



## Advancement in HIV Treatment: A Comprehensive Review of Therapeutic Strategies and Emerging Innovations

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### Abstract

The Human Immunodeficiency Virus (HIV), a global health threat, continues to challenge medical science despite decades of research. This review provides a comprehensive overview of HIV/AIDS, from its historical context and scientific intricacies to the implications for individual and public health. It outlines the progression of understanding and treatment, delving into HIV transmission, pathogenesis, and the evolution of antiretroviral therapy (ART). The review highlights persistent challenges in HIV treatment, such as drug resistance and accessibility, while exploring promising emerging therapies. Addressing the psychological and social dimensions of living with HIV, the review emphasizes the importance of a holistic approach. Finally, it examines the global response to the epidemic, spotlighting international collaborations and progress in treatment and prevention. By examining successes, setbacks, and ongoing challenges, this review contributes to a nuanced understanding of the HIV epidemic's trajectory and future prospects.

**Keywords:** HIV; AIDS; Antiretroviral Therapy; Emerging Therapies; Drug Resistance; Global Health; Public Health; Social Stigma; Mental Health; Treatment Adherence; Prevention

### Introduction

The Human Immunodeficiency Virus (HIV), which affects millions of people worldwide continues to rank among the most serious threats to global health [1]. Acquired immunodeficiency syndrome (AIDS) is a medical condition caused by the human immunodeficiency virus (HIV). Most people believed that arising of HIV/AIDS is dependent on two features: the natural history of the HIV infection (the number of CD4+ cells and HIV RNA copies plotted over the time) and the virus replication cycle (from the virus entry to the virus assembly, budding and maturation) [2].

### Importance of studying HIV and its treatment

HIV has intricated scientific and medical aspects, but it also has socioeconomic, cultural, and ethical ramifications. Due to its

capacity to compromise the immunological defenses that the body depends on for protection, the virus has presented particularly difficult problems. Acquired Immunodeficiency Syndrome (AIDS), which is characterized by a weaker immune system and greater vulnerability to opportunistic infections and some malignancies, was developed as a result of this intricate relationship. But during the last two decades, enormous progress has been achieved in understanding the virus, creating efficient treatment plans, and raising the standard of living for HIV-positive people [3].

### Purpose and scope of the review

The goal of this review is to present a thorough examination of HIV and the landscape of its treatments, ranging from its historical backdrop to the most recent advances and research in the area.

This study tries to clarify the complex nature of the virus and its effects on both individual health and global public health by digging into the complexities of HIV transmission, pathogenesis, and the advancement of antiretroviral therapy (ART) [4].

Additionally, the review will delve into the challenges that persist in HIV treatment, such as drug resistance, treatment adherence, and issues of accessibility in diverse settings. It will explore emerging therapies that hold promise in altering the course of the disease, moving beyond symptom management to approaches that may potentially offer a functional cure or long-term remission. Moreover, the psychological and social dimensions of living with HIV cannot be overlooked. Social stigma, discrimination, and mental health implications form a significant part of the narrative surrounding HIV/AIDS. The review will address the importance of addressing these aspects in a holistic approach to HIV treatment and management [5].

Lastly, this review will discuss the global response to the HIV epidemic, spotlighting international collaborations, organizations, and the progress made in both treatment and prevention. By examining successes, setbacks, and the ongoing challenges, this review seeks to contribute to a nuanced understanding of the trajectory of the HIV epidemic and the road ahead [6].

In essence, this review endeavors to provide a comprehensive and up-to-date overview of the multifaceted realm of HIV and its treatment. Through a synthesis of scientific research, clinical practice, and sociocultural insights, we aim to shed light on the past, present, and future of HIV management, highlighting the remarkable achievements and the work that remains to be done [6].

### Brief overview of HIV (Human Immunodeficiency Virus)

The Human Immunodeficiency Virus (HIV) is a lentivirus that targets the immune system, in particular the CD4 cells (also called T cells), which are crucial for the body's ability to fight off infections. HIV over time weakens the immune system, making the body more vulnerable to a variety of opportunistic infections and illnesses that a healthy immune system would typically be able to fend off. HIV is mainly spread via coming into touch with bodily fluids such as blood, semen, vaginal fluids, rectal fluids, and breast milk from an infected individual. Unprotected sexual contact, sharing of needles or syringes among drug users, and transmission from mother to child during childbirth or breastfeeding are the most typical mechanisms of transmission.

People who have HIV infection may have a variety of symptoms in the early stage, often known as acute HIV infection. Fever, exhaustion, rash, sore throat, enlarged lymph nodes, and muscle aches are a few of these symptoms. However, other people might not exhibit any symptoms at all during this stage [7].

HIV infection can proceed to AIDS (acquired immunodeficiency syndrome) a more severe form, if untreated. Due to the profound immunodeficiency that characterizes AIDS, the body is extremely vulnerable to opportunistic infections and some malignancies. The immune system has weakened to the point where even relatively simple infections can now be fatal. Antiretroviral therapy (ART) was created as a result of improvements in HIV/AIDS care. A mixture of drugs is used in ART to limit the spread of the disease, boost immune system performance, and suppress the body's ability to replicate the virus. ART can greatly increase the lifetime of people with HIV and enhance their quality of life, even though treatment cannot cure the virus [8].

Prevention strategies are essential for limiting HIV transmission. These include using condoms during sexual contact, abstaining from sharing needles or syringes, undergoing routine HIV testing, and utilizing pre-exposure prophylaxis (PrEP) for those who are at high risk of contracting the disease. Despite improvements in prevention and treatment, HIV/AIDS continues to be a problem for world health. Combating the effects of HIV on people and communities around the world requires ongoing efforts to increase awareness, encourage testing, and offer access to treatment and education [9].

### Importance of studying HIV and its treatment

The Human Immunodeficiency Virus (HIV) continues to be one of the biggest threats to global health, needing continued study and investigation into its makeup, transmission, and management. It is critical to comprehend the significance of researching HIV and its therapy for a number of reasons [10].

- **Impact on Public Health:** The pandemic that HIV started has claimed millions of lives and changed the course of countless others. It is crucial to have knowledge on HIV transmission, prevention, and therapy in order to stop its spread and lessen its negative effects on public health.
- **Medical Developments:** Research on HIV has sparked major

advances in virology, immunology, genetics, and the creation of antiviral drugs, among other fields.

- HIV research has provided new information that has sparked advancements in other medical specialties [10].
- **Treatment Advances:** Ongoing research has produced anti-retroviral medications (ART) that can successfully suppress the virus, enabling people with HIV to live longer, healthier lives [10]. Ongoing research is necessary to improve these medicines, making them more available, inexpensive, and individualized.
- **Drug Resistance:** HIV's capacity for fast mutation can result in drug resistance, which reduces the efficacy of treatment. Research aids in the discovery and comprehension of these alterations, enabling the creation of novel medications and therapeutic approaches to combat drug-resistant bacteria [10].
- **Prevention Strategies:** Understanding how HIV is transmitted and how it interacts with the immune system is critical for developing effective prevention strategies. This includes education, condom distribution, needle exchange programs, and pre-exposure prophylaxis (PrEP) for high-risk individuals [11].
- **Vaccine Development:** Global Health Equity: Studying HIV highlights health disparities and inequalities, particularly in vulnerable populations. Addressing these disparities is crucial for achieving global health equity and ensuring that everyone, regardless of their background, has access to essential healthcare [11].
- **Social and Psychological Impact:** HIV is not only a medical issue but also a social and psychological challenge. Understanding the psychosocial aspects of living with HIV helps in providing comprehensive care and support for affected individuals and communities.
- **Stigma Reduction:** Education and research play a crucial role in combating the stigma associated with HIV. Accurate information helps dispel myths and misconceptions, leading to increased acceptance and support for those affected by HIV [11].
- **Lessons for Other Diseases:** The study of HIV has provided valuable lessons for addressing other infectious diseases. The collaborative efforts, research networks, and community engagement models developed for HIV research have been used as templates for tackling other health challenges [11].

In conclusion, studying HIV and its treatment is of paramount importance for the advancement of medical knowledge, the improvement of global public health, and the betterment of the lives of individuals living with HIV. The ongoing pursuit of understanding this complex virus has far-reaching implications that extend beyond the realm of virology, touching various aspects of healthcare, society, and human well-being. The review of HIV and its treatment serves as a comprehensive exploration of the multifaceted aspects surrounding this viral infection, encompassing its virological, epidemiological, clinical, social, and global dimensions. This purposeful examination provides valuable insights into the ongoing efforts to combat HIV, improve treatment strategies, and enhance the overall quality of life for those affected. The scope of such a review is broad, touching upon various key areas:

- **Virological Understanding:** The review delves into the intricate mechanisms of HIV's replication, mutation, and interaction with the human immune system. It examines the viral life cycle, identifying potential targets for therapeutic interventions and elucidating the challenges posed by the virus's ability to adapt and evolve [12].
- **Treatment Modalities:** An essential component of the review involves assessing the existing antiretroviral therapies (ART) and investigational treatment options. This encompasses a critical evaluation of their efficacy, safety, dosing regimens, and potential side effects. The scope extends to novel therapeutic approaches, including gene therapies, immune-based interventions, and long-acting drug formulations.
- **Drug Resistance and Management:** Understanding HIV's propensity for developing drug resistance is crucial. The review explores the mechanisms underlying resistance and discusses strategies to monitor, prevent, and manage resistance. It considers the implications of resistance on treatment outcomes and public health efforts.
- **Health Equity:** An examination of health disparities is a critical aspect of the review. It scrutinizes how socioeconomic factors, race, gender, and access to healthcare contribute to unequal HIV outcomes. Strategies to address these disparities and promote health [13].
- **Community Engagement:** The scope includes a discussion of the importance of involving affected communities in research, policy development, and program implementation. Community engagement fosters trust, empowers individuals, and ensures that interventions are culturally sensitive and relevant.

- **Lessons for Future Challenges:** Beyond HIV, the review considers how insights gained from studying this virus can inform the approach to other infectious diseases. It emphasizes the importance of interdisciplinary collaboration and the application of successful research models to tackle emerging health threats.

In essence, the purpose and scope of reviewing HIV and its treatment are to provide a comprehensive understanding of this complex global health challenge. By examining various dimensions, from molecular mechanisms to societal impact, the review informs the development of evidence-based strategies that can effectively combat HIV, improve treatment outcomes, and contribute to the broader field of public health and medical research [14].

## Historical context

### Discovery of HIV and its early impact

The Human Immunodeficiency Virus (HIV) discovery marked a watershed moment in medical history. In the early 1980s, a cluster of rare and severe infections, coupled with an inexplicable collapse of immune function, alerted the medical community to a new and puzzling health threat. The subsequent identification of HIV as the causative agent revolutionized our understanding of infectious diseases and their long-term implications.

During the initial years, HIV's impact was profound and devastating. Medical professionals struggled to comprehend the virus's intricate mechanisms and rapid transmission dynamics. The virus targeted the immune system's CD4 T cells, leading to a progressive breakdown of the body's defense mechanisms. Opportunistic infections and certain cancers began to afflict individuals with compromised immune systems, resulting in unprecedented rates of illness and mortality [15].

Infections that were typically manageable became life-threatening, and entire communities faced the dire consequences of this new epidemic. Fear and uncertainty permeated society as HIV transmission modes were unraveled, primarily through unprotected sexual contact, contaminated blood products, and mother-to-child transmission [16].

Stigmatization and discrimination emerged as unfortunate responses to the epidemic. People living with HIV faced ostracism

and prejudice due to a lack of understanding about the virus's modes of transmission. This environment hindered open discussions about the disease, making prevention and education efforts challenging [16].

The early years of the HIV epidemic also galvanized scientific research and collaboration on an unprecedented scale. The identification of HIV's genetic material and the development of diagnostic tests were pivotal milestones, enabling the accurate detection of the virus and facilitating epidemiological studies [16].

The urgency to find effective treatments led to the development of the first antiretroviral drugs. While these early medications offered limited benefits, they paved the way for more sophisticated treatment strategies that emerged in subsequent years [17]. Moreover, the search for an HIV vaccine gained momentum as researchers and organizations recognized the global significance of curbing the epidemic through preventive measures [17].

In conclusion, the discovery of HIV and its early impact marked a pivotal juncture in the medical and social landscapes. It exposed vulnerabilities in healthcare systems, challenged societal norms, and spurred transformative research endeavors [17]. The lessons learned from these formative years continue to shape our approach to infectious diseases, public health communication, and the imperative of scientific collaboration in the face of emerging health crises [17].

### Initial challenges in understanding the virus and its transmission

The early years of the HIV epidemic were marked by a series of formidable challenges as medical experts and researchers grappled with the complex nature of the virus and its modes of transmission [18]. These challenges presented significant hurdles in unraveling the mysteries of HIV and formulating effective strategies for containment and prevention [18].

- **Unidentified Causative Agent:** In the initial stages, the medical community faced the daunting task of identifying the causative agent behind the emerging epidemic. The elusive nature of the virus, coupled with a lack of advanced diagnostic tools, impeded swift recognition [18].

- **Variable and Nonspecific Symptoms:** HIV presented with a wide range of symptoms that were often nonspecific, making it difficult to diagnose early cases accurately [18]. Symptoms such as fatigue, weight loss, and opportunistic infections were indicative of a compromised immune system but could be attributed to various other conditions [18].
- **Lack of Diagnostic Tests:** The absence of reliable and accessible diagnostic tests hindered timely detection of HIV. The initial tests were cumbersome, expensive, and had limited accuracy, posing challenges for both diagnosing individuals and tracking the epidemic's progression [19].
- **Unknown Transmission Routes:** Deciphering how HIV was transmitted posed a significant challenge. While sexual contact, blood transfusions, and mother-to-child transmission were identified as primary routes, understanding the nuances of transmission dynamics and risk factors required meticulous research [19].
- **Limited Treatment Options:** The absence of specific anti-retroviral therapies during the early years left medical professionals with few options to treat HIV-infected individuals [19]. The available treatments mainly focused on managing opportunistic infections and symptoms rather than targeting the virus itself [19].
- **Research and Resources:** Given the novelty of HIV, research funding and resources were initially limited. Scientists faced challenges in securing financial support and conducting comprehensive studies to unravel the virus's complexities [20].
- **Lack of Regulatory Frameworks:** The absence of regulatory frameworks for clinical trials and drug development in the context of HIV hindered the progress of research and the evaluation of potential treatments [20].
- **Healthcare System Strain:** The sudden emergence of HIV strained healthcare systems globally. Hospitals and medical facilities struggled to provide appropriate care, leading to a heightened demand for specialized medical personnel, treatment facilities, and support services [20].

Despite these challenges, the determination of scientists, healthcare workers, activists, and affected communities eventually led to significant strides in understanding HIV and its transmission [20]. Over time, concerted efforts in research, education, treatment development, and advocacy reshaped the global response to the

epidemic, illustrating the power of collective action in the face of a complex and evolving health crisis [20].

### Incidence and prevalence

According to the recently published India HIV Estimation 2019 report, since the epidemic's peak in 2000, India's estimated adult (15-49-Year-old) HIV prevalence trend has been declining and has stabilized in recent years. In 2019, the estimate for this indicator was 0.17-0.29%, or 0.22%. HIV prevalence was estimated to be 0.24% (0.18-0.32%) among adult males (15-49 years old) and 0.20% (0.15-0.26%) among adult females in the same year [21].

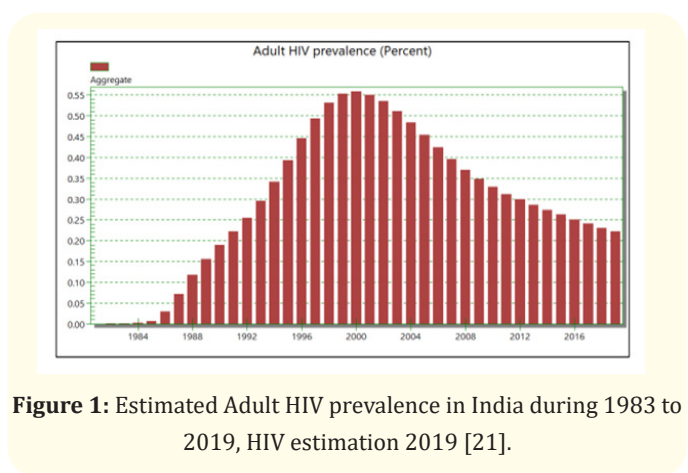


Figure 1: Estimated Adult HIV prevalence in India during 1983 to 2019, HIV estimation 2019 [21].

State/Union Territory	Estimated Prevalence (%)	95% Confidence Interval (%)
Mizoram	2.32	1.85 – 2.84
Nagaland	1.45	1.15 – 1.78
Manipur	1.18	0.97 – 1.46
Andhra Pradesh	0.69	0.54 – 0.89
Meghalaya	0.54	0.46 – 0.63
Telangana	0.49	0.35 – 0.66
Karnataka	0.47	0.37 – 0.59
Delhi	0.41	0.33 – 0.50
Maharashtra	0.36	0.25 – 0.53
Puducherry	0.35	0.20 – 0.58
Goa	0.27	0.19 – 0.46
Punjab	0.27	0.22 – 0.35
Dadra and Nagar Haveli	0.23	0.14 – 0.37
Tamil Nadu	0.23	0.16 – 0.29

Table 1: Adult HIV Prevalence Exceeding the National Average in Select Indian States/Union Territories (2019 Estimates).

In 2019, the estimated number of people living with HIV in the country was 23.49 lakh (17.98 lakh - 30.98 lakh), with an adult (15-49 years old) HIV prevalence of 0.22% (0.17-0.29%). This includes about 79 thousand CLHIV, or 3.4% of the estimated total number of PLHIV. 9.94 lakh women (15 years of age or older) were estimated to be living with HIV, making up approximately 44% of all PLHIV. In 2019, there were 69.22 thousand (37.03 thousand - 121.50 thousand) new cases of HIV infection. This represents a 37% decrease from 2010 and an 86% decline from the peak in 1997. In 2019, the number of deaths related to AIDS was 58.96 thousand (33.61 thousand - 102.16 thousand). This number has decreased by 66% since 2010 and by 78% since reaching its highest point in 2005. An estimate of HIV incidence was 0.05 per 1,000 people [21].

### HIV Transmission and Pathogenesis

#### Modes of transmission (sexual, blood contact, mother-to-child):

- **HIV Transmission:** HIV is primarily transmitted through specific bodily fluids that contain high viral loads, with the most common routes being.
- **Sexual Transmission:** Unprotected sexual intercourse, particularly anal and vaginal, is the most prevalent mode of HIV transmission. The virus can enter the body through mucous membranes and small abrasions, infecting CD4 T cells within the genital and rectal tissues. Through oral sex, which is theoretically feasible if an HIV-positive man's ejaculate gets past an HIV-negative person's oral membrane but is incredibly uncommon. Using syringes or needles on an HIV-positive person [22].
- **Parent-to-Child Transmission:** During pregnancy, childbirth, or breastfeeding, an HIV-positive mother can pass the virus to her unborn child. Antiretroviral therapy (ART) and cesarean deliveries are two effective interventions that can significantly lower the risk of transmission [22].
- **Blood Contact:** Sharing contaminated needles or syringes among intravenous drug users can lead to HIV transmission. Additionally, blood transfusions or organ transplants from infected donors were historically sources of transmission, but stringent screening measures have significantly reduced this risk [22].
- **Occupational Exposure:** Healthcare workers can be exposed to HIV through accidental needlesticks or contact with infected bodily fluids, highlighting the importance of proper safety precautions [22].

Pre-exposure prophylaxis, or PrEP, is a strategy to lower the risk of HIV transmission by taking antiretroviral drugs prior to possible exposure. This method is particularly effective for individuals in high-risk categories.

### HIV pathogenesis

HIV pathogenesis is characterized by a number of complex interactions between the virus and the immune system of the host.

- **Entry:** HIV enters the body by binding to CD4 receptors on the surface of immune cells, primarily CD4 T cells, macrophages, and dendritic cells. The virus further gains entry by binding to coreceptors, most notably CCR5 and CXCR4 [23].
- **Reverse Transcription:** The viral enzyme reverse transcriptase converts the HIV RNA genome into DNA once it has entered the host cell. An additional enzyme known as integrase then incorporates this viral DNA into the genome of the host cell [23].
- **Replication:** The integrated viral DNA directs the host cell's machinery to produce new viral RNA and proteins. These components assemble into new virus particles, which are then released from the host cell through a process called budding [23].
- **Immune Response:** The immune system recognizes the presence of infected cells and produces antibodies to neutralize the virus. However, HIV's high mutation rate allows it to evade immune detection and contributes to the development of diverse viral strains [23].
- **Chronic Inflammation:** HIV infection triggers a chronic state of immune activation and inflammation, contributing to various health complications, including cardiovascular diseases and neurocognitive impairments [23].

Understanding the intricate interplay between HIV transmission and pathogenesis is essential for developing targeted interventions that prevent transmission, delay disease progression, and improve the quality of life for those living with HIV [24]. Advances in this understanding continue to shape the landscape of HIV research, treatment, and prevention strategies [24].

## Pathophysiology

### The viral structure

Viruses can only exist and multiply inside of living cells; they cannot exist or replicate on their own [25]. The structure of viruses is straightforward. Since viruses don't have the complex parts that bacteria or human cells do, HIV is only interested in finding its target and infecting it.

A common characteristic shared by human, bacterial, and viral cells is their genetic material, which has all the information required to create and sustain an organism [25].

This is referred to as deoxyribonucleic acid (DNA) in humans and bacteria, and it is made up of two twisted strands of genetic material. The genetic material found in viruses like HIV is arranged into single strands and is known as ribonucleic acid (RNA) [25].

A capsid, or protein covering, envelops and protects the RNA that is present in a virus. Enzymes that the virus uses to replicate and infect its host are found outside the capsid. An envelope made of glycoproteins envelops these structures, aiding the virus in locating and attaching to its target [25].

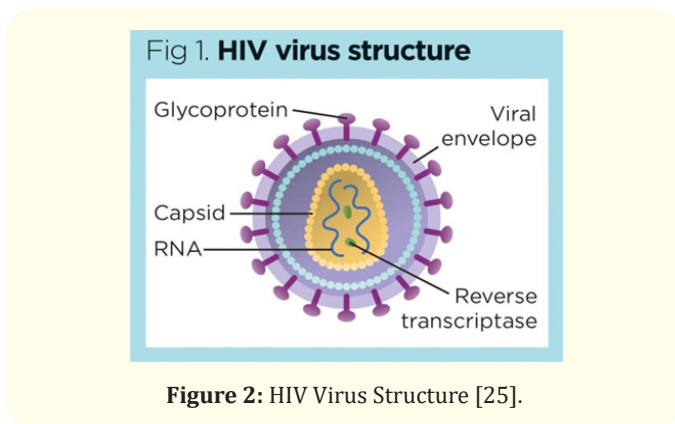


Figure 2: HIV Virus Structure [25].

### Viral targets

HIV specifically targets and infects CD4 "helper" cells, a subset of T-cells. These get their name from the fact that they signal to and enlist the help of other immune cells to combat foreign antigens rather than destroying or neutralizing them.

HIV finds CD4 cells quickly after entering a host's body and infects them [26].

The purpose of CD4 cells is to replicate the virus multiple times; on a daily basis, 10 million to 10 billion new virus cells can be created [26]. After becoming infected, CD4 cells live much shorter lives before being eliminated; their steadily declining quantity within the host leads to immunological failure and increased vulnerability to infection.

These are all targets for HIV medications that interrupt the life-cycle of the virus and inhibit infection and replication. Use of these medications is known as anti-retroviral therapy [26].

### Treatment

Antiretroviral therapy, or ART, is a form of HIV treatment that involves following a doctor's prescription for medication. HIV treatment helps you maintain your health by lowering the amount of HIV in your body [27].

HIV cannot be cured, but it can be managed with medication. Within six months, the majority of people can get the virus under control (Dybul, *et al.* 2002). Other STDs can still spread even after receiving HIV treatment [27].

It is possible to manage HIV infection effectively by combining various medications. Antiretroviral therapy (ART) is the collective term for this mode of treatment. "Highly active antiretroviral therapy," or HAART, is a regimen of at least three medications used in standard antiretroviral therapy [27].

### Antiretroviral therapy (ART)

Classes of antiretroviral drugs (NRTIs, NNRTIs, protease inhibitors, integrase inhibitors, etc.).

Evolution of ART regimens and guidelines [28].

Antiretroviral Therapy (ART) has revolutionized the management of Human Immunodeficiency Virus (HIV) infection since its introduction in the mid-1990s. This groundbreaking approach involves using a combination of medications to suppress viral replication, preserve immune function, and improve the overall quality of life for individuals living with HIV [28]. ART has transformed HIV infection from a potentially fatal illness to a chronic manageable condition, marking one of the most significant achievements in modern medicine [28].

### Principles of ART

Combination Therapy: ART typically involves using a combination of three or more antiretroviral drugs from different classes. This approach, known as highly active antiretroviral therapy (HAART) or the “AIDS cocktail,” targets different stages of the viral life cycle, reducing the likelihood of drug resistance and increasing treatment efficacy [29].

Suppressing Viral Replication: ART aims to reduce the viral load in the bloodstream to undetectable levels [29]. By inhibiting viral replication, the immune system’s CD4 T cells are preserved, leading to improved immune function and a reduction in the risk of opportunistic infections and other HIV-related complications [29].

### Adverse effects of ART

One of the major challenges that patients and physicians face with ART is the incidence of adverse drug reactions (ADR). ADR is defined as “a response to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for modification of physiological function” [30].

The major adverse effects of ART can be grouped into the following categories:

- **Gastrointestinal:** Nausea, diarrhea, vomiting, taste perversion, constipation, dyspepsia, abdominal pain, hepatotoxicity, and pancreatitis [30].
- **Central nervous system:** Headache, vision problems, dizziness, insomnia, paresthesia, pain/numbness/tingling in extremities, peripheral neuropathy, excessive sleep at night, memory problems, loss of olfactory function, and hearing impairment [30].
- **Hematological:** Anemia, bilirubinemia, increased urate, and blood in the urine [30].
- **Psychological:** Anxiety, confusion, depression, nightmares, and delusions [30].
- **Metabolic:** Abnormal fat distribution (lipodystrophy), anorexia, dyspnea, fatigue, lethargy, and weight gain [30].
- **Dermatological:** Skin rash, facial discoloration, and pruritus [30].
- **Musculoskeletal:** Body aches and vague chest pain [30].
- **Miscellaneous:** Hypersensitive reactions, oral ulcerations, fever, and irregular menstrual cycles

- **Restoring Immune Function:** As viral replication is suppressed, CD4 T cell counts tend to rise, indicating immune recovery. This helps individuals regain their ability to fight off infections and diseases [31].
- **Preventing Transmission:** Achieving and maintaining an undetectable viral load through ART greatly reduces the risk of transmitting HIV to sexual partners. This concept is known as “Undetectable = Untransmittable” (U=U) [31].

### Classes of antiretroviral drugs

**Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs):** These drugs inhibit reverse transcriptase, an enzyme required for viral DNA synthesis. They act as faulty building blocks, preventing the virus from replicating accurately [31].

- **Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs):** NNRTIs bind to reverse transcriptase, distorting its shape and inhibiting its function. These drugs are effective against specific strains of the virus [31].
- **Protease Inhibitors (PIs):** Protease is an enzyme that cleaves viral proteins, allowing them to mature into infectious particles. PIs block this process, preventing the formation of functional viral particles [31].
- **Chemokine Receptor 5 Antagonist**
- This group of drugs prevents the infection by blocking the chemokine receptor 5 (CCR5) antagonist receptor present on CD4 cells. In the absence of vacant CCR5 receptors, HIV fails to gain entry and infect the cell. Maraviroc is an example of a CCR5 antagonist used in HIV treatment [32].

### Integrase strand transfer inhibitors

Strand transfer inhibitors prevent the integration of viral DNA into the host genome of CD4 cells by an integrase enzyme. Blocking integrase prevents HIV from replicating. Raltegravir, elvitegravir, and dolutegravir are some medications in this category [32].

### Entry inhibitors

These drugs block the virus from entering host cells by interfering with viral attachment or fusion [32].

### Classes

The antiviral agents available against viruses can be classified as: (a) nucleoside analogs- Nucleoside/nucleotide reverse transcriptase inhibitors and non-nucleoside reverse transcriptase



inhibitors (b) protease inhibitors (c) integrase inhibitors (d) interferons fusion inhibitors, capsid inhibitors, gp120 attachment inhibitors, ccR5 antagonist [33].

**Nucleoside analogs**

Nucleoside analogs act by inhibiting the enzyme viral polymerase which are generally activated by phosphorylation by cellular or viral kinases.

Drug Name	Mechanism of Action	Uses	Side Effects
Acyclovir	Inhibits viral DNA synthesis by acting as a faulty building block	Treats chickenpox, shingles, cold sores, and genital herpes	Vomiting, diarrhea, headache, nausea, lightheadedness, drowsiness, kidney problems, mental/mood swings, shaky movements, difficulty speaking, allergic reactions [33].
Valacyclovir	Prodrug of acyclovir, converted to acyclovir in the body	Treats herpes zoster, cold sores, genital herpes, and chickenpox	Confusion, hostility, shaky feeling, speech difficulties, hallucinations, seizures [33].
Ganciclovir	Inhibits viral DNA synthesis	Treats CMV retinitis, CMV pneumonitis, and prevents CMV infection in transplant patients	Anemia, thrombocytopenia, fever, nausea, vomiting, diarrhea, abdominal pain, anorexia, headache, confusion, hallucinations, seizures, pain, phlebitis, perspiration, rash, itching, elevated serum creatinine, and blood urea concentration [33].
Zalcitabine	Inhibits reverse transcriptase	Treats HIV infection	Headache, fatigue, nausea, vomiting, diarrhea, constipation, stomach pain [33].
Lamivudine	Inhibits reverse transcriptase	Treats HIV-1 and hepatitis B	Headache, lightheadedness, nausea, diarrhea, difficulty sleeping [33].
Abacavir	Inhibits reverse transcriptase	Treats HIV infection	Fever, rash, nausea, vomiting, diarrhea, stomach pain, general illness, fatigue, body aches, sore throat, cough, dyspnea, mitochondrial toxicity [33].
Emtricitabine (FTC)	Inhibits reverse transcriptase	Treats HIV in combination with other antiretrovirals	Headache, dizziness, nausea, vomiting, diarrhea, fatigue, skin rash, changes in skin color [33].
Tenofovir alafenamide fumarate (TAF)	Inhibits reverse transcriptase	Treats HIV and chronic hepatitis B	Nausea, vomiting, diarrhea, headache, fatigue, abdominal pain, decreased bone mineral density [33].
Tenofovir disoproxil fumarate (TDF)	Inhibits reverse transcriptase	Treats HIV and chronic hepatitis B	Nausea, vomiting, diarrhea, headache, fatigue, abdominal pain, decreased bone mineral density, kidney problems [33].
Zidovudine (AZT)	Inhibits reverse transcriptase	Treats HIV infection	Nausea, vomiting, headache, fatigue, anemia, muscle weakness, neuropathy [33].

**Table 2:** Non-Nucleoside reverse transcriptase inhibitors.

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs).

NNRTIs represent a crucial class of antiretroviral drugs used to manage HIV infection.

These agents function by directly targeting and binding to the reverse transcriptase enzyme, a viral protein essential for HIV replication. By inhibiting reverse transcriptase, NNRTIs disrupt the conversion of viral RNA into DNA, effectively preventing the virus from integrating into the host cell’s genome and replicating.

NNRTIs are known for their potency and ability to achieve rapid viral suppression. They are often used in combination with other antiretroviral drugs as part of highly active antiretroviral therapy (HAART) to effectively control HIV infection and reduce the risk of disease progression. However, NNRTIs can be susceptible to the development of drug resistance, highlighting the importance of adherence to prescribed treatment regimens and the potential need for combination therapy with other antiretroviral classes [34].

Drug Name	Mechanism of Action	Uses	Side Effects
Nevirapine	Inhibits reverse transcriptase by binding to a hydrophobic pocket near the active site	Treats HIV-1 infection in adults and children	Rash, hepatotoxicity, Stevens-Johnson syndrome, elevated liver enzymes, fatigue, headache, nausea [34]
Efavirenz	Inhibits reverse transcriptase by binding to a hydrophobic pocket near the active site	Treats HIV-1 infection in adults and children	Rash, central nervous system effects (dizziness, insomnia, abnormal dreams), psychiatric symptoms, elevated liver enzymes [34].
Etravirine	Inhibits reverse transcriptase by binding to a hydrophobic pocket near the active site; active against many NNRTI-resistant HIV strains	Treats HIV-1 infection in adults who have experienced virologic failure with other NNRTIs	Rash, nausea, diarrhea, elevated liver enzymes, peripheral neuropathy [34].
Rilpivirine	Inhibits reverse transcriptase by binding to a hydrophobic pocket near the active site	Treats HIV-1 infection in adults	Rash, headache, depression, insomnia, elevated liver enzymes [34]
Doravirine	Inhibits reverse transcriptase by binding to a hydrophobic pocket near the active site	Treats HIV-1 infection in adults	Headache, nausea, diarrhea, fatigue, elevated liver enzymes [34].

**Table 3:** Non-Nucleoside Reverse Transcriptase Inhibitors, mechanism, uses and side effects.

**Protease Inhibitors:**

These are a broad class of agents that are widely used to prevent and treat HIV infections and acquired immunodeficiency syndrome. They bind to the catalytic HIV protease thus preventing the cleavage of viral polyprotein precursor into mature functional protein which is a requisite for viral replication. The most common protease inhibitors are ritonavir, indinavir, nelfinavir, saquinavir, amprenavir, atazanavir, fosamprenavir, tipranavir, darunavir [35].

**Integrase inhibitors**

INSTIs are a relatively newer class of antiretroviral drugs that have become a mainstay in HIV treatment due to their high efficacy, tolerability, and barrier to resistance. These medications target the HIV integrase enzyme, a critical viral protein responsible for inserting the viral DNA into the host cell’s genetic material. By inhibiting this step in the viral lifecycle, INSTIs effectively block HIV replication and reduce the viral load within the body [36].

Drug Name	Mechanism of Action	Uses	Side Effects
Ritonavir	Inhibits HIV protease	Treats HIV-1 and AIDS, boosts other PIs, part of COVID-19 treatment with Nirmatrelvir	Nausea, vomiting, diarrhea, abdominal pain, taste disturbances, hyperlipidemia, hepatotoxicity, drug interactions [35].
Indinavir	Inhibits HIV protease	Treats HIV-1 infection in combination with other antiretrovirals	Kidney stones, nausea, vomiting, diarrhea, headache, fatigue, hyperglycemia, hyperlipidemia, fat redistribution [35]
Nelfinavir	Inhibits HIV protease	Treats HIV-1 and HIV-2 infection	Diarrhea, nausea, vomiting, abdominal pain, asthenia, rash, hyperlipidemia, increased bleeding in people with hemophilia [35].
Atazanavir	Inhibits HIV protease	Treats HIV-1 infection	Nausea, vomiting, diarrhea, headache, abdominal pain, jaundice, hyperbilirubinemia, rash, prolonged PR interval [35].
Darunavir	Inhibits HIV protease	Treats HIV-1 infection, including drug-resistant strains	Nausea, vomiting, diarrhea, rash, headache, fatigue, increased liver enzymes, drug interactions [35].
Lopinavir/ritonavir	Lopinavir inhibits HIV protease, ritonavir boosts lopinavir levels	Treats HIV-1 infection	Nausea, vomiting, diarrhea, abdominal pain, headache, fatigue, hyperlipidemia, pancreatitis, hepatitis [35].
Fosamprenavir	Prodrug of amprenavir, inhibits HIV protease	Treats HIV-1 infection	Nausea, vomiting, diarrhea, rash, headache, fatigue, hyperlipidemia, increased liver enzymes [35].
Tipranavir	Inhibits HIV protease	Treats HIV-1 infection in adults with drug-resistant virus	Nausea, vomiting, diarrhea, rash, headache, fatigue, hepatotoxicity, intracranial hemorrhage, increased triglycerides [35].

**Table 4:** HIV protease inhibitors.

INSTIs are often preferred for first-line HIV treatment due to their favorable side effect profile and minimal interactions with other medications. However, like all medications.

### Chemokine receptor antagonist

Chemokine receptor antagonists are a specialized class of antiretroviral medications that target specific receptors on immune

Drug Name	Mechanism of Action	Uses	Side Effects
Bictegravir	Inhibits HIV-1 integrase	Treats HIV-1 and HIV-2 infection in combination with emtricitabine and tenofovir alafenamide (as part of a single-tablet regimen)	Nausea, diarrhea, headache, fatigue, insomnia [36].
Dolutegravir	Inhibits HIV-1 integrase	Treats HIV-1 infection in adults and children; also used in post-exposure prophylaxis (PEP)	Headache, insomnia, fatigue, nausea, diarrhea, rash, hypersensitivity reactions (rare) [36]
Elvitegravir	Inhibits HIV-1 integrase	Treats HIV-1 infection in combination with cobicistat, emtricitabine, and tenofovir alafenamide or disoproxil fumarate (as part of a single-tablet regimen)	Nausea, diarrhea, headache, fatigue, insomnia, rash [36].
Raltegravir	Inhibits HIV-1 integrase	Treats HIV-1 infection	Nausea, diarrhea, headache, fatigue, insomnia, myopathy, rhabdomyolysis (rare), increased risk of certain cancers (rare) [36].
Cabotegravir (long-acting injectable)	Inhibits HIV-1 integrase	Treats HIV-1 infection in combination with long-acting injectable Rilpivirine (administered every 1 or 2 months)	Injection site reactions, fever, fatigue, headache, nausea, diarrhea, depression, insomnia [36].

**Table 5:** Integrase inhibitors.

cells, namely CCR5 and CXCR4. These receptors serve as entry points for the human immunodeficiency virus (HIV) to infect cells. By blocking these receptors, chemokine antagonists prevent HIV from attaching to and entering immune cells, thus inhibiting viral replication and slowing disease progression.

CCR5 antagonists, like maraviroc, specifically target the CCR5 co-receptor, which is primarily used by HIV during the early stages of infection. CXCR4 antagonists, such as plerixafor, block the CXCR4 co-receptor, which HIV may utilize in later stages or in certain individuals. The use of chemokine antagonists represents a targeted therapeutic approach to HIV management, aiming to disrupt the viral entry process and protect the immune system [37].

### Challenges and Considerations:

- **Adherence:** ART requires strict adherence to the medication regimen. Skipping doses or not taking medications consistently can lead to viral resistance and treatment failure [38].
- **Drug Interactions:** Some antiretroviral drugs interact with other medications, affecting their efficacy or leading to unwanted side effects [38].

- **Side Effects:** ART can cause side effects such as nausea, fatigue, diarrhea, and lipid abnormalities. However, newer drug formulations aim to minimize these effects [38].
- **Resistance:** Prolonged viral exposure can lead to drug-resistant strains of HIV. Regular viral load monitoring helps detect resistance early and guide treatment adjustments [38].
- **Access and Affordability:** While ART has transformed HIV care in many parts of the world, ensuring access to treatment remains a challenge in resource-limited settings [38].

### Impact and future directions

ART has significantly improved the life expectancy and quality of life for individuals living with HIV. People on effective treatment can lead healthy lives and have near-normal life expectancies [39]. Ongoing research focuses on developing more convenient drug regimens (such as long-acting formulations), reducing side effects, addressing treatment disparities, and exploring strategies towards an HIV cure or functional cure [39].

In conclusion, Antiretroviral Therapy represents a remarkable milestone in HIV management, demonstrating the power of scientific innovation and multidisciplinary collaboration [39]. While

Drug Name	Receptor Target	Mechanism of Action	Uses	Side Effects
Maraviroc	CCR5	Blocks interaction between HIV-1 gp120 and CCR5, preventing viral entry	Treats CCR5-tropic HIV-1 infection in combination with other antiretrovirals	Cough, dizziness, fever, rash, abdominal pain, upper respiratory tract infection, musculoskeletal symptoms, liver problems (rare) [37]
Plerixafor	CXCR4	Blocks binding of SDF-1α to CXCR4, mobilizing stem cells from bone marrow	Mobilizes hematopoietic stem cells for transplantation, treats certain types of lymphoma and multiple myeloma	Diarrhea, nausea, injection site reactions, dizziness, headache, fatigue, insomnia, changes in blood tests, allergic reactions (rare) [37].
Vicriviroc	CCR5	Blocks interaction between HIV-1 gp120 and CCR5, preventing viral entry	Investigational drug for the treatment of HIV-1 infection (not currently approved)	Headache, dizziness, fatigue, nausea, diarrhea, cough, upper respiratory tract infection [37].
Cenicriviroc	CCR5 and CCR2	Blocks interaction of HIV-1 gp120 with CCR5 and CCR2, preventing viral entry	Investigational drug for the treatment of HIV-1 infection and non-alcoholic steatohepatitis (NASH) (not currently approved)	Headache, fatigue, nausea, diarrhea, cough, upper respiratory tract infection, increased liver enzymes [37].

**Table 6:** Chemokine Receptor Antagonist.

challenges remain, ART continues to play a pivotal role in transforming HIV from a once-debilitating disease into a chronic condition that can be managed effectively with proper medical care and adherence to treatment protocols.

### Challenges in HIV Treatment

- Drug resistance and its mechanisms
- Adherence to ART and its implications
- Access to treatment, especially in resource-limited settings
- Side effects and long-term consequences of ART
- Challenges in HIV Treatment: Navigating Complexities for Optimal Care [40].
- Despite significant advancements in antiretroviral therapy (ART) and the transformation of HIV from a once-debilitating disease into a manageable chronic condition, several challenges persist in the realm of HIV treatment [40]. These challenges encompass medical, social, economic, and systemic factors that impact both individuals living with HIV and the broader healthcare landscape [40].

### Adherence to treatment

Ensuring consistent and proper adherence to ART regimens is crucial for maintaining viral suppression and preventing drug resistance [40]. Factors such as pill burden, side effects, and complex dosing schedules can make adherence difficult, leading to treatment failure and increased health risks [40].

### Access and affordability

While ART has become more accessible in many parts of the world, disparities in access persist, particularly in low- and middle-income countries. Economic barriers, lack of healthcare infrastructure, and challenges in drug distribution hinder widespread availability of treatment [40].

### Mental health and well-being

Living with a chronic condition like HIV can take a toll on mental health. Depression, anxiety, and stigma-related stress can impact treatment adherence and overall well-being [41].

### Comorbidities

People living with HIV are at an increased risk of certain comorbidities, such as cardiovascular disease, diabetes, and certain cancers. Treating these conditions alongside HIV requires a comprehensive and coordinated approach [41].

### Aging and long-term health

As individuals with HIV live longer due to effective treatment, addressing age-related health concerns becomes critical. Issues related to bone health, cognitive function, and other age-associated conditions require attention [41].

### Limited cure

While ART effectively suppresses viral replication, it does not cure HIV. Efforts to develop a complete cure or a functional cure

(where the virus is suppressed without continuous treatment) remain ongoing but face complex challenges related to viral reservoirs and immune responses [41].

### Pediatric and adolescent care

Children and adolescents living with HIV require specialized care and tailored treatment approaches. Pediatric formulations, adherence support, and psychosocial considerations are vital in this population [42].

### Drug interactions and long-term effects

ART can interact with other medications, leading to potential complications. Long-term effects of certain antiretroviral drugs, including impacts on organ health and metabolic profiles, require ongoing research and management [42].

### Global health disparities

HIV disproportionately affects marginalized populations, including LGBTQ+ individuals, people of color, and those living in poverty. Addressing disparities in healthcare access, education, and prevention efforts is essential.

- **Evolving Viral Strains:** HIV's ability to mutate and evolve presents ongoing challenges in treatment and vaccine development. New strains of the virus may have different drug resistance patterns and treatment responses [42].
- **Treatment Fatigue:** Long-term engagement with healthcare, frequent medical appointments, and adherence can lead to treatment fatigue, where individuals may become disillusioned or overwhelmed by the demands of managing their condition [42].

Addressing these challenges requires a multifaceted approach that includes not only medical interventions but also social support, education, policy changes, and advocacy. Collaborative efforts between healthcare providers, researchers, policymakers, and affected communities are essential to overcoming these hurdles and ensuring that individuals living with HIV receive the comprehensive care that they deserve [42].

### Emerging therapies and research

- Novel drug development and approaches
- Functional or sterilizing cure research
- Gene therapy and genetic editing for HIV treatment

- Immunotherapies and vaccines in HIV treatment
- Emerging Therapies and Research in HIV Treatment: Pioneering the Future of Care
- The field of HIV research and treatment continues to evolve rapidly, with ongoing efforts aimed at improving existing therapies, exploring novel treatment modalities, and ultimately working towards an HIV cure. Emerging therapies and research initiatives hold the potential to reshape the landscape of HIV management and contribute to the global goal of ending the HIV epidemic [43].

### Long-acting therapies

Long-acting antiretroviral therapies have gained significant attention for their potential to improve adherence and simplify treatment regimens [43]. Injectable formulations that require administration every few months offer convenience and may enhance treatment outcomes [43].

- **Gene Therapies:** Gene editing technologies like CRISPR-Cas9 hold promise in HIV research. They offer the potential to modify a patient's own cells, making them resistant to HIV infection [59]. While still in experimental stages, this approach could revolutionize HIV treatment and prevention.
- **Broadly Neutralizing Antibodies (bNAbs):** bNAbs are naturally occurring antibodies that can neutralize a wide range of HIV strains (Mascola and Haynes, 2013). Research into developing and using bNAbs for both treatment and prevention is advancing, offering an alternative to traditional antiretroviral drugs [43].
- **Immune-Based Therapies:** Boosting the immune system's response to HIV is an area of active investigation. Therapies that enhance immune surveillance and stimulate the body's ability to control viral replication are being explored [43].
- **HIV Cure Strategies:** Research efforts are directed towards achieving an HIV cure or functional cure. Strategies include targeting viral reservoirs (cells where HIV lies dormant), using latency-reversing agents, and harnessing the immune system to clear infected cells [43].
- **Treatment Simplification:** Developing regimens with fewer pills, reduced side effects, and less frequent dosing remains a priority. Simplified treatment options can improve adherence and overall quality of life [44].

Personalized Medicine: Advances in understanding viral genetics and host factors are driving the exploration of personalized

treatment approaches. Tailoring treatments to an individual's genetic profile and immune response may optimize outcomes [44].

### Digital health and telemedicine

Digital tools, such as mobile apps and telemedicine platforms, are being leveraged to enhance treatment adherence, provide real-time support, and improve patient engagement [44].

- **Community Involvement and Engagement:** Including affected communities in research, clinical trials, and decision-making ensures that interventions are relevant, culturally sensitive, and responsive to their needs [44].
- **Microbicides and Vaginal Rings:** Research into microbicides (topical agents) and vaginal rings for HIV prevention continues. These methods empower individuals, particularly women, with additional tools to protect themselves from infection [44].
- **Targeting Resurgence of Latent Virus:** Novel approaches are being explored to reactivate and target latent HIV reservoirs, with the aim of reducing the size of the viral reservoir and potentially achieving sustained viral remission [44].

As these emerging therapies and research initiatives progress, it's important to approach them with careful consideration of safety, efficacy, ethical concerns, and equity in access.

Collaborative efforts between researchers, healthcare providers, policymakers, and affected communities are pivotal in driving innovation, translating research findings into clinical practice, and ultimately advancing the goal of ending the HIV epidemic.

### Co-Infections and Comorbidities

- Impact of HIV on other health conditions (tuberculosis, hepatitis, cardiovascular diseases, etc.)
- Co-infection of HIV and tuberculosis: HIV weakens the immune system, increasing susceptibility to TB. HIV accelerates TB progression, complicates diagnosis, and raises mortality risks.
- Challenges include accurate diagnosis, potential drug interactions in treatment, and the need for integrated care [45].
- Co-infection of HIV and hepatitis (hepatitis B (HBV) and hepatitis C (HCV)): Co-infected individuals may experience accelerated liver disease progression, higher rates of liver-related complications, and increased mortality [45].

- Challenges include accelerated liver disease, higher mortality rates, and potential drug interactions in treatment. Managing co-infection requires integrated care, addressing both infections simultaneously [45]. Preventive measures, such as vaccination, are vital. Overcoming challenges involves improving testing accessibility, developing tailored treatment regimens [45].
- Co-infection of HIV and cardiovascular diseases (CVD): People with HIV may face an elevated risk of cardiovascular problems, potentially due to chronic inflammation and the effects of antiretroviral medications [45].
- Challenges include early onset of CVD, underdiagnosis, and the need for tailored prevention and treatment approaches. Addressing these challenges involves integrating cardiovascular risk assessment into HIV care, promoting healthy lifestyles, and managing potential drug interactions [46].
- Co-infection of HIV and Human papillomavirus (HPV): The simultaneous occurrence of HIV and human papillomavirus (HPV) involves a complex interplay. HIV-induced immune compromise heightens vulnerability to HPV, fostering persistent infections and elevating the risk of HPV-related cancers.
- Challenges encompass an increased incidence of HPV-related cancers, accelerated disease progression, and difficulties in HPV prevention and treatment. Managing co-infection necessitates an integrated healthcare approach, incorporating regular screenings for HPV-related cancers, HPV vaccination, and optimizing HIV management to bolster the immune response against HPV [46].

### Psychological and social aspects

#### Mental health challenges among HIV-positive individuals

The heightened focus on psychological and psychiatric issues related to HIV infection in the past decade stems from the profound emotional repercussions of the disease, influencing various facets of an individual's life, including personal, sexual, occupational, and social dimensions. Beyond the evident impact on mental health, intricate connections exist between HIV infection and psychiatric disorders, necessitating a nuanced exploration of their interplay [47]. Numerous studies highlight higher rates of mental health disorders among people living with HIV compared to the general population. In a US multisite study (2800+ participants), 36% had major depression, and 15.8% had generalized anxiety disorder, significantly exceeding rates in the general population (6.7% and 2.1%, respec-

tively). In Ontario, Canada, electronic records revealed 41% of HIV-positive individuals with mental health conditions, contrasting with 22% in non-HIV infected adults. A study in India found 59% of people living with HIV showing signs of major depression, emphasizing the global impact of this issue.

Psychiatric disorders associated with HIV [47].

### AIDS phobia

Early reports highlight HIV/AIDS-related fears, especially among the “worried well” in the late ‘80s, primarily seen in homosexual men and intravenous drug users. Anxiety disorders, panic, hypochondriacal beliefs, and obsessive-compulsive disorders are linked to HIV. Heterosexuals in India with risky behavior also exhibit AIDS-related phobias, often associated with misinformation, inadequate knowledge, and an anxious temperament [47].

### Bereavement and grief

The severity of HIV/AIDS leads to bereavement, impacting mental health. Homosexual men with AIDS witnessing multiple deaths experience recurrent bereavement episodes [48]. Symptoms, such as sadness and insomnia, overlap with major depression, but survivor guilt, hostility, and preoccupation with images of the deceased differentiate [48]. If bereavement persists for over two months with functional impairment, a major depressive episode may be diagnosed. Unresolved grief, often due to stigma and incomplete funeral rituals in HIV-related deaths, poses a risk for family grief, especially in India and Africa [48]. Further research is needed for culturally sensitive management.

### Anxiety disorders

Throughout HIV infection, anxiety disorders may range from 2% to 38%, with prevalence increasing as the illness progresses. A South Indian study on 51 seropositive individuals found 36% with anxiety disorders, mainly generalized anxiety disorder. Factors contributing to anxiety included pain, alcohol abuse, poor family support, and spousal AIDS presence, accounting for 57% of the variance [48]. Higher rates compared to Western studies may be attributed to physical suffering, cultural factors, and limited healthcare access. The study assessed individuals soon after HIV revelation, potentially influencing higher anxiety incidence.

### Depression in HIV

Depression is prevalent in HIV-infected individuals, with rates ranging from 5% to 25% or higher. A South Indian study revealed

40% suffering from syndromal depression. Of those with depressive symptoms, 90% also had prominent anxiety, meeting criteria for generalized anxiety disorder [48]. Among depressed individuals, 20% expressed death wishes, 12% reported occasional suicidal ideations, and 6% persistent suicidal ideations. Notably, suicide attempts were linked to a past history of psychiatric illness.

### PTSD in HIV

Some individuals facing AIDS-related multiple losses experience post-traumatic stress disorders. HIV-positive women often exhibit a higher prevalence of PTSD symptoms. When evaluating anxiety in HIV-infected individuals, consider various medical conditions presenting with anxiety symptoms. Medications used for HIV/AIDS treatment may have anxiety as a possible side effect. Additionally, assess the impact of both prescribed and recreational psychoactive substances on anxiety [49].

Stigma and discrimination associated with HIV.

Efforts to address HIV-related stigma and discrimination are critical for creating a more compassionate and inclusive society [49].

### Social stigma

This may include fear of being misunderstood, myths and misconceptions etc. Fear and misunderstanding surrounding HIV often arise from a pervasive lack of knowledge about the virus’s transmission. Myths and misconceptions about casual transmission or everyday contact can lead to an unwarranted sense of fear, resulting in social exclusion and strained relationships [49]. Moreover, the stigma associated with HIV is exacerbated by the phenomenon of blame and judgment. Individuals with HIV may find themselves unfairly held responsible for their condition, as others make assumptions about their lifestyle or behaviors [49]. By challenging stereotypes and promoting accurate information, societies can work towards creating an environment that supports those affected by HIV without perpetuating fear, blame, or judgment [49].

### Isolation and rejection

Social exclusion is a distressing consequence, as those with HIV may encounter isolation and exclusion from their communities, friends, and even family members due to unfounded fears of transmission. This fear, often rooted in misinformation, can lead to a pervasive sense of alienation, exacerbating the emotional burden

borne by those already dealing with a complex health condition [49]. To address these issues, it is essential to foster open and non-judgmental conversations within communities, emphasizing accurate information about HIV transmission [49].

### Employment discrimination

Stigmatization in the workplace is a concerning reality for people living with HIV, as they often encounter discrimination that goes beyond the professional realm and infiltrates their personal lives [50]. Individuals with HIV may face employment challenges, including the denial of job opportunities, unfair treatment, or even termination, all stemming from misconceptions about HIV transmission [50]. Unfair treatment or termination based on HIV status perpetuates the broader issue of workplace discrimination. Legal protections and anti-discrimination policies must be robustly enforced to ensure that individuals living with HIV are not unfairly treated in the workplace [50].

### Family dynamics

Family rejection upon disclosure of one's HIV status is a deeply distressing consequence that can strain relationships and inflict emotional distress on individuals. The revelation of an HIV-positive status may trigger unfounded fears and misconceptions within families, leading to a sense of isolation for the individual affected [51]. Family education programs that focus on dispelling myths about HIV transmission, providing accurate information, and fostering empathy are essential. Counseling services can help families navigate the emotional challenges associated with a member's HIV-positive status, promoting open communication and understanding [51].

### Community attitudes

The perpetuation of stigma through gossip and rumors within communities poses a significant challenge, contributing to a hostile environment for individuals living with HIV [51]. The spread of misinformation, often fueled by fear and misunderstanding, can lead to the stigmatization of those with HIV, creating a climate of judgment and exclusion. Public awareness campaigns can play a crucial role in dispelling myths about HIV, fostering understanding, and challenging stigmatizing narratives [51]. By fostering a culture of openness, understanding, and support within communities, it is possible to counteract the negative impact of gossip and rumors, ultimately contributing to a more inclusive and compassionate environment for individuals living with HIV [51].

## Global Response to HIV Epidemic

### Overview of international efforts to combat HIV/AIDS

In the fight against HIV/AIDS, prevention of HIV infection and increasing access to antiretroviral treatment for AIDS patients are critical. Encouraging people to effect change at the individual and group levels is necessary for sustainable endeavors [52]. The spread of HIV/AIDS has been halted in a number of places, including Europe, Australia, Senegal, Uganda, Brazil, Thailand, and North America. These efforts have been achieved through a variety of preventative measures, such as behavior modification, health education, and the creation of environments that support self-defense. The initiatives include blood safety programs, HIV testing, counseling, reducing mother-to-child transmission, condom promotion, needle exchange, and treatment of STDs. To address areas with high HIV/AIDS prevalence, USAID and Development Alternatives launched pilot projects in Zimbabwe utilizing micro-enterprise and microfinance programs.

Through a variety of organizations, AIDS activists in the US have worked together to change public opinion, lessen stigma and discrimination, and prioritize HIV/AIDS-related issues. They have also lobbied for their interests, especially AIDS treatment, in public policy decisions [52].

### Role of organizations like UNAIDS and WHO Successes, setbacks, and lessons learned

Numerous nongovernmental organizations (NGOs), foundations, and key partners play pivotal roles in the global response to HIV and AIDS. These entities contribute significantly to prevention, treatment, and support initiatives worldwide, working collaboratively to address the multifaceted challenges posed by the HIV/AIDS pandemic [52]. Their efforts encompass a range of activities, including funding research, implementing prevention strategies, providing medical assistance, supporting affected communities, and advocating for policy changes to enhance the overall response to HIV/AIDS on a global scale.

### The global fund

The Global Fund is a cooperative effort that was started in 2002 with the goal of accelerating the end of the AIDS, TB, and malaria epidemics. This global organization addresses underlying injustices, strengthens health systems in more than 100 countries, and mobilizes and allots over US\$4 billion yearly to combat these in-



fectious diseases. Specifically, the Global Fund contributes 30% of global financing for HIV programs, with a substantial investment of \$24.2 billion in HIV/AIDS prevention and treatment programs by June 2022. Since its inception, the Global Fund partnership's health programs have saved an impressive 59 million lives. Notably, the organization's investments have experienced significant growth, as evidenced by a 22% increase in HIV prevention services in 2022 compared to the previous year. COVID-19 has represented a significant setback, a critical disruption across various sectors. Despite strides in programmatic outcomes after the COVID-19 pandemic, they are insufficient to align with the trajectory needed for achieving the Sustainable Development Goal 3 (SDG 3) target of eliminating AIDS, TB, and malaria by 2030 [53].

### International AIDS society

The International AIDS Society (IAS), representing HIV professionals in over 170 countries, is the largest association in its field. The International AIDS Society stands as the foremost independent association of HIV professionals globally, boasting a membership exceeding 16,000 individuals from over 196 countries. These dedicated members operate at various tiers of the global response to AIDS, representing diverse disciplines such as research, clinical practice, nursing, laboratory technology, education, social services, healthcare, advocacy, law, media, and policy planning. This inclusive network demonstrates the International AIDS Society's comprehensive and multidisciplinary approach to addressing the issues related to HIV/AIDS. Renowned conferences like the International AIDS Conference, the HIV Research for Prevention Conference, and the IAS Conference on HIV Science are organized by it. The IAS has formed a Commission on The Future of the HIV Response and Global Health in partnership with The Lancet [53].

### UNAIDS

UNAIDS serves as the vanguard in the worldwide endeavor to eradicate AIDS as a public health threat by 2030, aligning with the Sustainable Development Goals. Over the past 35 years, amidst the global HIV pandemic that has affected 78 million individuals and claimed 35 million lives, UNAIDS has played a pivotal role since its inception in 1996. Functioning as a catalyst for global, regional, national, and local efforts, UNAIDS has fostered leadership, innovation, and partnerships to propel HIV towards history. As a dynamic problem-solver, UNAIDS prioritizes the inclusion of people living with HIV and those affected by the virus in decision-making processes. This approach places them at the forefront of designing, de-

livering, and monitoring the AIDS response. UNAIDS not only charts pathways for countries and communities to accelerate progress through its Fast-Track initiative but also advocates fearlessly for addressing legal and policy barriers hindering effective responses to the AIDS epidemic. The Global Alliance to End AIDS in Children, the Global HIV Prevention Coalition, the Education Plus Initiative, and the Global Partnership to Eliminate Stigma and Discrimination are among the major focus areas on which UNAIDS focuses its efforts. These strategic initiatives underscore UNAIDS' commitment to education, fostering global alliances to eradicate AIDS in children, collaborative efforts in HIV prevention, and dedicated partnerships aimed at eliminating the stigma and discrimination associated with HIV. Through these targeted focus areas, UNAIDS aims to address diverse aspects of the HIV/AIDS response and create a comprehensive and impactful approach toward its ultimate goal of ending the epidemic by 2030 [54].

### World health organization

The World Health Organization (WHO), a vital United Nations agency, serves as a bridge connecting nations, partners, and individuals. Its overarching mission is to promote global health, ensure global safety, and support the vulnerable, working towards enabling everyone to achieve the highest level of health [55]. Within WHO, the Department of Global HIV, Hepatitis, and Sexually Transmitted Infections Programmes plays a crucial role in addressing and managing these specific health challenges on a worldwide scale. As of the end of 2022, approximately 39.0 million individuals were living with HIV globally, with two-thirds, or 25.6 million, located in the WHO African Region. In the same year, 630,000 people succumbed to HIV-related causes, while 1.3 million acquired the virus. While there is no cure for HIV, effective prevention, diagnosis, and treatment, including care for opportunistic infections, have transformed HIV into a manageable chronic health condition, enabling individuals to lead long and healthy lives. Global health organizations, such as WHO, the Global Fund, and UNAIDS, align their strategies with SDG target 3.3 to end the HIV epidemic by 2030. Their collective aim for 2025 is that 95% of all people living with HIV should be diagnosed, 95% of those diagnosed should receive life-saving antiretroviral treatment (ART), and 95% of those on treatment should achieve a suppressed viral load, benefiting both individual health and reducing onward transmission. In 2022, these percentages were 86%, 89%, and 93%, respectively [55]. These statistics provide insights into the progress made and areas that require intensified efforts to achieve the ambitious 2030 goal.

The nonprofit Kaiser Family Foundation (KFF) is committed to addressing domestic health concerns and US participation in international health policy. In particular, providing current data and information about the U.S. role in global health is a key component of KFF's work on global health policy [55]. With a focus on important issues that are important to journalists, non-governmental organizations, policymakers, and other stakeholders in the global health arena, this initiative seeks to provide a comprehensive understanding of the U.S. global health policy landscape. The largest HIV testing partnership in the United States was formed in 2011 by KFF's Greater Than HIV and Walgreens. By collaborating with community organizations and health departments, this productive partnership transcends conventional boundaries. Together, they have facilitated the provision of over 82,700 FREE rapid HIV tests. These tests are conducted not only in stores but also through the distribution of self-test kits, emphasizing accessibility and community engagement on National HIV Testing Day (NHTD), observed on June 27. This enduring partnership underscores a commitment to widespread HIV testing, reducing barriers, and promoting public health initiatives in the fight against HIV/AIDS [55].

### Future directions

#### Prospects for a functional cure or eradication of HIV

Apart from sustained effectiveness, the enduring success of HIV treatments will also hinge on ensuring safety and tolerability over the long term. Additionally, future clinical development is expected to prioritize the streamlining of antiretroviral regimens for further simplicity. The traditional strategy of using a two-NRTI backbone combined with a third agent is being challenged by the development of at least two 2-drug single-tablet regimens (DTG/RPV and 3TC/DTG). Positive outcomes have been noted with the 3TC/DTG combination after 24 weeks of treatment in a small proof-of-concept study in treatment-naïve patients [56]. The progress in creating novel antiretroviral therapies and treatment approaches will coincide with the growing accessibility of generic antiretrovirals. Given the absence of a highly effective vaccine, the crucial strategy to address the global AIDS epidemics involves the widespread and efficient utilization of antiretrovirals for both treatment and prevention. Hence, these innovations will play a vital role in realizing the ambitious objectives set for the global implementation of antiretroviral therapy. Concurrently with advancements in antiretroviral therapy, there is an expanding focus on research and development endeavors aimed at novel therapeutic strategies to

address persistent HIV reservoirs. These efforts seek to achieve prolonged periods of drug-free remission and, potentially, a cure for HIV infection [56].

#### Improving access to treatment and healthcare infrastructure

Involves a multifaceted approach addressing various challenges associated with the prevention, diagnosis, and management of the disease. Here are detailed aspects of this initiative.

#### Antiretroviral Therapy (ART) access

- **Affordability and Availability:** Ensuring that antiretroviral medications are affordable and widely available is crucial. This may involve negotiating lower drug prices, promoting generic alternatives, and collaborating with pharmaceutical companies to make treatment more accessible globally.
- **Supply Chain Management:** Establishing robust supply chain systems is essential to prevent stockouts and interruptions in the availability of antiretroviral drugs. This includes improving distribution networks and procurement processes [57].

#### Geographical accessibility

Rural and Remote Areas: Implementing strategies to reach individuals in rural and remote areas is vital. This may involve mobile clinics, telemedicine initiatives, and community outreach programs to provide healthcare services where traditional facilities may be scarce [57].

#### Healthcare infrastructure strengthening

- **Facility Upgrades:** Investing in the upgrade and construction of healthcare facilities to meet the increasing demand for HIV-related services. This includes equipping clinics and hospitals with necessary diagnostic tools, laboratories, and personnel [57].
- **Training Healthcare Workers:** Ensuring that healthcare professionals, including doctors, nurses, and community health workers, are adequately trained to provide comprehensive and sensitive care to individuals living with HIV.
- **Integrated Services:** Integrating HIV services into existing healthcare systems to reduce stigma and discrimination, and to encourage individuals to seek care within broader healthcare settings [57].

### Prevention and education

- **Community Outreach:** Conducting community-based education and awareness programs to promote HIV prevention, encourage regular testing, and reduce the stigma associated with the virus.
- **Pre-Exposure Prophylaxis (PrEP) Programs:** Promoting and expanding access to PrEP, a preventive measure for individuals at high risk of contracting HIV, can significantly contribute to reducing new infections [58].

### Data management and monitoring

Health Information Systems: Implementing robust health information systems to monitor and evaluate the effectiveness of HIV programs. This includes tracking treatment adherence, viral load suppression, and other key indicators to ensure the quality of care [58].

### Policy and advocacy

- **Policy Reforms:** Advocating for policy changes that support HIV treatment and care. This includes policies that reduce discrimination, protect the rights of individuals living with HIV, and improve overall healthcare infrastructure [58].

### Collaboration and funding

- **International Collaboration:** Facilitating collaboration among governments, non-governmental organizations, international agencies, and private sector entities to pool resources, share best practices, and coordinate efforts for a more effective response to HIV/AIDS [59].
- **Funding Initiatives:** Securing sustained funding for HIV programs through international aid, government budgets, and philanthropic contributions is crucial for the long-term success of improving access to treatment and healthcare infrastructure [59].

### Addressing social and economic disparities in HIV management

Mitigating social and economic disparities in HIV management involves a multifaceted scientific approach aimed at ensuring equitable access to prevention, treatment, and support services across diverse socio-economic strata [59]. This comprehensive initiative encompasses several key scientific aspects.

### Social determinants of health

Educational Interventions: Implementing evidence-based educational strategies to enhance awareness of HIV transmission, prevention, and treatment. Educational efforts serve as a scientific means to empower individuals and reduce societal stigma and discrimination associated with HIV.

### Access to healthcare

Universal Health Coverage (UHC): Advocating for and scientifically implementing universal health coverage to facilitate access to essential health services, including scientifically backed HIV testing, treatment, and support.

Community Health Worker Models: Employing scientifically validated community health worker models to bridge the healthcare accessibility gap, ensuring scientifically informed education, support, and linkage to care for individuals living with HIV [59].

### Economic empowerment

- **Employment Initiatives:** Implementing evidence-based economic initiatives to create employment opportunities for individuals impacted by HIV. Scientifically supported programs include job training, support for small business ventures, and evidence-based anti-discrimination policies in workplaces [59].
- **Microfinance Programs:** Scientifically endorsing and supporting microfinance programs as an evidence-based approach to empower individuals, particularly women, through small business initiatives to enhance economic resilience in affected communities [59].

### Housing and food security

- **Secure Housing Strategies:** Scientifically formulating and implementing strategies to ensure secure and stable housing for individuals living with HIV, recognizing the scientific impact of stable housing on treatment adherence and overall health.
- **Nutritional Support Programs:** Scientifically designing programs to address food insecurity, providing scientifically validated nutritional support for individuals living with HIV, crucial for the effectiveness of antiretroviral therapy and overall health [60].

### Legal Protections and Human Rights:

- **Legal Advocacy and Reforms:** Engaging in scientific advocacy for legal reforms that scientifically protect the rights of individuals living with HIV. This includes scientifically endorsed non-discrimination laws, confidentiality protections, and scientifically backed access to healthcare without legal repercussions [60].
- **Community Legal Support Services:** Scientifically establishing community-based legal support services to assist individuals in navigating scientifically relevant legal challenges related to HIV, ensuring awareness and exercise of their rights [60].

### Gender equality and vulnerable populations

- **Gender-sensitive Approaches:** Scientifically incorporating gender-sensitive approaches to address the scientifically documented disproportionate impact of HIV on women. Empowering women, addressing gender-based violence, and scientifically promoting women's rights are integral to this approach [60].
- **Vulnerable Populations Research:** Scientifically tailoring interventions through research to address the unique social and economic challenges faced by vulnerable populations, such as sex workers, men who have sex with men, transgender individuals, and people who inject drugs.

### Data collection and research

- **Disaggregated Data Methods:** Scientifically ensuring that data collection methods are inclusive and provide scientifically valuable disaggregated information. This scientific approach aids in identifying and understanding social and economic disparities, forming the basis for targeted, evidence-based interventions [60].
- **Scientific Research on Interventions:** Conducting rigorous scientific research to assess the effectiveness of different interventions in addressing social and economic disparities in HIV management, emphasizing an evidence-based approach [60].

### Community engagement and participation

Scientifically Led Initiatives: Encouraging and scientifically supporting community-led initiatives that actively involve affected

communities in the scientifically rigorous design, implementation, and evaluation of programs. This ensures culturally sensitive and scientifically informed interventions [60].

### Global collaboration and funding

- **International Scientific Cooperation:** Facilitating scientific collaboration between governments, research institutions, non-governmental organizations, international agencies, and donors to address social and economic disparities on a global scale.
- **Scientific Funding Initiatives:** Mobilizing financial resources through scientifically rigorous means to support programs scientifically aimed at mitigating social and economic disparities in HIV management [60].

### Integration of services

- **Holistic Scientific Care:** Integrating HIV services with other scientifically validated healthcare services, including mental health, sexual and reproductive health, and substance use treatment [60]. Holistic care, informed by scientific principles, addresses the complex needs of individuals and contributes to better scientific health outcomes.

### Importance of ongoing research and collaboration

Future Directions in HIV Research and Treatment: Navigating Toward Progress and Possibilities.

The future of HIV research and treatment holds promise for continued advancements that can transform the landscape of HIV care and prevention. As scientific knowledge deepens and technologies evolve, several key directions are shaping the trajectory of HIV management, with the overarching goal of ending the HIV epidemic [60].

- **HIV Cure and Remission:** Achieving a cure for HIV remains a long-term aspiration. Researchers are exploring innovative strategies to eliminate or control viral reservoirs, including gene editing, latency-reversing agents, and immunotherapies. While complete cure may still be distant, sustained viral remission is a realistic objective.

- **Precision Medicine:** Advancements in genetics and personalized medicine are shaping the future of HIV treatment. Tailoring therapies to an individual's genetic makeup and immune response can optimize treatment outcomes and minimize side effects [60].
  - **Innovative Delivery Methods:** Efforts to enhance treatment adherence and reach underserved populations are driving the development of innovative drug delivery methods. Long acting injectables, implants, and other novel formulations offer convenience and may overcome adherence challenges [60].
  - **Combination Prevention Approaches:** Combining different prevention strategies, such as PrEP, condoms, and behavioral interventions, can amplify their effectiveness. This approach addresses the multifaceted nature of HIV transmission [60].
  - **Integrated Health Services:** Integrating HIV services with other healthcare needs, such as sexual and reproductive health, mental health, and substance use treatment, ensures comprehensive care for individuals living with HIV [60].
  - **Digital Health and Telemedicine:** Digital tools and telemedicine are revolutionizing healthcare delivery. These technologies can enhance treatment adherence, provide real-time support, and facilitate communication between patients and healthcare providers [60].
  - **Addressing Disparities:** Efforts to reduce health disparities and ensure equitable access to care remain a priority. Tailoring interventions to the needs of marginalized populations is essential for ending the epidemic [60].
  - **Global Collaboration:** Continued international collaboration is essential in sharing knowledge, expertise, and resources. Global partnerships facilitate research, treatment access, and policy development [60].
  - **Social and Behavioral Interventions:** Incorporating social and behavioral interventions into HIV programs addresses the broader determinants of HIV transmission and encourages community engagement [60].
  - **Expanding Access to Testing:** Innovative approaches to HIV testing, including self-testing kits and community-based testing, can enhance early diagnosis and linkage to care [60].
  - **Empowering Marginalized Communities:** Supporting LG-BTQ+ individuals, people of color, women, and other marginalized groups is crucial in achieving the goals of HIV prevention and treatment. Empowering these communities through education, advocacy, and healthcare access can make a substantial impact [60].
  - **Cross-Disciplinary Collaboration:** Collaboration between different scientific disciplines, such as virology, immunology, genetics, and behavioral science, fosters a holistic understanding of HIV and drives comprehensive solutions [60].
  - **Advocacy and Awareness:** Sustained advocacy efforts and public awareness campaigns are essential to combat stigma, dispel myths, and ensure that accurate information about HIV is disseminated [60].
- The future of HIV research and treatment is dynamic and multifaceted, driven by the combined efforts of scientists, healthcare providers, policymakers, affected communities, and individuals at risk. While challenges persist, the ongoing pursuit of innovative solutions, guided by compassion and scientific rigor, continues to pave the way toward a world where HIV is no longer a global health threat [60].

## Conclusion

Navigating Challenges and Opportunities in HIV Treatment and Research. In summary, this comprehensive review has explored the multifaceted landscape of HIV treatment and research, highlighting both remarkable progress and persistent challenges. Key points discussed encompassed the discovery of HIV, the vital importance of studying the virus and its treatment, and the early impact of the epidemic. The review delved into the complexities of HIV transmission, pathogenesis, and the revolutionary role of Antiretroviral Therapy (ART) in suppressing viral replication and preserving immune function.

The challenges within HIV treatment were thoroughly examined, emphasizing the critical areas where advancements are needed. Adherence to treatment, drug resistance, and the often-uneven access to care were identified as ongoing challenges that impact individuals globally. Stigma, mental health concerns, and the intersection of HIV with co-morbidities and aging highlighted the need for a holistic approach to care. Global health disparities and disparities in access to care were underlined as complex issues that demand continued attention and action.

However, within these challenges lie opportunities for progress and innovation. Emerging therapies, such as long-acting treatments and gene therapies, have the potential to transform the way HIV is managed. Advancements in precision medicine, personalized treatment regimens, and the integration of digital health tools

offer avenues for improving treatment outcomes and quality of life. Research into HIV cure strategies and combination prevention approaches show promising potential for controlling the epidemic.

The review ultimately emphasizes that the fight against HIV is far from over. The collective efforts of researchers, healthcare providers, policymakers, and affected communities are essential in navigating the complexities and capitalizing on the opportunities that lie ahead. While challenges persist, the ongoing dedication to scientific advancement, advocacy, and global collaboration offers a path towards ending the HIV epidemic, improving treatment options, and ensuring a brighter and healthier future for all individuals impacted by HIV.

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