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Immunological effectiveness of antiretroviral therapy in key groups of men

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Abstract. As of 3 September 2025, there were 15,095 people living with human immunodeficiency virus (HIV) registered in the Kyrgyz Republic. Antiretroviral therapy is received by 6,393 people living with HIV, of whom 5,374 (84.06%) have achieved a viral load of <50 copies/ml. The modern treatment regimen of two nucleoside reverse transcriptase inhibitors + dolutegravir is taken by 5,100 (79.77%) patients. Among people who inject drugs, in 2025, compared to 2018, there was a 14.09% decrease in the proportion of men with a CD4 count <200 cells/μl who were in the first clinical stage of HIV infection. In the group of men with probable heterosexual transmission, the proportion of patients with low immune status at the first clinical stage decreased by 5.69% over the same period. The most pronounced decrease in this indicator was recorded among men with homosexual transmission – by 24.96% compared to 2018. The aim of the study was to

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evaluate the immunological effectiveness of antiretroviral therapy among key groups of men. Data from 15,095 registered HIV cases and 9,006 men ≥18 years of age were analysed. Changes in CD4+ T-cell levels were studied over time: before the start of antiretroviral therapy and on 3 September 2025, with comparison to 2018 data. Among men who have sex with men, the proportion of patients with CD4 levels > 500 cells/μl increased from 23.25% (2018) to 62.28% (2025), reflecting a 33.4% increase in immunological effectiveness. Among people who inject drugs, the increase was 34.5%, and among men infected through heterosexual contact, it was 30.5%. Early initiation of antiretroviral therapy demonstrates advantages: better immune recovery dynamics, reduced risk of AIDS and associated pathologies, and reduced mortality compared to late initiation of treatment

Keywords: HIV; CD4; immunological efficacy; heterosexual men; viral load

Introduction

Human immunodeficiency virus (HIV) remains one of the major global public health challenges: to date, this virus has claimed 40.4 million (32.9-51.3 million) lives, and transmission continues worldwide; with a number of countries seeing an increase in new infections, whereas previously this figure had been declining. At the end of 2022, an estimated 39.0 million people worldwide were living with HIV, two-thirds of whom were in the African region (World Health Organisation (WHO). In 2022, 630,000 people died from HIV-related causes, and 1.3 million new HIV infections were reported [1].

There is no cure for HIV infection. However, as access to effective prevention, diagnosis, treatment and care for HIV and opportunistic infections has expanded, HIV infection has become a controllable chronic disease, and people living with HIV can live long and healthy lives [1]. The testing, treatment and viral suppression cascade for 2023 was 70-79-90. Survival among women receiving antiretroviral therapy (ART) is higher than among men (confidence interval (CI) 1.5-1.8; $p < 0.05$). Virological (CI 1.3-1.7; $p < 0.05$) and immunological (CI 0.7-0.9; $p < 0.05$) efficacy is higher in women than in men. Timely initiation of ART increases survival, especially among women (CI 123-124, $p < 0.05$) [2].

Antiretroviral therapy (ART) has been shown to reduce mortality among infected individuals, and efforts are being made to make it more accessible in low- and middle-income countries. Results have shown that in recent years, thanks to appropriate treatment, the survival rate of HIV-infected patients has increased [3]. High risk factors for death were people with low CD4+ T-cell counts, lack of antiretroviral therapy, low education levels, male gender, and people who inject drugs. These people need more attention in order to be tested for HIV-related indicators and receive appropriate treatment [4]. HIV-infected patients who have not been treated in the later stages have a shorter life expectancy than those who have received early treatment with highly active antiretroviral therapy (HAART). Early treatment provides better immunological recovery, reduced AIDS progression, reduced risk of comorbidities, and lower mortality compared to starting HAART in the later stages of the disease [5].

According to data from the Republican Centre for the Control of Blood-borne Viral Hepatitis B, C and HIV Infection in the Kyrgyz Republic, as of 3 September 2025, 15,095 people with HIV were registered in the Kyrgyz Republic, with 9,006 cases registered among men aged 18 and older, accounting for 59.66% of the total number of people identified with HIV in the Kyrgyz Republic. In terms of routes of infection among the total number of HIV-infected men over the age of 18, 4,001 (44.42%) cases were found to be heterosexual; 720 (7.99%) cases were found to be homosexual; in 3,783 (42%) cases, parenteral transmission through injecting drug use was identified. The aim of the study was to investigate the immunological efficacy of antiretroviral therapy in key groups of men to identify factors influencing the dynamics of the immune response.

Materials and Methods

The research materials consisted of data from the Republican Centre for Combating Haemocontact Viral Hepatitis B, C, D and HIV from the electronic surveillance system for HIV cases in the Kyrgyz Republic. On 3 September 2025, certificate No. 01-10/560 was issued by the Osh Regional Centre for the Control of Blood-borne Viral Hepatitis and Human Immunodeficiency Virus, confirming access to information on people living with HIV (PLHIV). The study design is descriptive. Data on 15,095 registered cases in the Kyrgyz Republic as of 3 September 2025 were processed. The inclusion criteria for the study were men with HIV aged 18 years and older who were receiving antiretroviral therapy as of 3 September 2025. CD4+ T-cell counts were analysed before the start of antiretroviral therapy and at the time of antiretroviral therapy. Exclusion criteria included all women living with HIV, children with HIV, all men not receiving antiretroviral therapy, and men who had died while receiving antiretroviral therapy. To calculate the reliability of the results, statistical methods were used with IBM SPSS statistics – determination of the p-value ($p \leq 0.05$), (95% CI: 0.04616- -0.2036) ($P < 0.05$)).

Results

As of 3 September 2025, a total of 6,408 people living with HIV in Kyrgyzstan are receiving antiretroviral therapy, 6,198 PLHIV aged 18 and older, 3,350 men (52.27%), women – 2,848 (44.44%), children under 18 – 210 (3.29%). Of the 3,350 men receiving antiretroviral

therapy (ART) in 1994 (59.52%) cases, heterosexual transmission (HST) was established; in 571 (17.04%) cases, parenteral transmission was established through the use of injectable drugs; in 460 (13.73%) cases among men, homosexual sexual transmission of HIV was established. Of the 3,450 men receiving ART, 3,311 (98.83%) were taking a regimen of two nucleoside reverse transcriptase inhibitors (NRTIs) + dolutegravir. 325 (9.71%) PLHIV were taking other ART regimens.

As of 31 March 2018, a total of 2,946 PLHIV were receiving ART, of whom 2,511 were aged 18 years and older (1,339 men, 1,172 women, and 435 children). 1,339 (45.45%) were men aged 18 years and older. In 445 (33.2%) cases among men, heterosexual transmission was established; 950 (58.99%) were identified as having been infected parenterally through injecting drug use; and in 86 (6.42%) cases among men receiving ART, the route of HIV infection was identified as homosexual (Fig. 1).

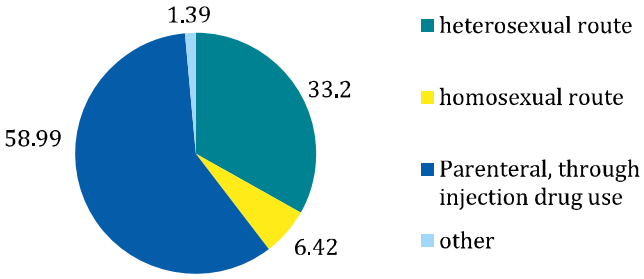

Figure 1. Distribution of HIV infection routes among men as of 31 March 2018
Source: created by the authors

As of 3 September 2025, among 3,350 men with HIV, 3,311 are receiving antiretroviral therapy on the 2NRTIs+dolutegravir regimen and 48 (1.39%). 48.92% of men were in the first clinical stage, 16.59% were in the second clinical stage, 26.07% were in the third clinical stage, and 8.42% were in the fourth clinical stage. 1,263 PLHIV received prophylactic therapy for opportunistic infections with cotrimazole, while 1,007 PLHIV completed it. 7.51% of men had a CD4 count of less than 200 cells/μl.

As of 31 March 2018, 1,240 (92.6%) of 1,339 men were receiving antiretroviral therapy with a 2NRTIs+efavirenz regimen, 51 (3.8%) were receiving 2NRTIs+/protease inhibitors (PI), 36.16% were in the first clinical stage, 16.07% were in the second clinical stage, 35.19% of men were in the third clinical stage, and 12.58% of men were in the fourth clinical stage. 608 men started preventive treatment for opportunistic infections with cotrimazole. 20.98% of men had a CD4 count of less than 200 cells/μl (Fig. 2).

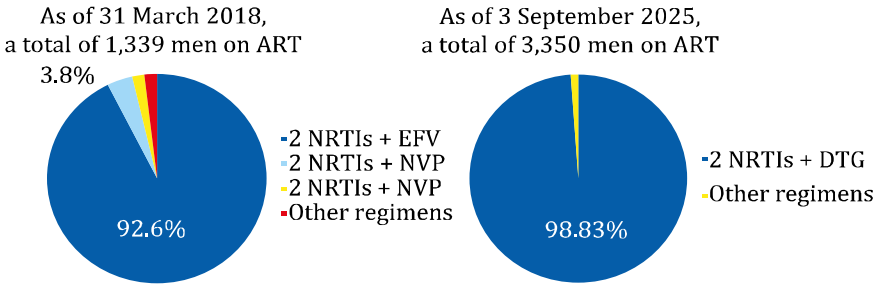

Figure 2. Comparative overview of antiretroviral therapy regimens among men with HIV as of 31 March 2018 and 3 September 2025
Source: created by the authors

The immunological efficacy of antiretroviral therapy among men with probable heterosexual transmission as of 31 March 2018 was calculated from the results of 434 (97.52%) CD4 tests before the start of antiretroviral therapy among 134 (30.87%), the CD4 level was below 200 cells/microlitre; on antiretroviral therapy, this CD4 level was observed among 89 (20.5%), i.e. the immunological efficacy among men with probable heterosexual transmission and CD4 counts below 200 cells/μl was 10.37% (95% CI: – 0.0167-0.2241 ($P < 0.05$)). In 59 (13.59%) men, the CD4 count was above 500 cells/μl before starting ART, and on antiretroviral therapy, it was observed in 103 (23.73%) men with established heterosexual transmission. The number of men with CD4 levels above 500 cells/μl increased by 10.14% (95% CI: -0.2086-0.0058 ($P < 0.05$)). In 48.97% of men, the first clinical stage was observed, in 19.95% of men, the second clinical stage was observed, in 26.63% of men, the third clinical stage was observed, and in 4.45% of men, the fourth clinical stage was observed.

As of 3 September 2025, calculated from 2,978 (88.89%) CD4 test results, 558 out of 1,713 (32.57%) men with probable heterosexual transmission had a CD4 count below 200 cells/μl before starting antiretroviral therapy. On antiretroviral therapy, the number of men with levels below 200 cells/ml was observed among 193 (11.26%) men, i.e. a 21.31% higher immunological effect was observed among men with CD4 levels below 200 cells/ml (95% CI: 0.0904-0.3216 (P > 0.05)). CD4 levels above 500 cells/μl were observed in 294 (17.16%) men with established heterosexual transmission prior to antiretroviral therapy, and among 864 (50.43%) men with heterosexual transmission. Immunological efficacy among men with established heterosexual transmission at a CD4 level above 500 cells/μl improved by 33.27% (95% CI: −0.443—0.199 (P < 0.05)). 54.62% of men were in the first clinical stage, 16.1% were in the second clinical stage, 21.09% of men were in the third clinical stage, and 8.19% of men were in the fourth clinical stage (Fig. 3).

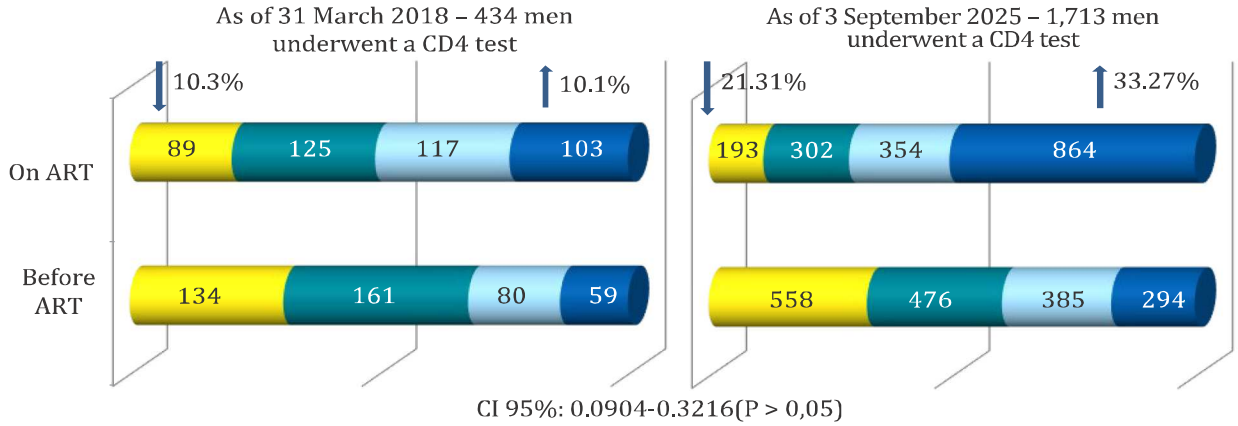

Figure 3. Immunological effectiveness of antiretroviral therapy among men with a heterosexual route of infection

Note: The lower bars show values before the start of antiretroviral therapy, while the upper bars show values at the time of antiretroviral therapy. Light grey indicates CD4 levels below 200 cells/μl, green indicates CD4 levels of 200–350 cells/μl, orange indicates CD4 levels of 350–500 cells/μl, and dark grey indicates CD4 levels above 500 cells/μl

Source: created by the authors

The immunological efficacy of antiretroviral therapy among men with probable homosexual transmission as of 31 March 2018 was calculated from the results of 86 (100%) CD4 tests before the start of antiretroviral therapy among 15 (17.44%), the CD4 level was below 200 cells/microlitre; on antiretroviral therapy, this CD4 level was observed in 9 (10.46%), i.e. the immunological efficacy among men with probable homosexual transmission and CD4 levels below 200 cells/μl was 6.98% (95% CI: 0.0462-0.1858 (P < 0.05)). In 20 (23.25%) men, the CD4 level was above 500 cells/μl before the start of ART, and on antiretroviral therapy, it was observed in 28 (32.55%) men with established homosexual transmission. The number of men with CD4 levels above 500 cells/μl increased by 9.3% (95% CI: 0.216-0.030 (P < 0.05)). 69.31% of men who have sex with men (MSM) with HIV were in the first clinical stage, 17.04% were in the second clinical stage, 11.36% were in the third clinical stage, and 2.29% were in the fourth clinical stage.

As of 3 September 2025, based on 411 (89.34%) CD4 analysis results, prior to antiretroviral therapy, 59 (14.96%) men with probable homosexual transmission had CD4 levels below 200 cells/μl. On antiretroviral therapy, the number of men with levels below 200 cells/μl was observed among 14 (3.56%) men, i.e., the immunological efficacy of ART improved by 10.95% among men with homosexual transmission with CD4 levels below 200 cells/μl (95% CI: 0.036-0.193 (P < 0.05)). CD4 levels above 500 cells/μl were observed among 114 (27.73%) men with established homosexual transmission before starting antiretroviral therapy, and among 256 (62.28%) men with heterosexual transmission on antiretroviral therapy, CD4 counts above 500 cells/μl were observed. The immunological efficacy of ART among men with confirmed homosexual transmission at a CD4 level above 500 cells/μl improved by 34.55% (95% CI: 0.04616-0.2036 (P < 0.05)). 77.26% of MSM were in the first clinical stage, 14.12% were in the second clinical stage, 6.62% were in the third clinical stage, and 2% were in the fourth clinical stage (Fig. 4).The immunological efficacy of antiretroviral therapy among men with probable parenteral transmission, using injectable drugs, as of 31 March 2018, was calculated from the results of 773 (81.36%) CD4 tests, before the start of antiretroviral therapy among 238 (30.78%) the CD4 level was below 200 cells/μl, on antiretroviral therapy this CD4 level was observed among 165 (21.34), i.e. 9.44% immunological efficacy among men with probable parenteral infection, when using

injectable drugs with CD4 levels below 200 cells/μl (95% CI: −0.0263-0.2151 (P < 0.05)). In 129 (16.68%) men, the CD4 count was above 500 cells/μl before starting ART, and on antiretroviral therapy, it was observed in 191 (24.7%) men with established parenteral transmission through injecting drug use. The number of men with CD4 levels above 500 cells/μl increased by 8.02% (95% CI: −0.1913-0.0309 (P < 0.05)). 26.52% of men infected through injecting drug use were in the first clinical stage, 16.63% were in the second clinical stage, 41.68% were in the third clinical stage, and 15.17% were in the fourth clinical stage.

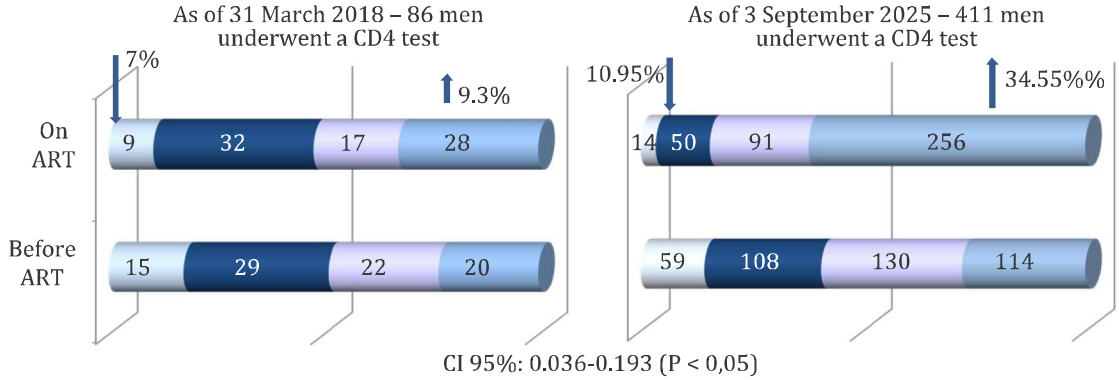

Figure 4. Immunological effectiveness of antiretroviral therapy among groups of men who have sex with men as of 31 March 2018 and 3 September 2025

Note: The upper values refer to data at the time of ART, while the lower values refer to data before the start of ART. Grey indicates CD4 levels below 200 cells/μl, blue indicates CD4 levels of 200–350 cells/μl, bright purple indicates CD4 levels of 350–500 cells/μl, and light blue indicates CD4 levels of 500 cells/μl and above

Source: created by the authors

As of 3 September 2025, based on 552 (96.67%) CD4 analysis results, prior to the start of antiretroviral therapy, among 187 (33.88%) men with probable parenteral infection, when using injectable drugs, had an SD4 level below 200 cells/μl. On antiretroviral therapy, the number of men with levels below 200 cells/μl was observed among 43 (7.78%) men, i.e., immunological efficacy improved by 26.1% among men with CD4 levels below 200 cells/μl (95% CI: 0.01681-0.3783 (P < 0.05)). CD4 levels above 500 cells/μl were observed in 92 (16.66%) men with established parenteral infection who used injection drugs before starting antiretroviral therapy, and among 290 (52.53%) men with parenteral transmission who used injection drugs. The immunological efficacy of ART among men with established parenteral infection, who used injection drugs, with a CD4 level above 500 cells/μl improved by 35.87% (95% CI: −0.4667–0.2227 (P < 0.05)). Of the men infected through injecting drug use, 21.83% were in the first clinical stage, 20.55% were in the second clinical stage, 43.83% were in the third clinical stage, and 13.79% were in the fourth clinical stage (Fig. 5).

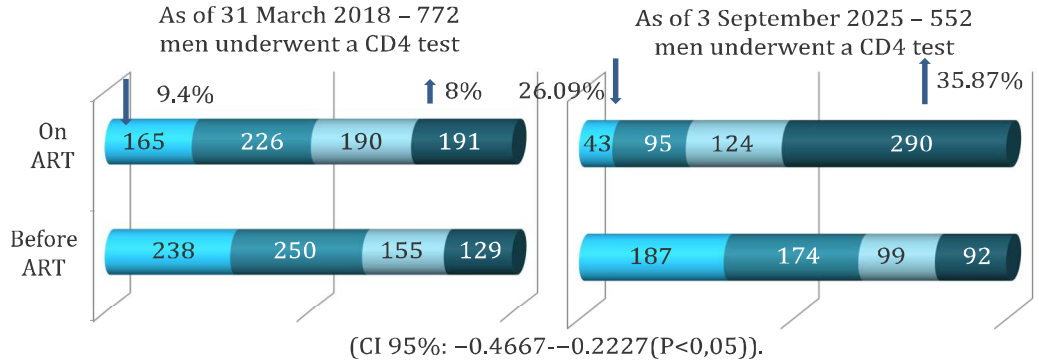

Figure 5. Immunological efficacy of antiretroviral therapy among men infected parenterally through injecting drug use

Note: The upper data in the column is data against the background of ART, the lower data in the column is data before the start of ART. Blue indicates data with a CD4 level of less than 200 cells/ml, orange indicates data with a CD4 level of 200-350 cells/ml, green indicates CD4 levels of 350-500 cells/μl, and bright purple indicates CD4 levels of 500 cells/μl and above

Source: created by the authors

Among men with heterosexual transmission (30.87%) and people who inject drugs (30.78%) before starting antiretroviral therapy with a CD4 count below 200 cells/microlitre is twice as common as in the MSM group (17.44%). A similar pattern can be observed against the background of ongoing antiretroviral therapy. Among men with heterosexual transmission (20.5%) and among people who inject drugs (PWID) (21.34%), a CD4 count below 200 cells/μl is twice as common. Consequently, among groups of men with heterosexual transmission (10.37%) and PWID (9.44%), immunological efficacy is observed at CD4 levels below 200 cells/μl. Meanwhile, among men who have sex with men (MSM), the immunological efficacy of ART at CD4 levels below 200 cells/μl improves by 6.98%. These figures explain that even before the start of ART, there were fewer people with CD4 levels below 200 cells/μl among MSM (Fig. 6).

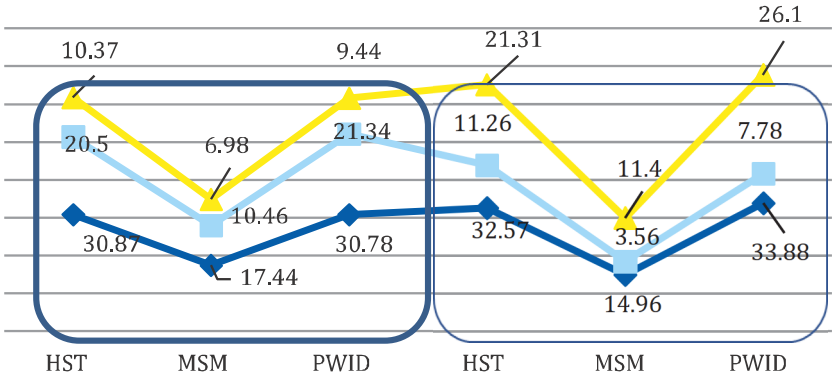

Figure 6. Dynamics of the immunological effectiveness of antiretroviral therapy by HIV infection routes in 2018 and 2025

Note: The black frame on the left describes the immunological effectiveness of ART in 2018, while the blue frame on the right shows the immunological effectiveness of ART in 2025. HST shown by the left vertical line in the right and left frames of the picture. MSM – men who have sex with men are represented by a vertical line in the middle of each frame. PWID – people who inject drugs are represented by a vertical line on the right side of each frame

Source: created by the authors

All three groups show more people in the first clinical stage, while among MSM, 7.95% (69.31% in 2018 and 77.26% in 2025) are in the first clinical stage, which may indicate early detection of HIV. Among men with probable heterosexual transmission, early detection of HIV improved by 5.65% (48.97% in 2018 and 54.62% in 2025). Among men with probable parenteral transmission, early detection decreased by 4.69% among injecting drug users (26.52% in 2018 and 21.83% in 2025).

Among people who inject drugs (PWID) in 2025, 187 (33.87%) had a CD4 count of less than 200 cells/μl and 20 of them (10.69%) were in the first clinical stage. In 2018, 238 (30.82%) had an SD4 level below 200 cells/μl, and 59 (24.78%) PWID were in the first clinical stage. Consequently, the number of men with low immune status at the first clinical stage of HIV infection decreased by 14.09%. Among men with probable heterosexual transmission in 2025, 537 (31.34%) had an CD4 count below 200 cells/μl and 144 (26.81%) were in the first clinical stage of HIV infection. In 2018, 160 (36.86%) men had CD4 counts below 200 cells/μl, and 52 of them (32.5%) were in the first clinical stage. Consequently, the number of men with low immune status at the first clinical stage of HIV infection decreased by 5.69%.

In 2025, 57 (13.86%) men with HIV infected through homosexual contact had an CD4 count below 200 cells/μl, and 35 (61.4%) of them were in the first clinical stage. In 2018, 22 MSM (25.58%) had CD4 counts below 200 cells/μl, and 19 (86.36%) of them were in the first clinical stage. Consequently, the number of men with low immune status at the first clinical stage of HIV infection decreased by 24.96%.

Discussion

Viral tropism determines the differential distribution of the viral reservoir among CD4(+) T-cell subpopulations. Despite viral tropism, effector and transient CD4(+) memory T-cell subpopulations are the main source of residual viraemia during suppressive ART, even though their contribution to the total proviral pool is small. However, the lack of correspondence between residual viraemia and viral variants causing de novo infection of CD4(+) T cells on ART may reflect the predominance of defective HIV RNA genomes in plasma. These findings highlighted the need to monitor multiple markers of viral RNA/DNA persistence based on their differential contribution to viral persistence [6].

In the primary population-level analysis, recent HIV testing was 31% higher in integrated care centres than in conventional care settings (adjusted prevalence ratio [PR] 1.31, 95% CI 0.95-1.81, p = 0.09). In intervention sites, the impact of integrated care centres was lower than expected (median impact of 40% in PWID care settings and 24% in MSM care settings). In intervention

sites, survey participants who attended integrated care centres were more likely to report recent HIV testing [7]. All integrase strand transfer inhibitors, except raltegravir, are approved for simplification of antiretroviral treatment in patients with virologically suppressed infection without resistance to integrase inhibitors (INIs). Data also support the use of dolutegravir and raltegravir in individuals with antiretroviral drug resistance as part of an optimised ART regimen. INIs are generally well tolerated by people living with HIV compared with older drug classes [8]. Although progress with new treatment strategies may be encouraging, challenges remain, and it is important to achieve a high threshold of safety and efficacy in the era of safe and effective ART. It is likely that achieving sustained remission or a cure for HIV will require a multifaceted approach, including a combination of strategies to enhance both adaptive and innate immunity [9]. Combined antiretroviral therapy (cART) not only reduces HIV replication and restores immunological status, improving immune function in patients with HIV-associated lymphomas, but also enables patients to tolerate standard doses of chemotherapy [10].

The authors of this study also documented a progressive increase in the proportion of viral load suppression as a result of expanded ART. Although CD4 T-cell counts prior to ART initiation have steadily increased in recent years, a significant proportion of PLHIV are still diagnosed at late stages of HIV infection. The number of new HIV diagnoses is declining rapidly, but to a lesser extent among men who have sex with men (MSM), and there is currently an increase in cases of infectious syphilis in this population. The majority (62%) of the included studies were retrospective cohort studies, which are prone to systematic bias in allocation and outcome assessment. A pooled analysis was not performed due to the heterogeneity of the studies and outcome definitions. No studies examined interventions targeting heterosexual men in the context of HIV treatment. However, in the included studies that examined retention among both men and women, high dropout rates were observed among men. More male-specific interventions need to be studied, preferably in randomized controlled trials (RCTs) [11].

The results of this study further confirm the high immunological efficacy of modern antiretroviral therapy regimens. The identified differences in the immunological effectiveness of antiretroviral therapy in key populations compared with men with a confirmed heterosexual route of infection show that, prior to starting ART, there were fewer patients with low immune status among MSM than among men with confirmed heterosexual routes of infection and among PWID. In addition, in the PWID and MSM groups receiving antiretroviral therapy, the proportion of patients with CD4 counts above 500 cells/μL was higher compared with men with a confirmed heterosexual route of infection [12].

Conclusions

The study assessed the immunological efficacy of antiretroviral therapy at the current stage among men with HIV infection, depending on the route of infection and baseline CD4 cell count. The results showed that in men with heterosexual transmission, the immunological efficacy of ART improved by 10.94% at CD4 levels below 200 cells/ml and by 19.13% at CD4 levels of 500 cells/ml and above. Among men with homosexual transmission, immunological efficacy improved by 4.42% at CD4 levels below 200 cells/μl and by 25.25% at CD4 levels of 500 cells/μl and above. In men with parenteral infection associated with injecting drug use, the improvement in immunological efficacy was 16.66% at a CD4 level of less than 200 cells/μl and 27.13% at a CD4 level of 500 cells/μl and above. It was found that in all groups of men, the use of modern antiretroviral therapy regimens (2 NRTIs + dolutegravir) was associated with higher immunological efficacy compared to the ART regimens used in 2018 (2 NRTIs + efavirenz). It was also found that among men with homosexual transmission, low immune status at the time of initial HIV detection is twice as rare compared to men in the PWID group and men with heterosexual transmission.

An analysis of baseline CD4 cell counts prior to ART initiation showed that, at the present stage, among men who have sex with men, there is a downward trend in the proportion of patients with CD4 counts below 200 cells/μl, while among people who inject drugs and men with heterosexual transmission, there is a tendency for this group to increase. At the same time, the proportion of patients with CD4 counts of 500 cells/μl and above before starting ART shows an upward trend among men who have sex with men and men infected through heterosexual contact, while no significant upward or downward trends have been identified among PWID. Against the background of antiretroviral therapy, CD4 counts of 500 cells/μl and above are more frequently recorded among men who have sex with men (62.28%) compared to MSM (52.53%) and men with heterosexual transmission (50.43%). In addition, in all groups of men with HIV infection, there was a decrease in the number of patients in the first clinical stage of the disease with low CD4 cell counts, with a simultaneous increase in the proportion of men in the first clinical stage of HIV infection.

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Conflict of Interest

The authors declare no conflict of interest.

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