, and successful treatments and prevention methods have been developed and disseminated [1]. Before the introduction of antiretroviral therapy (ART) in the late 1990s, HIV infection had a high mortality rate and a devastating effect on people of almost every race, country and class worldwide. The availability of combined ART (cART) has significantly reduced the prevalence and mortality of HIV infection, which has become a chronic disease with long-term survival [1].

The Joint United Nations Programme on HIV/AIDS (UNAIDS) has declared a fight against HIV transmission. In 2014, the UNAIDS proposed the 90–90–90 target, i.e., to diagnose 90% of people living with HIV (PLWH) worldwide, provide ART to 90% of PLWH, and achieve viral suppression in 90% of PLWH, by 2020 [2]. The strategy was to diagnose HIV infection early, before PLWH could

become immunocompromised, and put them on ART to achieve sustained viral suppression, thereby halting disease progression, improving morbidity and survival, and reducing HIV transmission [2]. By 2020, the UNAIDS estimated that 84% of PLWH worldwide have been diagnosed, 87% have been offered ART and 90% have achieved viral suppression [2,3]. In December 2020, the UNAIDS raised the target to be achieved by 2025 to 95–95–95, with at least 86% of all PLWH achieving viral suppression [3].

The Korean Centers for Disease Control and Prevention has set a goal of achieving 95–95–95 by 2030, with the aim of reducing the number of new infections in 2030 by 50% compared to 2023 [4]. In this review, I summarize the epidemiology of HIV/AIDS and the use of ART in Korea [5].

Methods

Ethics statement

As this is a literature review study, it does not require approval from an institutional review board or individual consent.

Study design

The present study is a narrative review of studies obtained through a web-based database search.

Literature search and strategy

The following search terms were used in PubMed and KoreaMed.

(Korea) AND {(HIV [tiab]) OR (human immunodeficiency virus [MESH terms]) OR (ADIS [tiab]) OR (acquired immunodeficiency syndrome [MESH terms])}.

The epidemiology of Korean HIV/AIDS

In 1985, the first HIV infection in Korea was reported in a foreigner [6]. Subsequently, the number of new infections has gradually increased every year, and since 1995, more than 100 cases have been reported annually. Since 1999, the number of new infections has increased rapidly every year, and since 2003, more than 500 new infections have been registered each year. Since 2007, the upward trend has slowed, with 700–800 new infections are still recorded each year [7]. In 2011, the upward trend resumed, with more than 1,000 new infections registered yearly since 2013 [8]. After peaking at 1,223 in 2019, the number of new infections decreased from 2020 to 2022 because of the coronavirus disease 2019 (COVID-19) pandemic, with approximately 1,000 new infections registered annually [9]. In 2023, there were 1,005 new HIV infections, a decrease of 61 (5.7%) compared to 2022. However, a recent study comparing HIV infection to diagnosis before and after the COVID-19 pandemic suggested that the actual incidence of HIV infection may have decreased more than the possibility that HIV diagnosis was delayed due to the COVID-19 pandemic because the median time from HIV infection to diagnosis decreased from 5.68 years before to 5.41 years after the COVID-19 pandemic [10]. Over the past decade, there has been an average of 1,100 new cases per year, with 1,191 in 2014, 1,206 in 2018 and 1,005 in 2023, with no clear upward or downward trend (Fig. 1) [11].

After the first diagnosis in 1985, 19,745 cumulative domestic infections were registered by the end of 2023, of which 18,495 (93.7%) were in men and 1,250 (6.3%) in women [10]. In 2023,

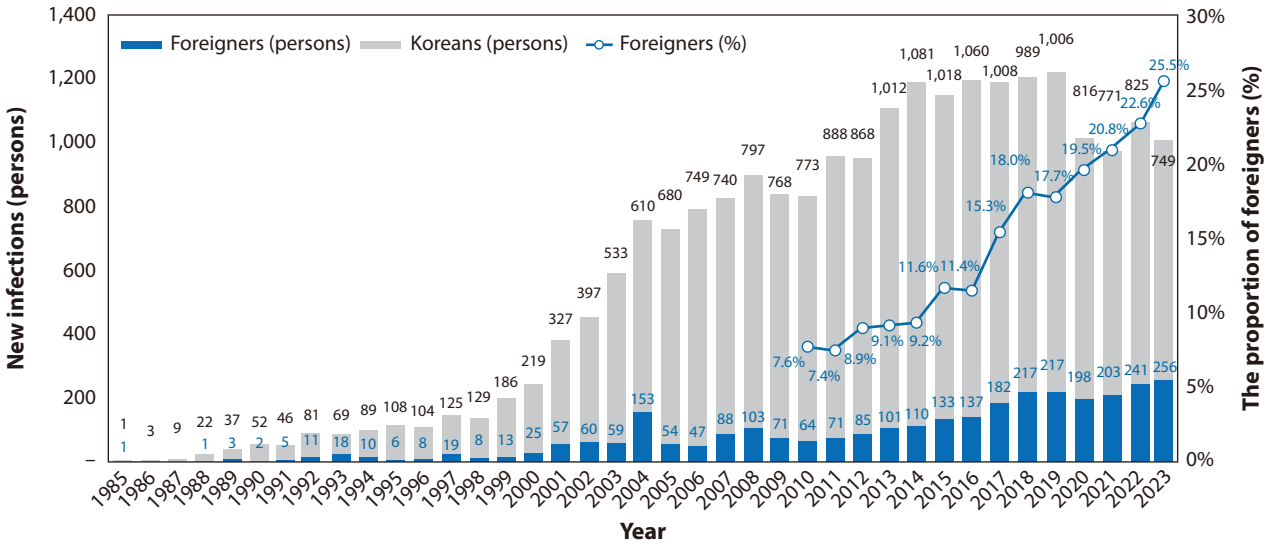

Fig. 1. New human immunodeficiency virus infections in Korea according to year. Adapted from Korea Centers for Disease Control and Prevention [10] with CC-BY.

130 new cases of AIDS were registered, an incidence rate of 0.254 per 100,000 HIV-infected persons. 17.4% of all notifications were of people living with AIDS [10]. Of the total number of infections, the average number of Koreans with HIV infection over the past 5 years was 834. The proportion of foreigners was 9.2% in 2014, 18.0% in 2018 and 25.5% in 2023, and increased each year [11].

The age distribution of new infections has continued to show an increase in the proportion of young people under the age of 40, from 53.3% in 2013 to 61.8% in 2017 and 81.0% in 2023 [11]. In particular, the proportion of young people in their 20s and 30s increased from 576 (53.3%) in 2014 to 572 (57.8%) in 2018 and 478 (63.8%) in 2023 [11,12]. In addition, 158 (15.7%) were in their 40s, 120 (11.9%) in their 50s, 55 (5.5%) their 60s and 16 (1.6%) were ≥70 years of age, with those aged ≥40 years accounting for 34.7% of the total [11]. In 2023 there were new infections in 903 men (89.9%) and 102 women (10.1%), for a gender ratio of 9:1 [11]. The proportion of men was 92.4% in 2014, 91.2% in 2018, and 89.9% in 2023, and showed a slightly decreasing trend.

According to an analysis of cases in which the transmission route of HIV infection was identified, sexual contact was the most common mode of transmission, accounting for 99.6% of infections, of which 54.3% were infected by homosexual contact and 42.0% by heterosexual contact in 2023 [11]. The proportion of transmission by homosexual contact increased from 53.8% in 2019 to 56.2% in 2020, 64.8% in 2021, and 65.4% in 2022 [11]. Although large numbers of transfusion and blood product-related infections were identified early in the HIV epidemic in developed countries such as the United States and Japan, only 46 such infections were identified in Korea, among which 13 were from transfusions performed overseas, 17 from blood products, and 16 from transfusions performed in Korea [8,11]. To reduce the rate of HIV transmission by blood transfusion, HIV antibody testing has been performed on blood donated in Korea since 1987. In addition, nucleic acid amplification testing has been performed on donated blood since February 2005 to prevent missed cases during the testing period. As a result, no case of HIV infection via blood or blood products has been reported since 2006 [11]. Infection via vertical transmission occurred sporadically until 2014, with a total of nine cases reported [8].

The number of deaths among Koreans has not changed significantly, with 142 in 2014, 136 in 2018 and 158 in 2023. There were 158 deaths among PLWH in 2023, an increase of 16 compared to the previous year [11]. However, the causes of death among PLWH have changed; AIDS-related deaths from opportunistic infections associated with immunosuppression and AIDS-defining cancers are declining gradually, whereas chronic diseases such as non-AIDS-defining cancers, liver disease, and cardiovascular disease (CVD) are emerging as important causes of death among PLWH [13]. A study of causes of death among PLWH using National Health Service data from 2004 to 2018 showed that although AIDS was the most frequent (59%) cause of death, chronic conditions such as non-AIDS-defining cancers (8.2%), suicide (7.4%), CVD (4.9%), and liver disease (2.7%) were also important causes [14].

The prevalence of non-communicable diseases among PLWH is projected to increase from 29% in 2010 to 84% in 2030 [15]. The proportion of AIDS-related deaths among PLWH is decreasing and the proportion of deaths from non-AIDS causes is increasing [16]. These findings underscore the importance of treating non-AIDS complications and comorbidities in addition to HIV infection.

Non-AIDS-defining comorbidities in Korean HIV/AIDS

Non-AIDS-defining comorbidities are increasing as a result of advances in treatment and the aging of the patient population [17–19]. In addition to conditions directly related to HIV infection (opportunistic infections, AIDS-specific cancers, central nervous system infections, HIV debilitating syndromes, and co-infection with hepatitis B or C), conditions that are increasingly frequent in patients with HIV and are of clinical concern and need to be treated together are defined as non-AIDS-defining comorbidities. These include CVDs, metabolic complications, kidney diseases, psychiatric disorders, malignancies, and so on [18]. This increase in comorbidities has led to the need for comprehensive internal medicine care for patients with HIV, not just treatment of the infection. There is also an increased need for consultative care with other specialists.

Because PLWH are living longer, the number of older patients is steadily increasing in Korea, and chronic diseases such as malignancies, CVD and diabetes are becoming important issues in HIV care [20]. In a study of the incidence of chronic diseases between PLWH and the general population using data from the National Health Insurance Service, PLWH had higher rates of malignancies, chronic kidney disease, osteoporosis, diabetes, hyperlipidemia and depression than the general population [21].

PLWH have higher rates of CVD, including myocardial infarction and hypertension, compared to people without HIV [18,22], and the mortality rate after acute myocardial infarction or stroke has been reported to be higher in PLWH [23]. A study with claims data from the National Health Insurance of the Korea reported that acute coronary syndrome was confirmed in 2.0% of PLWH, which was 1.3-fold higher than in the general population. The overall mortality rate was 7.1% [24]. In a Korean study, the incidence of CVD in PLWH was 4.11 per 1,000 person-years and CVD was more common in the elderly and in patients with diabetes mellitus [25]. Older PLWH should be encouraged to adopt lifestyle modifications such as regular exercise and a balanced diet.

HIV patients with diabetes need to avoid antiretroviral drugs that can worsen diabetes, including proteinase inhibitors (PIs), which induce insulin resistance and decrease insulin secretion [26]. Weight gain is reportedly greater among PLWH receiving integrase strand transfer inhibitor (INSTI)-based cART as initial therapy [27,28]. In a Korean study, individual INSTI-based regimens were associated with weight gain at the 24-month follow up in both the

treatment-naïve and treatment-experienced groups [20].

In a meta-analysis, bone mineral density was found to be 6.4-fold lower and the rate of osteoporosis 3.7-fold higher in PLWH than in individuals not infected with HIV [29]; the rate of fractures has been reported to be 60% higher [30]. In addition to risk factors for osteopenia and osteoporosis in the uninfected population, the risk of osteopenia associated with HIV medications, including PIs and tenofovir, should be considered [29,31]. In a Korean study, middle-aged men living with HIV had lower hip bone density and higher cortical and trabecular bone deficit rates compared to controls [32]. This finding suggests the need for a tailored strategy for the early detection and prevention of bone deficit in middle-aged men living with HIV.

Although kidney diseases can be caused by HIV infection itself such as HIV nephropathy, several antiretrovirals are associated with renal insufficiency, including tenofovir disoproxil fumarate (TDF), and boosted atazanavir [33]. The most common renal insufficiency observed in clinical practice is associated with the use of TDF [33,34]. In a Korean cohort study of renal insufficiency in male PLWH based on a Korean HIV/AIDS cohort of 830 patients, 32 (3.9%) cases of renal insufficiency occurred during 9,576 person-years of follow-up [35]. Diabetes mellitus, dyslipidemia, exposure to tenofovir or non-nucleoside reverse transcriptase inhibitors (NNRTIs) for >1 year, and AIDS-defining illness were risk factors for renal insufficiency.

PLWH often experience psychological stigma, which is more severe in Korea than in developed countries [36]. This stigma is related to symptoms of both depression and anxiety. Brief screening for depression is recommended for all PLWH [37]. Cognitive behavioral therapy for adherence and depression performed by clinical psychologists is effective for treating depression in PLWH [38]. A Korean study showed that a nurse-delivered cognitive behavioral therapy for adherence and depression was feasible and acceptable for PLWH and could improve their depression and quality of life [39]. HIV-associated neurocognitive disorder screening and the identification of modifiable factors are needed to improve patient compliance with therapy [40]. Among 194 Korean PLWH, the prevalence of HIV-associated neurocognitive disorders was 26.3%. Asymptomatic neurocognitive impairment and minor neurocognitive disorder accounted for 52.9% and 47.1%, respectively, of these patients [41].

Studies on cancer survival in PLWH using data from the National Health Insurance Service found that cancer rates were approximately 1.7-fold higher in PLWH than in the general population, with a decreasing trend in AIDS-related cancers and a gradual increase in non-AIDS-related cancers [42–44]. The incidence rates of HPV-related cancers, including cervical, anal, and oral cancers, were 4.98-, 104.2- and 2.97-fold higher, respectively, than in the general population, and have increased recently [43–45]. Compared with the general population, the incidence rates of lung and liver cancer were higher, whereas that of stomach cancer tended to be lower, among PLWH [42–44]. These findings highlight the need for multifaceted cancer prevention and early detection, including increased cancer screening, HPV vaccination, and smoking cessation.

Antiretroviral therapy for HIV/AIDS in Korea

Zidovudine was the first treatment for HIV infection to be approved by the US Food and Drug Administration (FDA), in 1987 [46]. Several agents were subsequently developed, and by the late 1990s it was recognized that long-term suppression of HIV was possible through a combination of three drugs [47]. This highly active ART is now the standard of care for HIV infection. To date, more than 30 antiretrovirals have been approved by the US FDA: abacavir, embricitabine,

lamivudine, and tenofovir alafenamide, and TDF; the nucleoside reverse transcriptase inhibitor (NRTI) class, which includes doravirine, efarirenz, etravirine, nevirapine, and rilpivirine; the NNRTI class, which includes atazanavir, darunavir, and lopinavir/ritonavir; the PI class, which includes atazanavir, darunavir, and lopinavir/ritonavir; the INSTI class, which includes bictegravir, dolutegravir, elvitegravir, raltegravir, and carbotegravir; the fusion inhibitor class, which includes enfuvirtide; the CCR5 antagonist class, which includes maraviroc; the CD4 post-attachment inhibitor class, which includes ibalizumab; the gp120 attachment inhibitor class, which includes fostemsavir; and the capsid inhibitor class, which includes lenacapavir [48]. In the past, each agent had to be administered separately, resulting in large numbers of pills to be taken daily; however, fixed-dose combinations of multiple drugs into a single formulation have been used more recently.

ART was introduced in Korea in 1991 with zidovudine monotherapy, followed by NRTIs such as didanosine, lamivudine, and stavudine as two-drug combination regimens. The introduction of PIs such as indinavir and later nelfinavir in 1997 and NNRTIs such as efavirenz in 1999 led to the development of triple therapies [49]. Subsequently, NRTIs such as abacavir and tenofovir; PIs such as atazanavir, lopinavir/ritonavir, and darunavir; and NNRTIs such as etravirine and rilpivirine were introduced. The introduction of the raltegravir as a integrase inhibitor in 2010 and its combination with elvitegravir in 2013 paved the way for single-tablet regimens [50]. Since then, several single-tablet regimens have been introduced, including dolutegravir, bictegravir, and doravirine [50]. Long-acting injectable antiretrovirals are used in other nations and will soon be introduced in Korea as a combination of carbotegravir and rilpivirine [51].

Continuous antiretroviral treatment can reduce viral replication in the blood to below the detectable level, leading to long-term suppression of HIV. A study of 141 PLWH in Korea who had received antiretroviral treatment for at least 1 year by 2005 found that 6 months after starting treatment, 73% of patients had suppressed viral replication to ≤400 copies/mL [52]. Antiretroviral treatment can fail due to patient non-adherence to the regimen, and HIV develops resistance-associated mutations. The incidence of resistance mutations in Korea is low, but increasing, and therefore requires attention [53]. Among 248 Korean PLWH, the rate of NNRTI resistance decreased between January 2010 and December 2020 (by 15.3% during 2012–2014, 8.7% during 2015–2017, and 2.4% during 2018–2020), whereas the rates of resistance to PIs and INSTIs increased from 0% until 2018 to 3.5% and 8.2% during 2018–2020, respectively [54]. Therefore, continuous monitoring of the pattern of ART resistance is necessary.

Conclusion

The availability of cART has significantly reduced the prevalence and mortality of HIV infection, which has become a chronic disease with long-term survival. Achieving the 95–95–95 target among those living with HIV in Korea requires multifaceted efforts to improve early diagnosis, early and proper treatment of HIV infection including the management of chronic diseases, and adherence to ART.

ORCID

Nam Su Ku: https://orcid.org/0000-0002-9717-4327

Authors' contributions

All work was done by Nam Su Ku.

Conflict of interest
No potential conflict of interest relevant to this article was reported.

Funding
Not applicable.

Data availability
Not applicable.

Acknowledgments
Not applicable.

Supplementary materials
Not applicable.

References

1. Joint United Nations Programme on HIV/AIDS. The path that ends AIDS: 2023 UNAIDS global AIDS update [Internet]. Geneva (CH): Joint United Nations Programme on HIV/AIDS; c2023 [cited 2024 Jan 13]. Available from: https://www.unaids.org/en/resources/documents/2023/global-aids-update-2023
2. Joint United Nations Programme on HIV/AIDS. 90-90-90: an ambitious treatment target to help end the AIDS epidemic [Internet]. Geneva (CH): Joint United Nations Programme on HIV/AIDS; c2024 [cited 2024 Jan 13]. Available from: https://www.unaids.org/en/resources/909090
3. Frescura L, Godfrey-Faussett P, Ali Feizzadeh A, El-Sadr W, Syarif O, Ghys PD, et al. Achieving the 95 95 95 targets for all: a pathway to ending AIDS. *PLoS One* 2022;17(8):e0272405. https://doi.org/10.1371/journal.pone.0272405
4. Korea Centers for Disease Control and Prevention. 2nd Strategies for the preventive management of HIV/AIDS (2024-2028). Cheongju: Korea Centers for Disease Control and Prevention; 2024.
5. Youn BB, Kang HC, Oh YW, Lee CH. A case report of an acquired immunodeficiency syndrome with multiple problems, such as fever, dyspnea, abdominal pain, oral candidiasis candida albicans esophagitis, etc. *N Med J* 1985;28:63-72.
6. Korea Centers for Disease Control and Prevention. Annual report on the notified HIV/AIDS in Korea, 2010. Cheongju: Korea Centers for Disease Control and Prevention; 2011.
7. Korea Centers for Disease Control and Prevention. Annual report on the notified HIV/AIDS in Korea, 2022. Cheongju: Korea Centers for Disease Control and Prevention; 2023.
8. Kim JM, Kim NJ, Choi JY, Chin BS. History of acquired immune deficiency syndrome in Korea. *Infect Chemother* 2020;52(2):234-244. https://doi.org/10.3947/ic.2020.52.2.234
9. Kim GS, Kim L, Baek S, Shim MS, Lee S, Kim JM, et al. Three cycles of mobile app design to improve HIV self-management: a development and evaluation study. *Digit Health* 2024;10:20552076241249294. https://doi.org/10.1177/20552076241249294
10. Korea Centers for Disease Control and Prevention. Annual report on the notified HIV/AIDS in

Korea, 2023. Cheongju: Korea Centers for Disease Control and Prevention; 2024.
11. Ann HW, Jun S, Shin NY, Han S, Ahn JY, Ahn MY, et al. Characteristics of resting-state functional connectivity in HIV-associated neurocognitive disorder. *PLoS One* 2016;11(4):e0153493.
https://doi.org/10.1371/journal.pone.0153493
12. Yoo M, Seong J, Yoon JG, Cha J, Chung YS, Kim K, et al. Characteristics of adolescents and young adults with HIV in the Republic of Korea from 2010 through 2015. *Sci Rep* 2020;10(1):9384.
https://doi.org/10.1038/s41598-020-66314-0
13. Lewden C, Salmon D, Morlat P, Bévilacqua S, Jougla E, Bonnet F, et al. Causes of death among human immunodeficiency virus (HIV)-infected adults in the era of potent antiretroviral therapy: emerging role of hepatitis and cancers, persistent role of AIDS. *Int J Epidemiol* 2005;34(1):121-130.
https://doi.org/10.1093/ije/dyh307
14. Park B, Choi Y, Kim JH, Seong H, Kim YJ, Lee M, et al. Mortality and causes of death among individuals diagnosed with human immunodeficiency virus in Korea, 2004–2018: an analysis of a nationwide population-based claims database. *Int J Environ Res Public Health* 2022;19(18):11788.
https://doi.org/10.3390/ijerph191811788
15. Smit M, Brinkman K, Geerlings S, Smit C, Thyagarajan K, Sighem A, et al. Future challenges for clinical care of an ageing population infected with HIV: a modelling study. *Lancet Infect Dis* 2015;15(7):810-818.
https://doi.org/10.1016/S1473-3099(15)00056-0
16. Smith CJ, Ryom L, Weber R, Morlat P, Pradier C, Reiss P, et al. Trends in underlying causes of death in people with HIV from 1999 to 2011 (D:A:D): a multicohort collaboration. *Lancet* 2014;384(9939):241-248.
https://doi.org/10.1016/S0140-6736(14)60604-8
17. Wong C, Gange SJ, Moore RD, Justice AC, Buchacz K, Abraham AG, et al. Multimorbidity among persons living with human immunodeficiency virus in the United States. *Clin Infect Dis* 2018;66(8):1230-1238.
https://doi.org/10.1093/cid/cix998
18. Guaraldi G, Orlando G, Zona S, Menozzi M, Carli F, Garlassi E, et al. Premature age-related comorbidities among HIV-infected persons compared with the general population. *Clin Infect Dis* 2011;53(11):1120-1126.
https://doi.org/10.1093/cid/cir627
19. Hsu DC, Sereti I. Serious non-AIDS events: therapeutic targets of immune activation and chronic inflammation in HIV infection. *Drugs* 2016;76(5):533-549.
https://doi.org/10.1007/s40265-016-0546-7
20. Kim J, Nam HJ, Jung YJ, Lee HJ, Kim SE, Kang SJ, et al. Weight gain and lipid profile changes in Koreans with human immunodeficiency virus undergoing integrase strand transfer inhibitor-based regimens. *Infect Chemother* 2022;54(3):419-432.
https://doi.org/10.3947/ic.2022.0063
21. Kim JH, Noh J, Kim W, Seong H, Kim JH, Lee WJ, et al. Trends of age-related non-communicable diseases in people living with HIV and comparison with uninfected controls: a nationwide population-based study in South Korea. *HIV Med* 2021;22(9):824-833.
https://doi.org/10.1111/hiv.13139

22. High KP, Effros RB, Fletcher CV, Gebo K, Halter JB, Hazzard WR FM, et al. Workshop on HIV infection and aging: what is known and future research directions. *Clin Infect Dis* 2008;47(4):542-553.
https://doi.org/10.1086/590150
23. Okeke NL, Hicks CB, McKellar MS, Fowler VG Jr, Federspiel JJ. History of AIDS in HIV-infected patients is associated with higher in-hospital mortality following admission for acute myocardial infarction and stroke. *J Infect Dis* 2016;213(12):1955-1961.
https://doi.org/10.1093/infdis/jiw082
24. Jung H, Lee E, Ro J, Lee JY, Bang J. Mortality after acute coronary syndrome in human immunodeficiency virus infection with optimal adherence: a nationwide study. *Infect Chemother* 2023;55(4):471-478.
https://doi.org/10.3947/ic.2023.0050
25. Bae JY, Kim SM, Choi Y, Choi JY, Kim SI, Kim SW, et al. Comparison of three cardiovascular risk scores among HIV-infected patients in Korea: the Korea HIV/AIDS cohort study. *Infect Chemother* 2022;54(3):409-418.
https://doi.org/10.3947/ic.2022.0048
26. Kalra S, Kalra B, Agrawal N, Unnikrishnan AG. Understanding diabetes in patients with HIV/AIDS. *Diabetol Metab Syndr* 2011;3(1):2.
https://doi.org/10.1186/1758-5996-3-2
27. Sax PE, Erlandson KM, Lake JE, McComsey GA, Orkin C, Esser S, et al. Weight gain following initiation of antiretroviral therapy: risk factors in randomized comparative clinical trials. *Clin Infect Dis* 2020;71(6):1379-1389.
https://doi.org/10.1093/cid/ciz999
28. Norwood J, Turner M, Bofill C, Rebeiro P, Shepherd B, Bebawy S, et al. Brief report: weight gain in persons with HIV switched from efavirenz-based to integrase strand transfer inhibitor-based regimens. *J Acquir Immune Defic Syndr* 2017;76(5):527-531.
https://doi.org/10.1097/QAI.0000000000001525
29. Brown TT, Qaqish RB. Antiretroviral therapy and the prevalence of osteopenia and osteoporosis: a meta-analytic review. *AIDS* 2006;20(17):2165-2174.
https://doi.org/10.1097/QAD.0b013e32801022eb
30. Triant VA, Brown TT, Lee H, Grinspoon SK. Fracture prevalence among human immunodeficiency virus (HIV)-infected versus non-HIV-infected patients in a large U.S. healthcare system. *J Clin Endocrinol Metab* 2008;93(9):3499-3504.
https://doi.org/10.1210/jc.2008-0828
31. Bonjoch A, Figueras M, Estany C, Perez-Alvarez N, Rosales J, del Rio L, et al. High prevalence of and progression to low bone mineral density in HIV-infected patients: a longitudinal cohort study. *AIDS* 2010;24(18):2827-2833.
https://doi.org/10.1097/QAD.0b013e328340a28d
32. Hong N, Kim JH, Treece G, Kim HC, Choi JY, Rhee Y. Cortical and trabecular bone deficit in middle-aged men living with HIV. *J Bone Miner Res* 2023;38(9):1288-1295.
https://doi.org/10.1002/jbmr.4873
33. Lucas GM, Ross MJ, Stock PG, Shlipak MG, Wyatt CM, Gupta SK, et al. Clinical practice guideline for the management of chronic kidney disease in patients infected with HIV: 2014 update by the HIV Medicine Association of the Infectious Diseases Society of America. *Clin Infect Dis* 2014;59(9):e96-e138.
https://doi.org/10.1093/cid/ciu617

34. Islam FM, Wu J, Jansson J, Wilson DP. Relative risk of renal disease among people living with HIV: a systematic review and meta-analysis. *BMC Public Health* 2012;12:234. https://doi.org/10.1186/1471-2458-12-234
35. Kim JH, Jang H, Kim JH, Song JY, Kim SW, Kim SI, et al. The incidence and risk factors of renal insufficiency among Korean HIV infected patients: the Korea HIV/AIDS cohort study. *Infect Chemother* 2022;54(3):534-541. https://doi.org/10.3947/ic.2022.0101
36. Kim K, Jang S, Rim HD, Kim SW, Chang H, Woo J. Attachment insecurity and stigma as predictors of depression and anxiety in people living with HIV. *Psychiatry Investig* 2023;20(5):418-429. https://doi.org/10.30773/pi.2022.0271
37. Gonzalez JS, Batchelder AW, Psaros C, Safren SA. Depression and HIV/AIDS treatment nonadherence: a review and meta-analysis. *J Acquir Immune Defic Syndr* 2011;58(2):181-187. https://doi.org/10.1097/QAI.0B013E31822D490A
38. Safren SA, O'Cleirigh CM, Bullis JR, Otto MW, Stein MD, Pollack MH. Cognitive behavioral therapy for adherence and depression (CBT-AD) in HIV-infected injection drug users: a randomized controlled trial. *J Consult Clin Psychol* 2012;80(3):404-415. https://doi.org/10.1037/a0028208
39. Kim JH, Kim JM, Ye M, Lee JI, Na S, Lee Y, et al. Implementation of a nurse-delivered cognitive behavioral therapy for adherence and depression of people living with HIV in Korea. *Infect Chemother* 2022;54:733-743. https://doi.org/10.3947/ic.2022.0118
40. Zipursky AR, Gogolishvili D, Rueda S, Brunetta J, Carvalhal A, McCombe JA, et al. Evaluation of brief screening tools for neurocognitive impairment in HIV/AIDS: a systematic review of the literature. *AIDS* 2013;27(15):2385-2401. https://doi.org/10.1097/QAD.0b013e328363bf56
41. Ku NS, Lee Y, Ahn JY, Song JE, Kim MH, Kim SB, et al. HIV-associated neurocognitive disorder in HIV-infected Koreans: the Korean NeuroAIDS project. *HIV Med* 2014;15(8):470-477. https://doi.org/10.1111/hiv.12137
42. Lee SO, Lee JE, Lee S, Lee SH, Kang JS, Son H, et al. Nationwide population-based incidence of cancer among patients with HIV/AIDS in South Korea. *Sci Rep* 2022;12(1):9974. https://doi.org/10.1038/s41598-022-14170-5
43. Park B, Ahn KH, Choi Y, Kim JH, Seong H, Kim YJ, et al. Cancer incidence among adults with HIV in a population-based cohort in Korea. *JAMA Netw Open* 2022;5(8):e2224897. https://doi.org/10.1001/jamanetworkopen.2022.24897
44. Lee SO, Lee JE, Sim YK, Lee S, Ko WS, Kim J, et al. Changing trends in the incidence and spectrum of cancers between 1990 and 2021 among HIV-infected patients in Busan, Korea. *J Infect Chemother* 2023;29(6):571-575. https://doi.org/10.1016/j.jiac.2023.01.018
45. Lee CH, Lee SH, Lee S, Cho H, Kim KH, Lee JE, et al. Anal human papillomavirus infection among HIV-infected men in Korea. *PLoS One* 2016;11(8):e0161460. https://doi.org/10.1371/journal.pone.0161460
46. Fischl MA, Richman DD, Grieco MH, Gottlieb MS, Volberding PA, Laskin OL, et al. The efficacy of azidothymidine (AZT) in the treatment of patients with AIDS and AIDS-related complex. *N*

Engl J Med 1987;317(4):185-191.
https://doi.org/10.1056/NEJM198707233170401
47. Hammer SM, Squires KE, Hughes MD, Grimes JM, Demeter LM, Currier JS, et al. A controlled trial of two nucleoside analogues plus indinavir in persons with human immunodeficiency virus infection and CD4 cell counts of 200 per cubic millimeter or less. *N Engl J Med* 1997;337(11):725-733.
https://doi.org/10.1056/NEJM199709113371101
48. Clinicalinfo. Guidelines for the use of antiretroviral agents in adults and adolescents with HIV [Internet]. Rockville (MD): Office of AIDS Research; c2023 [cited 2023 Nov 22]. Available from: https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/whats-new
49. Lee SH, Kim KH, Lee SG, Chen DH, Jung DS, Moon CS, et al. Trends of mortality and cause of death among HIV-infected patients in Korea, 1990-2011. *J Korean Med Sci* 2013;28(1):67-73.
https://doi.org/10.3346/jkms.2013.28.1.67
50. Shin YH, Park CM, Yoon CH. An overview of human immunodeficiency virus-1 antiretroviral drugs: general principles and current status. *Infect Chemother* 2021;53(1):29-45.
https://doi.org/10.3947/ic.2020.0100
51. Swindells S, Andrade-Villanueva JF, Richmond GJ, Rizzardini G, Baumgarten A, Masiá M, et al. Long-acting cabotegravir and rilpivirine for maintenance of HIV-1 suppression. *N Engl J Med* 2020;382(12):1112-1123.
https://doi.org/10.1056/NEJMoa1904398
52. Kim MS, Shin SY, Park YS, Kim YA, Ku NS, Kim JH, et al. Therapeutic response of HAART and analysis of related factors in Korean HIV-infected persons. *Infect Chemother* 2007;39(3):142-150.
53. Kim MH, Song JE, Ahn JY, Kim YC, Oh DH, Choi H, et al. HIV antiretroviral resistance mutations among antiretroviral treatment-naive and -experienced patients in South Korea. *AIDS Res Hum Retroviruses* 2013;29(12):1617-1620.
https://doi.org/10.1089/aid.2013.0184
54. Oh SM, Bang J, Park SW, Lee E. Resistance trends of antiretroviral agents in people with human immunodeficiency virus in Korea, 2012 - 2020. *Infect Chemother* 2023;55(3):328-336.
https://doi.org/10.3947/ic.2022.0150