



## Literature Review: Development of Antiretroviral Therapy in Hiv/Aids Treatment

Nur Ainun Amir<sup>1</sup>, Pratiwi Nasir Hamzah<sup>2</sup>, Muhammad Jabal Nur<sup>2</sup>

<sup>1</sup>General Practitioner Professional Education, Faculty of Medicine, Muslim University of Indonesia

<sup>2</sup>Department of Internal Medicine, Faculty of Medicine, Muslim University of Indonesia

\*Corresponding Author: Nur Ainun Amir

E-mail: [nurainunamr@gmail.com](mailto:nurainunamr@gmail.com)



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### Abstract

Human Immunodeficiency Virus (HIV) is a virus that attacks the human immune system. The United Nations Joint Program for HIV/AIDS (UNAIDS) in 2019, stated that the largest HIV-infected population in the world is on the African continent (25.7 million), then in Southeast Asia (3.8 million), and in the Americas (3.5 million). HIV/AIDS symptoms consist of 4 stages, namely stage 1, this phase is referred to as asymptomatic HIV infection where the initial HIV symptoms are still not felt. The goal of antiretroviral therapy (ARV) is to increase the number of CD4<sup>+</sup> in T cells, reduce viral load, so that it is expected to reduce mortality. Recommendations for ARV administration are always evolving. Currently, ARVs are given to patients with PLWHA at any clinical stage and CD4<sup>+</sup> count. This study aims to determine the development of Antiretroviral therapy (ARV) in the treatment of HIV/AIDS. The method used was literature review with narrative review design to identify and summarise previously published articles on the development of Antiretroviral (ARV) therapy in the treatment of HIV/AIDS. From the 10 articles summarised, it was found that there was an influence of the development of Antiretroviral (ARV) therapy in the treatment of HIV/AIDS over time.

## Introduction

Human Immunodeficiency Virus (HIV) is a virus that attacks the human immune system. Symptoms of HIV infection can cause various serious conditions, caused by decreased immunity due to damage to the immune system. This condition makes individuals more susceptible to severe infections, HIV can damage white blood cells, a vital component of the immune system that plays an important role in fighting infections and diseases. When HIV destroys these cells, the immune system becomes weak, making individuals more susceptible to disease. When the immune system is reduced to a serious level, this condition is known as AIDS (Natasya et al., 2025; Edelman & Zolla-Pazner, 1989). The United Nation Joint Program for HIV/AIDS (UNAIDS) in 2019 stated that the largest HIV-infected population in the world is in the African continent (25.7 million), then in Southeast Asia (3.8 million), and in America (3.5 million). The HIV/AIDS and Sexually Transmitted Diseases (STIs) Development Report for Quarter IV (2019) noted that the number of HIV cases in Indonesia peaked in 2019, which was 50,282 cases. Although it tends to fluctuate, data on HIV/AIDS cases in Indonesia continues to increase from year to year (Wahyuni et al., 2023; Riono & Challacombe, 2020).

HIV/AIDS symptoms consist of 4 stages, namely stage 1, this phase is called asymptomatic HIV infection where early HIV symptoms are still not felt. This phase is not yet categorized as

AIDS because it does not show symptoms. If there are symptoms that often occur, it is swollen lymph nodes in several parts of the body such as the armpits, neck, and groin. Patients (PLWHA) in this phase still look healthy and normal, but the sufferer is already infected and can transmit the virus to others (Tiffany & Yuniartika, 2023; Balatif, 2020).

The goal of antiretroviral therapy (ARV) is to increase the number of CD4 + in T cells, reduce viral load, so that it is expected to reduce mortality. In order to achieve the goal, successful ARV treatment is needed. The success of ARV treatment in HIV patients can be assessed from three things, namely clinical success is assessed from clinical changes in HIV patients such as weight gain and improvement in opportunistic infections, immunological success is assessed from changes in the number of CD4 lymphocytes towards an increase, and virological success is assessed from a decrease in the number of viruses as low as possible or below the detection limit known as the number of undetectable viruses in the blood of HIV patients after ARV administration (Yoo et al., 2023; World Health Organization, 2023; Vojnov et al., 2022). Recommendations for ARV administration are always evolving. Currently, ARVs are given to patients with PLWHA in the clinical stage and with the number of CD4 + cells found. In PLWHA without symptoms of opportunistic infections, ARVs are started immediately within 7 days of diagnosis and clinical assessment. In pregnant PLWHA, ARVs are offered to start on the same day the HIV diagnosis is made. Currently, ARVs must also be started in pregnant and lactating women regardless of clinical status and CD4 + cell count, because pregnancy itself is an indication for ARV administration. Initiation in pregnant and lactating mothers also has three synergistic goals, namely improving maternal health, preventing transmission of HIV from mother to child, and preventing transmission of HIV from mother to partner. Late administration of ARVs in pregnancy can be seven times more risky for transmitting the virus from mother to child (Widjaja, 2022; Qu et al., 2023; Lyatuu et al., 2021). This study aims to determine the development of Antiretroviral (ARV) therapy in the treatment of HIV/AIDS.

## Methods

This study is a literature review study with a narrative review design. This method is used to identify, examine, evaluate, and interpret all available research. By using this method, a systematic review and identification of journals can be carried out, which in each process follows the steps or protocols that have been set. The type of data in this study is secondary data, namely databases from various references, such as research journals, journal reviews, annual reports, books and data related to the development of Antiretroviral (ARV) therapy in the treatment of HIV / AIDS. In the initial stage of searching for journal articles obtained through electronic databases, namely Google Scholar, 531 articles were found, Clinical Key 4 articles, PubMed 6 articles, Taylor & Francis 753 articles, ScienceDirect 2734 articles and national survey results such as RISKESDAS and WHO were searched using the keywords: Antiretroviral, HIV and AIDS. After screening, 10 relevant articles were obtained and became the material for analysis in this study. Content analysis was conducted using a synthesis table by comparing research methods, research subjects and objects, and the variables studied including the development of Antiretroviral (ARV) therapy in the treatment of HIV/AIDS.

## Result and Discussion

Table 1. Literature Review Results

| No | Authors                | Title   | Publisher   | Method                        | Result  |
|----|------------------------|---|---|-------------------------------|---|
| 1  | Febriani et al. (2019) | Evaluation of Antiretroviral (ARV) Use Based on CD4 Indicators in HIV Patients at | The Indonesian Journal of Infectious Disease (2020) | Cross-sectional study design. | Sociodemographic analysis mostly aged 26-45 years 73.8%, male gender 92.9%, bachelor's degree education |

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|   |                       | RSPI Prof. Dr. Sulianti Saroso   |   |   | 69%, already working 88.1% and already married 76.2%. Based on compliance in treatment obtained 78.6% compliant. The most widely used drug combination is TDF (300) + 3TC (300) + EFV (600) in the form of FDC (fixed-dose combination). The results of the Wilcoxon Test showed a significant difference between initial CD4 and final CD4 with a p value of 0.000 ( $p < 0.05$ ). Statistical tests with chi square obtained marital status, compliance, employment status and educational status showed a significant relationship with changes in CD4 (Pvalue $< 0.05$ ) while age, gender, and drug combination were not significant (Pvalue $> 0.05$ ). |
| 2 | Saniputra (2022)      | Meta-Analysis of Mean Differences in HIV/AIDS Treatment in Indonesia                 | Preventif: Public Health Journal (2022)               | Unobtrusive research with meta-analysis method. | The summary effect results show that ARV therapy results in changes in the number of CD4 cells in the body.   |
| 3 | Lailiah et al. (2024) | Development of Resilience Model in People with HIV Undergoing Antiretroviral Therapy | International Journal of Public Health Science (2024) | Cross-sectional design.                         | This resilience model is relevantly able to increase compliance in PLWHA. Emotional response is a factor that has the strongest influence   |

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|   |                   |  |  |                            | in forming PLWHA resilience in compliance mechanisms and quality of life.   |
| 4 | Shu et al. (2022) | Real-World Evidence-Based Management of HIV by Differential Duration HAART Treatment and its Association with Oral Lesions     | Current HIV Research (2022)                | Retrospective study        | In 246 patients with HIV, CD4 counts increased significantly after ART compared with pre-ART in all three treatment groups ( $P<.001$ ), while CD8 counts decreased significantly ( $P<.05$ ) in all three treatment groups. A significant association between ART and the CD4/CD8 ratio was observed ( $P<.001$ ). A significant increase in CD4 counts was observed between the 12-month and 18-month treatment groups ( $P<.05$ ). Oral lesions were significantly reduced in the treatment group. |
| 5 | Yiping Li, et al. | Effect of Switching Antiretroviral Treatment Regimen in Patients With Drug-Resistant HIV-1: Retrospective Observational Cohort | JMIR Public Health and Surveillance (2022) | Retrospective cohort study | Our study found that PI-based ART regimens were beneficial for reducing mortality in PLHIV and HIV-1 drug resistance. Our study found that PI-based ART regimens were beneficial for reducing mortality in PLHIV and HIV-1 drug resistance. More efforts are needed to detect HIV-1 drug  |

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|   |                            |   |  |                            | resistance earlier to ensure timely adjustment to PI-based ART, thereby maximizing the benefits of early treatment switching for PLHIV and HIV-1 drug resistance.   |
| 6 | Ahmed et al. (2020)        | Effectiveness of Same-Day ART Initiation on Retention in HIV Care in Ethiopia       | BMC Public Health (2020)                       | Retrospective study        | Reduced retention in care may threaten the benefits of “same-day test and treat” policies. These policies need to be implemented carefully with greater emphasis on assessing and preparing PLWHA for ART to ensure treatment readiness before starting same-day ART and close patient monitoring during follow-up. |
| 7 | Gebremichael et al. (2020) | Incidence and Predictors of Initial ART Regimen Change Among HIV Adults in Ethiopia | HIV/AIDS – Research and Palliative Care (2020) | Retrospective study        | The incidence of initial ART regimen changes was found to be low. HIV disclosure status, concurrent ART treatment, occurrence of side effects on initial regimen, low initial CD4 count, initial ambulatory and bedridden functional status were found to be predictors.  |
| 8 | JL Adams, et al.           | Comparative Effectiveness of ARV Classes in Patients With High Viral Load           | British HIV Association (2020)                 | Retrospective cohort study | Patients with high viral loads who started taking NNRTIs were more likely to achieve viral suppression within 6 months of   |

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|    |                          |  |   |  | ART compared with patients taking integrase strand transfer inhibitors and protease inhibitors.   |
| 9  | A. Dravid, et al.        | Efficacy and Safety of Switching to TDF/3TC/EFV 400 mg in Virologically Suppressed Patients in India | HIV Medicine (2020)                           | Retrospective study                                    | TLE400 STR demonstrated excellent efficacy and safety as a switching strategy and should be introduced in India's National ART Program, especially for PWH who are virologically suppressed on TLE600 STR.  |
| 10 | Rifqian & Mediana (2024) | HIV/AIDS Knowledge Improves ARV Adherence  | Trisakti University Scientific Journal (2024) | Analytical observational study, cross-sectional design | Most respondents were male, aged 20-25 years, had secondary education, high level of HIV/AIDS knowledge, and had good level of ARV adherence. There was a significant relationship between education, HIV/AIDS knowledge and adherence to taking ARV medication.                  |
| 11 | Yongli Yang, et al.      | ART Initiation Time and CD4 Count Effects on AIDS Mortality in China                                 | Global Health Action (2021)                   | Retrospective cohort study                             | Patients who initiated ART within 90 days of HIV/AIDS diagnosis (sHR: 0.24, 95% CI: 0.22–0.27) or had an initial CD4 + count >500 cells/ $\mu$ L (sHR: 0.23, 95% CI: 0.19–0.28) were associated with a lower risk of AIDS-related mortality. Patients with ART initiation time >1 |

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|    |                       |  |  |                                 | year but CD4 + count >350 cells/μL (sHR: 4.42, 95% CI: 3.30–5.91) had a higher risk of AIDS-related mortality than those with ART initiation time >90 days but CD4 + count ≤350 cells/μL (sHR: 4.33, 95% CI: 3.58–5.23).   |
| 12 | Addisu et al. (2023)  | Trends Analysis of HIV and ART Outcomes in Amhara, Ethiopia (2015–2021)          | HIV/AIDS – Research and Palliative Care (2023) | Descriptive retrospective study | A total of 145,639 people accessed antiretroviral therapy. HIV test positivity has been declining since 2015, peaking at 0.76% in 2015 and declining to 0.60% in 2020. High positivity rates were reported in voluntary counseling and testing compared to provider-initiated testing and counseling services. Once HIV positive, there is increased linkage to HIV care and treatment. High levels of viral load suppression indicate testing coverage is increasing over time. Viral load monitoring coverage was 70% in 2021, with a viral suppression rate of 94%. |
| 13 | Teshale et al. (2021) | Mortality Incidence and Predictors Among HIV Adults on ART in Northwest Ethiopia | HIV/AIDS – Research and Palliative Care (2021) | Retrospective cohort study      | <ul style="list-style-type: none"> <li>• Number of Deaths: 45 patients (9.5%) died during the study period.</li> <li>• Mortality Incidence: 5.3 per</li> </ul>   |

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|    |                        |  |  |                    | <p>100 person-years (95% CI: 3.4–7.1).</p> <ul style="list-style-type: none"> <li>• Significant Predictors of Mortality; WHO Stage III/IV Final: Patients with advanced stage had a 15-fold higher risk of death compared to those with stage I/II (AHR = 15.02; 95% CI: 5.79–38.92), Anemia at Baseline: Patients who were anemic at ART initiation had more than double the risk of death compared to those who were not anemic (AHR = 2.21; 95% CI: 1.02–4.78), Poor Final Adherence: Patients with poor adherence had more than three times the risk of death compared to those with good adherence (AHR = 3.29; 95% CI: 1.39–7.78).</li> </ul> |
| 14 | Shumetie et al. (2021) | Determinants of Virological Failure in HIV-Infected Children on First-Line ART in Ethiopia | HIV/AIDS – Research and Palliative Care (2021) | Case-control study | <ul style="list-style-type: none"> <li>• Failure to Disclosure HIV Status to Children: Children who did not know their HIV status were at higher risk of virologic failure (AOR = 4.26; 95% CI: 2.09–8.70).</li> <li>• Initial Viral Load &gt;1000 copies/mL: Children with high initial viral load were at greater risk of virologic failure (AOR = 10.82; 95% CI: 5.4–21.67).</li> </ul>  |



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|    |                      |  |  |                       | <ul style="list-style-type: none"> <li>• Poor Adherence to Treatment: Poor adherence to ARV therapy significantly increased the risk of virologic failure (AOR = 6.05; 95% CI: 1.70–21.55).</li> <li>• Missing Clinic Appointments: Children who missed clinic appointments were at higher risk of virologic failure (AOR = 8.03; 95% CI: 3.88–16.65).</li> </ul>   |
| 15 | Kaudha et al. (2023) | Anemia in HIV Patients on ART at Hoima Hospital: Prevalence, Morphology, and Factors | HIV/AIDS – Research and Palliative Care (2023) | Cross-sectional study | <ul style="list-style-type: none"> <li>• Prevalence of Anemia; Found in 16.8% of HIV patients undergoing ART therapy.</li> <li>• Morphological Classification of Anemia<br/>From the results of blood morphology examination;<br/>Normocytic normochromic: 47.4% (the most common type),<br/>Microcytic hypochromic: 42.1%, Normocytic hypochromic: 7%,<br/>Macrocytic normochromic: 3.5%</li> <li>• Factors Significantly Associated with Anemia; Age: Higher risk in the age group of 18 years and above,<br/>Marital status: Divorced patients are more at risk of anemia. Chronic disease: The</li> </ul> |

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|    |                       |   |   |                  | <p>presence of comorbidities increases the risk. Family history of anemia: Genetic factors play a role. History of malaria in the last 1 month: Infection increases the risk of anemia, Opportunistic infections: Very significant (OR = 58, <math>p &lt; 0.001</math>), Use of antihelminthic drugs in the last 3 months: Has a protective effect (OR = 0.10), Uncontrolled viral load: Risk of anemia increases drastically (OR = 10.74).</p>  |
| 16 | Jamie Colloty, et al. | Advances in HIV Treatment and Prevention: What You Need to Know | British Journal of Hospital Medicine (2022) | Narrative review | <ul style="list-style-type: none"> <li>• Simplification of Therapy Regimens: The development of complex regimens with multiple pills to fixed-dose combinations that allow for once-daily administration has improved patient compliance.</li> <li>• Long-acting Injectable Therapy: The development of long-acting injectable drugs, such as cabotegravir and rilpivirine, that allow for bimonthly dosing, providing an alternative for patients who have difficulty with daily oral therapy.</li> <li>• Pre-Exposure Prophylaxis (PrEP): The introduction of</li> </ul> |

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|----|------------------------|--|-----------------|------------------|--|
|    |                        |  |                 |                  | <p>PrEP as an HIV prevention strategy, including the use of long-acting oral and injectable drugs such as cabotegravir, has shown high efficacy in preventing HIV infection in high-risk populations. • Vaccine and Microbicide Development: Current research is focused on the development of vaccines and microbicides for HIV prevention, although no products are yet widely available.</p>  |
| 17 | Nuwagaba et al. (2025) | 30 Years of HIV Therapy: Current and Future Drug Targets | Virology (2025) | Narrative review | <p>1. Development of Antiretroviral Therapy (ARV)<br/>Highly Active Antiretroviral Therapy (HAART) has transformed HIV-1 into a manageable chronic condition. HAART involves a combination of drugs that target different stages of the HIV life cycle, including:</p> <ul style="list-style-type: none"> <li>• Reverse Transcriptase: An enzyme that converts viral RNA into DNA.</li> <li>• Protease: An enzyme that processes viral proteins into functional forms.</li> <li>• Integrase: An enzyme that helps</li> </ul> |

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|  |  |  |  |  | <p>integrate viral DNA into the host cell genome.</p> <ul style="list-style-type: none"> <li>• Viral Entry: The initial process of infection in which the virus enters the host cell.</li> </ul> <p>Although effective, HAART faces challenges such as lifelong adherence, toxicity, drug interactions, and drug resistance.</p> <p>2. New Therapies and Future Targets</p> <p>This article highlights new therapies and potential targets for the treatment of HIV:</p> <ul style="list-style-type: none"> <li>• Lenacapavir: A new drug that targets the HIV capsid, showing promise as a long-term therapy.</li> <li>• CCR5 co-receptor: Target for functional therapies, including the <math>\Delta 32</math> mutation known to confer resistance to HIV.</li> <li>• Tat and Rev proteins: Non-enzymatic proteins that are important in regulating HIV transcription and RNA export. Targeting these proteins could pave the way for new therapies that inhibit HIV replication</li> </ul> |
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|    |                     |  |                                       |                  | without causing excessive toxicity.  |
| 18 | Nayan et al. (2023) | Advances in Long-Acting Antiretroviral Therapies | Advanced Drug Delivery Reviews (2023) | Narrative review | <p>1. The Need for Long-Term ARV Therapy</p> <p>Adherence to daily ARV therapy is a significant barrier to HIV treatment and prevention. To address this limitation, a variety of long-term ARV formulations have been developed, including:</p> <ul style="list-style-type: none"> <li>• Long-Term Injections: Drugs such as cabotegravir and rilpivirine that can be given every 1–2 months.</li> <li>• Vaginal Implants and Rings: Devices that release drugs slowly over a period of time.</li> <li>• Microarray Patches and Ultra-Long-Term Prodrugs (ULAs): New technologies in development to extend the duration of drug effectiveness.</li> </ul> <p>2. Pharmacological Advances</p> <p>This article highlights advances in extending the half-life of ARV drugs and optimizing drug delivery to viral reservoirs in cells and tissues. These approaches include:</p> <ul style="list-style-type: none"> <li>• Nanoformulations and Prodrugs: Using nanotechnology and</li> </ul> |

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|    |                         |   |                |                  | <p>prodrugs to improve drug stability and efficacy.</p> <ul style="list-style-type: none"> <li>• Targeting Viral Reservoirs: Directing drugs to locations where the virus hides, such as in CD4+ T cells and macrophages.</li> </ul> <p>3. Challenges and Future Prospects</p> <p>Although long-term ARV therapy offers many advantages, there are challenges that need to be addressed, such as:</p> <ul style="list-style-type: none"> <li>• Dosing Interval: Increasing the duration between doses to reduce the frequency of administration.</li> <li>• Access and Cost: Ensuring the availability and affordability of this therapy in countries with limited resources.</li> <li>• Side Effects and Injection Site Reactions: Reducing side effects and increasing patient comfort.</li> </ul> |
| 19 | Ndashimye et al. (2023) | New ARV Inhibitors and HIV-1 Drug Resistance: Focusing on 90% of HIV-1 Isolates | Viruses (2023) | Narrative review | <p>1. HIV-1 Subtype Differences and Their Impact on Drug Resistance</p> <p>Most HIV-1 drug resistance research has focused on subtype B, which is predominant in high-income countries. However, approximately 90% of global HIV-1</p>   |

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|  |  |  |  |  | <p>infections are caused by non-B subtypes, such as A, C, D, G, and recombinants. Genetic variation between these subtypes can affect the effectiveness of antiretroviral (ARV) therapy and the rate of emergence of drug resistance.</p> <p>2. Resistance to Protease Inhibitors (PIs)</p> <p>Some naturally occurring mutations in non-B subtypes can affect sensitivity to PIs. For example, the D30N mutation in subtype C can reduce viral replication, whereas in subtype B, this mutation is a primary resistance mutation to PIs. In addition, the L90M mutation in subtype B can increase genetic resistance to PIs, but in subtype C, this mutation is less common and may affect the effectiveness of therapy.</p> <p>3. Resistance to Integrase Inhibitors (INSTIs)</p> <p>Mutations at key resistance sites such as Q148, N155, and Y143 can occur in all HIV-1 subtypes. However, differences in secondary mutations between B and non-B subtypes can</p> |
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|  |  |  |  |  | <p>affect response to INSTIs. For example, the G140S mutation is more common in B subtypes, while the G140A mutation is more common in non-B subtypes.</p> <p>4. Resistance to Nucleoside Reverse Transcriptase Inhibitors (NRTIs) and Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)</p> <p>Mutations such as M184V/I can reduce sensitivity to NRTIs, while mutations such as V106A/M and K103N can affect the effectiveness of NNRTIs. The differences in frequency and impact of these mutations between B and non-B subtypes highlight the need for a tailored therapeutic approach based on the viral subtype.</p> <p>5. Development of New Inhibitors and the Challenge of Resistance</p> <p>The development of new inhibitors such as temsavir and ibalizumab has shown therapeutic potential. However, studies have shown that temsavir has high variability in sensitivity among HIV-1 subtypes, with some non-B</p> |
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|    |                           |  |                |                  | subtypes showing natural resistance to the drug. Ibalizumab has also shown variable effectiveness depending on the viral subtype, with subtype B showing higher sensitivity compared to other subtypes.   |
| 20 | Charpentier et al. (2023) | Future of ARVs and HIV-1 Drug Resistance Evolution | Viruses (2023) | Narrative review | <ul style="list-style-type: none"> <li>• Long-acting ARV Development: Discusses innovations in the development of longer-acting ARVs, such as lenacapavir, which can be given subcutaneously every six months.</li> <li>• Drug Resistance: Analyzes the evolution of HIV-1 drug resistance, both transmitted and acquired, and its implications for therapeutic effectiveness.</li> <li>• WHO 95-95-95 Goal: Evaluates challenges and strategies to achieve the WHO target of testing, treating, and achieving 95% viral load suppression by 2025.</li> </ul> |

One of the strengths of some of these articles is the use of nationally and internationally representative data with the latest editions and a large sample size sufficient to analyze the development of Antiretroviral (ARV) therapy in the treatment of HIV/AIDS. One limitation that needs to be considered is that it requires a relatively large or large number of research subjects, assuming that there are quite a lot of independent variables that are less able to describe the development of Antiretroviral (ARV) therapy in the treatment of HIV/AIDS. The data sources available in literature studies may not be complete to answer all research questions. In addition, some articles use less population coverage. Thus, the authors suggest future research with better methodology, larger sample sizes, and more variables. Further

research is needed to describe the development of Antiretroviral (ARV) therapy in the treatment of HIV/AIDS.

In terms of preventive therapy services, the "test and treat" approach recommends starting ARV treatment immediately when the test result is reactive. This has been proven effective in reducing the risk of HIV transmission and improving the quality of life of PLHIV. In addition to screening that has not covered all transgender sex workers due to obstacles to health access, involvement, and social factors such as stigma and expulsion. However, it is also related to the orientation of policy makers, which is actually directed at reducing the number of HIV/AIDS cases where the success of the program is not only measured by the decrease in cases but is adjusted to the context of the program (Agung et al., 2024; Elendu et al., 2025; Simooya et al., 2025).

Cases of HIV and AIDS, which were initially considered 'strange diseases', began to emerge in New York and California, United States, in 1981 when young gay men who were known to be healthy were diagnosed with Kaposi's sarcoma, a type of cancer usually found in men who are much older. Some also suffer from rare types of pneumonia (Kemnic & Gulick, 2025; Brima et al., 2021).

A year later, the mysterious disease was named Acquired Immune Deficiency Syndrome or AIDS, which destroys the immune system and makes the body susceptible to all kinds of infections. In 1983, scientists discovered the virus that causes AIDS. They then named it human immunodeficiency virus or HIV. And to this day, they continue to race to find a cure to stop this deadly epidemic. HIV turns out to be difficult to kill. One of them attacks immune cells called T cells, which help protect the body from invaders like HIV. If enough T cells are destroyed, the body is defenseless against viruses and other opportunistic infections (Kemnic & Gulick, 2025). HIV is a retrovirus that is different from viruses such as cold and flu viruses. Retroviruses are more efficient at tricking host cells in the body and can replicate themselves and cause lifelong infections. By 1987, HIV had infected 32,000 people in the United States and more than half of them died (Kemnic & Gulick, 2025).

### **HIV Drug Breakthrough**

Researchers have discovered that the failed 1960s cancer drug zidovudine can stop the spread of HIV and help people with AIDS live longer. Also called azidothymidine (AZT), it became available in 1987. AZT works by blocking a protein called an enzyme that the virus needs to replicate itself. The FDA in the United States approved AZT in less than 4 months, speeding up a process that usually takes years (Kemnic & Gulick, 2025). However, AZT had the disadvantage that it did not work well on its own and caused side effects such as liver problems and low blood cell counts that could lead to death. AZT was also the most expensive prescription drug in history at the time, with a year's cost of \$16,500 in today's dollars. Over the next few years, the FDA in the United States approved several other drugs that work similarly to AZT, including in a class of drugs called nucleoside reverse transcriptase inhibitors (NRTIs) (Kemnic & Gulick, 2025).

### **New Class of Antiretrovirals**

In the early 1990s, HIV was the leading cause of death among people aged 25 to 44 living in the United States. This was because, with single-drug treatments such as AZT, the virus learned to change, or mutate, so that over time the drugs stopped working (Kemnic & Gulick, 2025).

In 1995, the FDA approved saquinavir, the first in a class of anti-HIV (antiretroviral) drugs called protease inhibitors. Like NRTIs, protease inhibitors stop the virus from multiplying, but at a different stage during infection. A year later, another class of antiretrovirals, called non-nucleoside reverse transcriptase inhibitors (NNRTIs), emerged, including nevirapine. Similar

to AZT, NNRTIs kill HIV by targeting an enzyme it needs to replicate (Kemnic & Gulick, 2025; Vanangamudi et al., 2023).

These drugs ushered in a new era of combination therapy for HIV and AIDS. Doctors began prescribing saquinavir plus AZT or other antiretroviral drugs. This combination therapy is called highly active antiretroviral therapy (HAART). This approach became the new standard of care for HIV in 1996, and HAART has significantly extended the lives of people with AIDS. HAART requires taking multiple pills every day. The multiple doses and side effects of the drugs prompted many people to stop taking HIV therapy. Then in 1997, the FDA approved a pill called Combivir, which contained two anti-HIV drugs and was easier to take. Nearly 2 decades after the emergence of HIV and AIDS, a dozen antiretroviral drugs are on the market (Kemnic & Gulick, 2025).

### **PrEP**

Another breakthrough in HIV treatment occurred in 2010. A study showed that taking antiretroviral drugs every day not only helped those who were HIV-positive, but also protected healthy people from getting infected. In 2012, the FDA approved a once-daily preventive drug known as pre-exposure prophylaxis (PrEP). In 2021, the injectable cabotegravir suspension was introduced, first given as two injections one month apart, and then every two months thereafter. When used according to guidelines, PrEP can reduce your risk of getting HIV to nearly zero. PrEP is recommended for anyone at risk of getting HIV, including men who have sex with men, heterosexual people who engage in risky sex without condoms, and those who inject drugs (Kemnic & Gulick, 2025).

### **Current HIV Treatments**

A new class of HIV drugs has emerged in recent years. In 2007, the US Food and Drug Administration approved the first integrase inhibitor, raltegravir. This class of drugs offers a different way to prevent HIV from replicating itself (Kemnic & Gulick, 2025).

### **Conclusion**

Based on the results of the identification and review in this literature review, it can be concluded that there has been development in Antiretroviral (ARV) therapy in the treatment of HIV/AIDS over time.

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