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Advancements in HIV/AIDS Cure Research: Effects on Patient Adherence and Behavioral Trends in the General Population a Scoping Review

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ABSTRACT

Introduction: Despite significant global efforts, HIV/AIDS remains a major health issue, with over 39 million people living with HIV worldwide (UNAIDS, 2024). Although Antiretroviral Therapy (ART) has improved management, a definitive cure remains elusive. Recent advancements in HIV cure research include functional and sterilizing cures. Functional cures aim to suppress the virus without daily ART, while sterilizing cures seek complete eradication. Breakthroughs in gene editing, stem cell transplants, and latency-reversing agents (LRAs) offer promise but face challenges.

Research Gap: The effect of cure-related optimism on patient behavior and ART adherence is underexplored. While optimism may enhance adherence by motivating patients, it could also lead to reduced compliance and risky behaviors. This review investigates how optimism about potential cures impacts ART adherence and behavioral tendencies in HIV-positive individuals.

Trends and Impact: Functional cures manage HIV with minimal ART, while sterilizing cures strive for total eradication. Gene editing, stem cell transplants, and LRAs are key recent advancements. Optimism about these cures may boost adherence but also risk reduced compliance and unsafe practices. This review aims to highlight the need for balanced public health strategies to maintain effective ART adherence amid evolving cure research.

Key words: HIV cure research; Antiretroviral therapy (ART) adherence; Functional HIV cure Sterilizing HIV cure; Gene editing (CRISPR)

INTRODUCTION

Background

Despite decades of combating HIV/AIDs through concerted efforts, its prevalence is still on the rise, though at a lower rate compared to the initial years of its discovery. Over 39 million people worldwide are HIV positive based on UNAIDS' (2024) research, showing that 1.3 million new cases were reported in 2023 alone. According to Haris and Abbas (2024), the epidemic has not been eradicated, even with Antiretroviral Therapy (ART) available in every country today, especially in low- and middle-income countries. As with many

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illnesses, the treatment of HIV has now become less of a challenge through the use of ART; hence, there is a continued search for a cure. Functional and sterilizing cure solutions – based on recent studies by the likes of Bailon et al. (2020), Gupta and Saxena (2021), and Hahn and Martins (2023) – have advanced dramatically in recent years, contributing to a significant advancement in HIV cure research. The concept of a functional cure in which the virus is effectively regulated and a sterilizing cure, where the virus is wiped off the face of the earth from the body, have brought hope among the patients and the healthcare givers. Such advancements include new strategies such as gene editing technologies, especially CRISPR–Cas 9, which targets HIV-infected cells for destruction (Hussein et al., 2023). Also, stem cell transplants and latency-reversing agents have been reported to show signs of working. For instance, the "Berlin Patient" was cured of HIV permanently after being treated by a bone marrow transplant (Gong & He, 2023), and such cases only encourage further search for possible cure avenues.

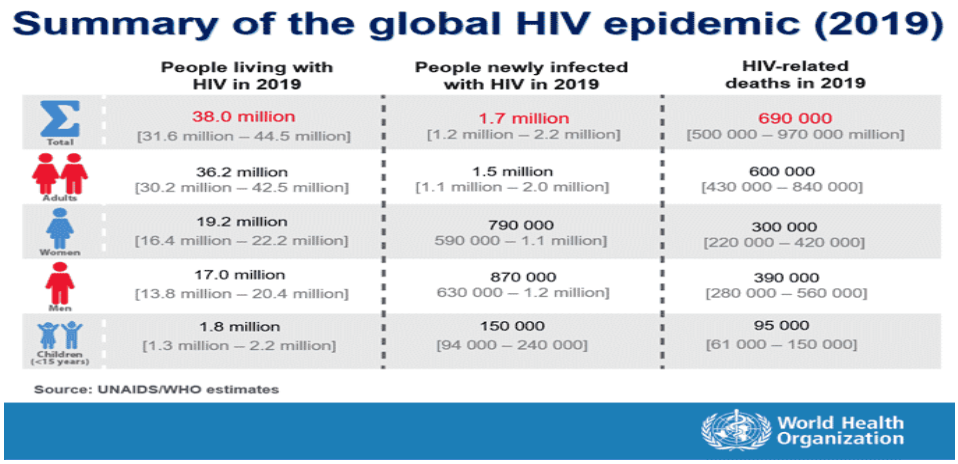

Figure 1. Evolution of HIV/AIDS Research and Treatment (1981-Present). The figure depicts key milestones in HIV/AIDS research, from early identification of HIV transmission and replication to the transformative impact of daily antiretroviral therapy (ART). Notable achievements include the "Berlin Patient" (2008) and the "London Patient" (2019), who were cured using stem cell transplants. Despite these advances, HIV remains a global challenge, with approximately 38 million people affected and no complete cure available.

Research Gap

Despite these developments, little is known about how cure-related optimism affects population-wide behavior and adherence to ART. Adherence to ART is one essential factor that determines the effectiveness of the treatment, avoiding viral replication, advancement of the disease, and transmission of the disease to other people [1], [2]. It is possible that such hopes can work in a twofold manner; such expectations increase the chances of discovering the cure, whereas optimism about getting better improves compliance, as the patients use ART to keep themselves symptom-free until the cure arrives. However, some patients may relax and have lower adherence due to decreased need for ART due to promises of a cure. More so, even though there are very effective medicines available for HIV/AIDs management, only 75% of people living with HIV (PLHIV) on antiretroviral therapy (ART) achieve viral suppression. Reduced compliance because of cure arrogance is poised to worsen the situation, resulting in the development of resistant strains and increased spread of the disease. The impact of cure research on the population's behavior is also least known per Obeagu and Obeagu's (2023) research [2]. The same study and others hint at the possibility of over-optimism with the cure in the offing and, thereby, developing high-risk sexual behaviors and failure to observe clinical measures such as using a condom or taking Pre-Exposure Prophylaxis (PrEP). This narrative review attempts to investigate the behavioral consequences of HIV cure due to the narrow scope of current research. In particular, it aims to explore the connections between cure-related optimism and ART consistency in people's adherence and its impact on such general population tendencies as risk assessment and prevention. To this end, the review aims to fill this gap and contribute with findings that will support public health approaches so that the progress on HIV cure research does not hinder other efforts in the fight against the epidemic, especially in Africa and developing countries, where prevalence is high.

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TRENDS IN HIV/AIDS CURE RESEARCH

Functional Cure vs. Sterilizing Cure

Functional Cure

A functional cure for HIV means managing the virus to have the patient free from ART, yet the virus is still in the body but in a suppressed state. In this approach, however, the virus is still present in the body, but its levels are maintained so low that it does not progress and cause disease or be transmitted [3], [4]. It is considered to be a more realistic target in comparison with a sterilizing cure, which implies the absence of daily ART while implying sustained viral suppression over a long period. Antiviral functional cure approaches focus on better controlling the virus using the immune system or stimulating therapeutic vaccines that evoke immune responses (Dubé et al., 2020). Integral to this approach is eliminating viral reservoirs; the virus infects these cells but does not manifest the viral infection then, and it may re-emerge later.

Sterilizing Cure

A sterilizing cure in HIV-infected subjects implies the total absence of the virus in the body and its eradication from all forms, including the viral reservoirs. It is relatively more straightforward said than done because HIV's genetic material merges with the DNA of the host cell, as described by Scoca and Di Nunzio's (2021) host nuclear invasion study; hence [5], it cannot easily be targeted and eliminated. However, attempts at a sterilizing cure have recently received steam with new technologies such as gene editing and complex immunotherapies [6]. A sterilizing cure means that HIV-positive patients are cured of the virus, and the possibility of re-emergence of the virus or transmission of the virus to other people cannot exist.

Recent Breakthroughs

Gene Editing

With the CRISPR-Cas9 method, gene editing holds great promise for HIV cure research. Considering the recent review by Vasconcelos Komninakis et al. (2024), scientists can accurately target and cut particular genome regions using CRISPR-Cas9 [7]. With this technology, it may be possible to target and remove HIV proviral DNA in host cells precisely. CRISPR can, therefore, alter the CCR5 gene, which codes for a receptor on immune cells that HIV uses to enter these cells, as recent investigations have shown [8][9]. Theoretically, altering this gene could provide HIV resistance in immune cells. Human trials are still in their early phases, but early animal research has demonstrated some effectiveness in utilizing CRISPR to eliminate HIV-infected cells. In animal models, CRISPR-Cas9 has shown promise [10], [11][12]; in certain instances, researchers have observed long-term control of viral replication. The technology still faces difficulties in safely and effectively targeting all human viral reservoirs, particularly in light of the variety and dispersion of these reservoirs throughout various tissues.

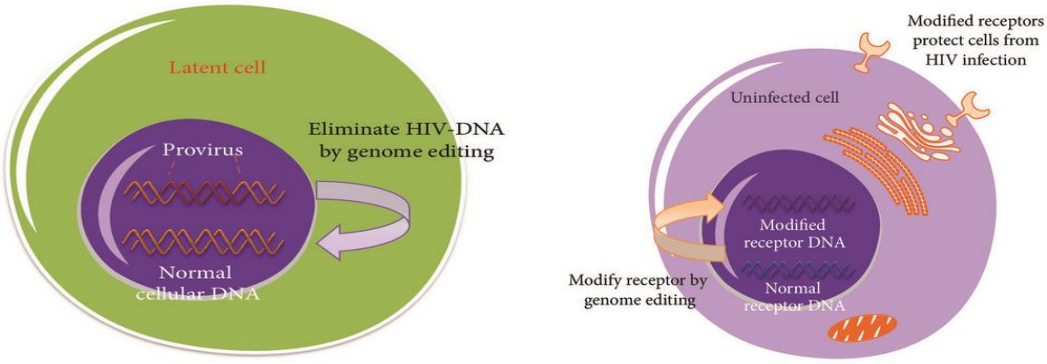

Figure 1 (a); Two major strategies for HIV cure by using genome editing. (a) Gene therapy strategies to eradicate HIV reservoirs. Using ZFN, TALENS, or CRISPR to eliminate the HIV provirus in latent cells. (b)

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Gene therapy strategies to prevent susceptible cells from HIV infection. Using gene editing to modify the receptor of susceptible cells and protect them from HIV infection. (b) Two major strategies for HIV cure by using genome editing. (a) Gene therapy strategies to eradicate HIV reservoirs. Using ZFN, TALENS, or CRISPR to eliminate the HIV provirus in latent cells. (b) Gene therapy strategies to prevent susceptible cells from HIV infection. Using gene editing to modify the receptor of susceptible cells and protect them from HIV infection.

Stem Cell Transplants

According to Li (2022), stem cell transplantation has drawn interest due to the success of the "Berlin Patient," who received a bone marrow transplant from a donor with a naturally existing CCR5 mutation. HIV cannot enter immune cells due to this mutation, and the patient's immune system was able to regenerate itself with HIV-resistant cells after the transplant. Several patients, including the "London Patient," as covered by Ling and LI (2020), have now experienced long-term remission using comparable techniques. These cases demonstrate that it is possible to attain a sterilizing cure in specific individuals [13]. Unfortunately, risks associated with stem cell transplants [14], such as the need for a matched donor and the intensive procedure, mean they are not a practical solution for the world's population. Although these rare accomplishments are promising, the process is costlier, risky, and unreliable if applied widely. Consequently, current research focuses on how these transplants' underlying principles, such as CCR5 gene modification, can be used more effectively and safely.

Latency-Reversing Agents (LRAs)

The body possesses dormant cells that harbor active HIV, and traditional antiretroviral therapy is powerless because this virus is not active in these cells. Another major challenge in HIV cure is how to 'activate' the mentioned virus reservoirs to make the virus detectable and capable of being cleared by the immune system or treated pharmaceutically [15], [16]. LRAs are drugs that aim at provoking otherwise dormant HIV by sensitizing it to specific treatments or the immune system. Scientists plan to eradicate such reservoirs and approach sterilization by reactivating latent viruses. Many clinical trials have reviewed different types of LRAs; histone deacetylase inhibitors (HDACis) work with proteins to change the state of viral latency [17][18]. Even while several LRAs have demonstrated the ability to awaken latent HIV, much more study needs to be done to match these agents with efficient methods of eradicating the reactivated virus. Managing the immune system's reaction to the newly active virus and preventing broad viral multiplication are the current issues associated with reactivation.

Combined Approaches

Researchers like Ward et al. (2021)[19] and Alum et al. (2024) widely believe that the most effective way to cure HIV is to combine techniques, including gene editing, immunotherapy, and latency-reversing drugs. The objective is to enhance the immune system's ability to combat the infection, inhibit viral replication, and simultaneously identify and eradicate viral reservoirs. Using multiple drugs in combination may help to evade the coordinates of the HIV lifecycle and the various copies of the virus present in the body.

IMPACT ON PATIENT ADHERENCE

Optimism and Adherence

The increasing perception that a cure for HIV/AIDS is around the corner has a significant impact on patients' compliance with ART. This means that the hope for a cure is one of the ways to enhance the level of adherence to the treatments. For instance, a study revealed that patients with high expectations for future treatment were more likely to follow ART regimens than any other group [20]. Hope for a cure can mobilize the patient, determine their treatment regime, and ensure that the patient communicates well and actively interacts with the healthcare providers. Borrowing from the study by Margolis et al. (2020), the expectation of the cure may keep patients' minds on their current health regimen, helping them deal with their future health. For instance,

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breakthrough research like that of the so-called "Berlin patient" who was eliminated from the HIV+ list by a stem cell transplant encouraged many people to stick to their ART treatments, awaiting such insightful ideas.

Complacency Risk

Optimism can lead to complacency among some patients. According to a past study by Chen (2013), if patients learn that the cure is near, they may think that ART is unnecessary. A more recent study established that there is an emerging behavior where patients reduce adherence to their ART regimen [21]; what comes from such and in line with recent advances in HIV cure, there is a link to the promising research, suggesting that they no longer need current ART treatments. More so, a promising cure can decrease psychological trauma and, therefore, have a positive impact on the mental well-being of the patients. For example, a study by Brown and Adeagbo (2022) established that mentally prepared people, coupled with optimism toward the eventual elimination of HIV, demonstrated lower depression and anxiety levels. This informed lot is poised to adhere to the ART, leading to positive outcomes. However, many cure optimizations, especially behavioral changes, have yet to be covered.

Psychological Effects

Accepting that one can recover sometime in the future helps a patient gain much psychological comfort; this knowledge promotes patient compliance. First, the hope that there is a cure around helps to lift some psychological burden, thus improving the mental health of such patients. For instance, one piece of research found that patients who had hope for a future cure were less depressed and anxious, implying that they were highly likely to stick to ART [22]. Second, the anticipation of improvement may increase patients' engagement. One study found that patients who positively perceive future treatments or disease management are more likely to patronize visits and acquire better efficiency in health management [23]. Therefore, adverse psychological effects are imminent among HIV patients.

Patients' attitudes and beliefs that compound curing in R&D sometimes threaten their compliance with medicines. First, people can easily get irritated by overstatements or early release of information on 'cures.' This was made clear by Al Khaja et al.'s (2018) study that found damaging mental effects on people who were exposed to drug-related exaggerated social media misinformation. Regarding potential cures for HIV, patients may be likely to become frustrated when the claims are not realized because it results in less compliance, which may be behind the increasing global virulence. Second, if provided inaccurately, the patients' misinformation causes a disconnection between the conclusions expected at the end of the treatment and the procedures being administered. For instance, going by the findings of Al Khaja et al. (2018), some patients may be inclined to relapse from their ART due to false information on the cure-finding period, hence leading to poor health outcomes. That is a gap that needs research in the advent of the ongoing HIV cures.

IMPACT ON GENERAL POPULATION BEHAVIOR

Risk Perception and Behavior

Awareness of Potential Cures

Public perception of HIV/AIDS may shift as word spreads about potentially effective treatments like gene therapy and stem cell transplants [24]. This perception shift can be either positive or negative. On the one hand, it can decrease the rates of such anxiety and fatalism typical for HIV-positive diagnoses previously and increase the utilization of medical services among those people. However, on the other hand, it may lower the perception of the seriousness of contracting HIV, as regards Brown (2021). The same was observed after the introduction of GA in the middle of the nineties antiretroviral therapy (ART). Before ART, HIV was considered a terminal illness; hence, the adherence to safe sex practices. However, after ART, some high-risk populations, for example, men who have sex with men (MSM) per Chuang et al. (2021), have increased risky behaviors such as erratic condom use and reduced practice of HIV prevention even though there is existing management of the disease differently compared to previous times.

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Decreased Use of Preventive Measures

Some people may become less diligent about using preventive measures like condoms and PrEP in the hopes of finding a cure. For example, according to probable considerations, those who know the HIV cure research have lesser concerns over the HIV risks and are, therefore, more likely to indulge in high-risk sexual behaviors described by Chuang et al. (2021). This is similar to what Ayerdi Aguirrebengoa et al. (2021) and Di Ciaccio et al. (2021) observed concerning the adoption of PrEP in recent years. Even though PrEP is one of the most effective preventive tools, it is observed from both studies that with the availability of the drug, individuals have decreased the usage of condoms and become at risk for other sexually transmitted infections (STIs).

Public Health Campaigns

Public health campaigns need to adjust to address this. A good example is the UK Terrence Higgins Trust's (n.d.) It Starts with Me media campaign that combines positive messages about today's effective HIV treatment with powerful prevention messages. This campaign conveys the message that whereas treatment research is ongoing, prevention is possible through condoms, testing, and PrEP [25]. Thus, the campaign and others alike are creating a positive message about the future of HIV treatment and care, but at the same time, reminding the public to use protection measures to avoid re-infection and new infections.

Stigma Reduction

Advances in Cure Research and Stigma

The possibility of a cure has the power to change public perception of HIV/AIDS. Most of the individuals who suffer from this disease have always been stigmatized, particularly those in the Black community, forcing them into isolation and also having a hard time being tested and treated (Hedge et al., 2021). There is a sign that the stigma has begun to be eroded by the progress achieved in treating the sickness. Such as how the appreciation of the U=U (Undetectable = Untransmutable) campaign, covered by Spinelli et al. (2021), has taken the public through the education process to understand and know that an HIV-positive person on ART and has an undetectable viral load cannot pass on HIV through sexual intercourse. The campaign of 'U=U' has also favored the fight by minimizing stigma and encouraging people not to fear rejection because of their status of HIV.

Encouraging Testing and Treatment

Research on cures contributes to this changing story by portraying HIV as a treatable illness rather than a death sentence. As seen in Denmark, the more people learn about treatments such as gene editing and stem cell transplants, the more they demand tests and early diagnosis. The CROI Conference in 2016 revealed that campaigns surrounding the discovery of a cure, as well as advancement in ART, boosted MSM's HIV testing rates due to a decrease in social persecution and increased optimism about living with HIV [9], [26]. Moreover, speaking about HIV, whose prevalence is high in South Africa, cure research is emerging as a hope for local communities there [27]. The same study done in Durban, South Africa, was made aware and engaged in local research on HIV cures, thus creating a positive attitude towards testing and treatment.

Persistent Stigma

Even with these encouraging developments, stigma is still ingrained in many cultures, particularly in those groups where HIV is seen as a moral sin or in areas with poor access to healthcare. For instance, HIV is still associated with immoral and deviant behavior in Sub-Saharan Africa, especially among conservative or religious societies [28]. It is possible to be still stigmatized for their HIV-positive status even if there is a cure. It means people may not come for testing or treatment as they fear they can still be fired from their jobs or isolated from family and friends. This is more so because the environment in countries like Nigeria, per Ayuk et al. (2022), is one that still bears much prejudice towards HIV-infected individuals. In Nigeria, even though HIV-positive patients receive free medical treatment, many still opt not to seek treatment due to the stigma that is associated with the disease, meaning that the advancement that has been made in the medical field is not

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being enjoyed thoroughly by patients in their respective countries or societies due to the culture and the beliefs held by the institutions.

Continued Efforts to Educate and Destigmatize

Campaigns to reduce stigma must coexist with advancements in science. For example, in the United States, the Let's Stop HIV Together campaign launched by the Centers for Disease Control (CDC) communicates messages about ART progress and current research with efforts to eliminate the stigma associated with testing and treatment [29]. This campaign states that it is possible to live with HIV today based on the fact that current science has made it possible for HIV-positive persons to live long, healthy lives similar to ordinary people. Likewise, HIV Cure Research Day, held annually, also introduces people to cure research and does not involve the stigma and fear of a virus in its work [30]. Though, the concerns relating to stigma call for more emphasis on population groups that may be on the margins of society. It, therefore, becomes the responsibility of governments and NGOs to support local endeavors in eradicating social and cultural beliefs that fuel stigma among HIV-positive persons.

PUBLIC HEALTH IMPLICATIONS

Communication Strategies

Clear Communication about Cure Research and Realistic Timelines

Handling public expectations in the face of promising research is crucial. Cures are also usually identified by certain breakthroughs, for example, gene editing or stem cell transplants, which qualify as cure developments, and this always creates much hype, which leads to people having a wrong perception of the cure and when it is available in the market [31]. For instance, news on the timeline featuring the first 'cured' HIV-positive patient, namely Timothy Ray Brown, also known as the 'Berlin patient, created awareness across the whole world. However, this case included very complex invasive interventions that cannot be replicated for the majority of HIV-positive individuals [32]. Therefore, the task for public health officials and scientists is to present the many-layered treatments required, always emphasizing that these advances are not a panacea readily available to millions of suffering humanity. Adherence to existing treatments may be compromised by false information on cure dates. When patients think that the cure is near, some of them will cut down on their adherence to ART since they will be able to quit the medications shortly anyhow. Awareness creation for the public should target the need to continue sticking to the ART while hoping for more advances to be realized [33]. For instance, based on Smith et al. (2020), the National Institute of Health (NIH) is responsible for developing statements periodically to help society appreciate the current status of cure research and the available options in the market. Educational information must closely describe timelines to expected milestones to ensure that people using ART understand that it is a lifesaving tool despite the new advancements in HIV treatment [22].

Emphasis on Continued Prevention and ART Adherence

Prevention techniques remain essential to public health initiatives even as research into cures increases. HIV education initiatives like the CDC's (2024) Ending the HIV Epidemic campaign ensure that the public does not forget that ART does not only save lives but also interrupts transmission. This has been very instrumental in reminding people living with HIV to adhere to their ART since taking the drugs will not infect others as long as the viral load is undetectable. Communication campaigns also have to sustain this two-pronged approach of encouraging the public to look forward to a better future where there will be cures for these diseases while at the same time being disciplined to take precautions and stick to the ART regimens in the present [34]. Moreover, prevention efforts must be directed towards the youth because people in their age brackets did not witness the worst outbreak of the HIV epidemic and hence may lack the perception that there will be an HIV cure. A 2021 study by Laher et al. established that younger populations, particularly those in the below 35-year age bracket, wrongly perceive the available cure. Thus, they are likely to drop preventative measures such as the use of condoms or PrEP. These groups should be reached out using straight talk with evidence-based messages about where cure research is and why prevention is still relevant [35].

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Policy Development

Supporting Cure Research while Strengthening ART Programs

Legislators must maintain potent antiretroviral therapy (ART) programs for HIV-positive individuals while simultaneously providing funding and support for research on HIV cures. Research efforts such as the HIV Cure Initiative under the NIH are a worthy investment, but they need a lot of resources [22]. The reasons above make it essential that more resources be committed to expanding the currently existing ART programs to help those already infected receive requisite care. For instance, in the United States, the primary services that are supported by federal programs (such as the Ryan White HIV/AIDS Program) include putting low-income persons on ART and other medical services [36]. Therefore, policymakers must ensure that funds for these programs are sustained despite the current trend of funneling more money toward cure-based research. The balancing act is much more difficult internationally, particularly in low- and middle-income countries (LMICs), where healthcare resources are few. In sub-Saharan Africa, which hosts the majority of the global HIV-positive population, interventions such as the PEPFAR (President's Emergency Plan for AIDS Relief) funded ART programs have been God-sent [37], [38]. Nevertheless, the emerging interest in developing an HIV cure ought not to be used to justify financing cuts for such essential initiatives. HIV/AIDS cure research has been described as needing innovative plans to go forward, while the Global Fund (2024) to Fight AIDS, Tuberculosis, and Malaria has hinted at the need to continue ART access. Policymakers must not set two research priorities in opposition; the former has to ensure that funding is provided to both.

Allocating Resources with a Balanced Approach

Allocating healthcare resources requires careful consideration of both immediate needs and long-term goals. Much as the focus on cure research is interesting, the importance of attention on people with HIV now cannot be overemphasized. This is the lesson that can be learned from the experience of ART rollout in LMICs. As ART was first made widely accessible, all organizations working in the global health field discovered that resource distribution disproportionately supported emergent treatment rollouts [39], [40]. However, this resulted in a stoppage of continued preventive interventions and long-term program planning and implementation, disrupting services as soon as the first few crisis intercessions ended. Similarly, focusing too much on the cure research may negatively deny present ART programs some of the funds they need, especially in developing countries (Dubé et al., 2020). Policymakers need to consider the global disparities in HIV care. In high-income nations, the ART distribution is almost complete, while dedicating more efforts towards seeking cures does not compromise present treatment. Nevertheless, where ART access remains suboptimal, as is currently the case in sub-Saharan Africa per Dovel et al. (2023), efforts to build up the ART framework and continue educational activities should remain the priorities. Moreover, policy strategies should also consider contextual factors that affect receipt of HIV care, including housing, food security, and health care. Like San Francisco, Getting to Zero (2022) has also revealed that linkage to ART and other social support services would significantly decrease new infections and enhance patients' lives. The governments have to focus on such needs in a multidimensional way and simultaneously support cure development as one of the components of the more comprehensive plan.

CONCLUSION

While there is great hope in the search for an HIV/AIDS cure, there are also significant obstacles to overcome. Population-level optimism held out by cure research can benefit patients, improve medication adherence, and decrease stigma; there will be adverse effects such as complacency contributing to poor adherence to ART among clients and receiving risk information within communities. These two findings highlight the need for careful communication from health officials to reduce expectations and increase ART and prevention adherence.

Public health initiatives must give equal weight to the long-term search for a cure and the immediate need to guarantee access to ART, lower the number of new infections, and tackle stigma. Policymakers and health organizations have to divide their resources and funds on the one hand in supporting new cures and research and, on the other, in the development and sustainability of current treatment and preventive interventions.

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HIV/AIDS continues to be a public health challenge to this day, and education, destigmatization, and providing full support to those diagnosed and living with the virus are as important as ever because the journey to find a cure is still ongoing.

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