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Review Article

Preventable Mortality in Advanced HIV Disease in the Era of Universal ART: A Narrative Review

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Abstract

The widespread adoption of universal antiretroviral therapy has transformed the global HIV response and led to substantial reductions in HIV-related mortality. However, advanced HIV disease continues to contribute disproportionately to deaths, even in settings with high treatment coverage. This narrative review examines preventable mortality among individuals presenting with or returning to care with advanced HIV disease in the era of universal ART, with a focus on clinical, programmatic, and structural determinants. Drawing on peer-reviewed literature, global guidelines, and major cohort studies, the review synthesizes evidence on the epidemiology of advanced HIV disease, pathways to early mortality, and the predominant role of opportunistic infections, particularly tuberculosis and cryptococcal disease. Despite the availability of effective diagnostics, prophylactic interventions, and WHO-recommended packages of care, implementation remains inconsistent. Gaps in service integration, delayed diagnosis, weak accountability, and limited prioritization of advanced disease within HIV programs continue to undermine outcomes for the most vulnerable patients. The persistence of preventable mortality highlights a disconnect between scientific advances and health system delivery. Universal ART alone is insufficient to eliminate HIV-related deaths without targeted, high-intensity care for individuals with severe immunosuppression. Reducing mortality will require reframing advanced HIV disease as a health system emergency and ensuring full implementation of comprehensive, evidence-based care.

1. Introduction

The scale-up of universal antiretroviral therapy has transformed HIV from a uniformly fatal infection into a manageable chronic condition for millions of people worldwide. The adoption of the Treat All policy, supported by simplified regimens and expanded access to testing, has resulted in substantial declines in HIV-related morbidity and mortality across diverse settings. Global indicators increasingly reflect high levels of treatment coverage and viral suppression, reinforcing optimism that HIV-related deaths can be further reduced and ultimately eliminated as a public health threat. Yet, beneath these aggregate successes, mortality remains unacceptably high among a distinct and vulnerable subgroup of people living with HIV: those who present with or return to care with advanced HIV disease [1].

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Advanced HIV disease continues to account for a disproportionate share of HIV-related deaths in the era of universal ART. Individuals with severe immunosuppression experience markedly higher early mortality, often within weeks of clinical presentation or treatment initiation. This pattern persists across regions and health systems, including countries with long-standing ART programs and high overall coverage. The continued burden of death among this population highlights a paradox at the center of contemporary HIV care. While effective therapies and preventive interventions are widely available, they are not consistently reaching those at greatest risk. Advanced HIV disease, therefore, should be understood not as a failure of antiretroviral efficacy, but as a manifestation of broader health system and programmatic shortcomings [2].

The World Health Organization defines advanced HIV disease in adults and adolescents as a CD4 cell count below 200 cells per microliter or the presence of stage 3 or 4 clinical conditions. This definition captures both individuals who are diagnosed late in the course of infection and those who have previously initiated ART but disengaged from care or experienced treatment interruptions. Importantly, the epidemiology of advanced HIV disease has shifted over time. In many settings, a substantial proportion of cases now occur among ART-experienced individuals, underscoring the need to address retention, re-engagement, and continuity of care alongside early diagnosis [3].

A growing body of evidence demonstrates that most deaths associated with advanced HIV disease are preventable. Opportunistic infections such as tuberculosis, cryptococcal disease, and severe bacterial infections can be detected early and managed effectively using existing diagnostic tools, prophylactic strategies, and treatment protocols. WHO-recommended packages of care for advanced HIV disease, which combine rapid ART initiation with targeted screening and prophylaxis, have been shown to reduce mortality when implemented comprehensively. However, real-world uptake of these interventions remains uneven, and critical gaps persist in diagnostics, clinical decision-making, and service integration [4].

This narrative review aims to critically synthesize current evidence on the causes and drivers of preventable mortality in advanced HIV disease in the universal ART era. It examines clinical, programmatic, and structural factors that contribute to ongoing deaths and explores why proven interventions have failed to achieve their full impact. By focusing on implementation gaps and policy-relevant solutions, this review seeks to reframe advanced HIV disease as an urgent health system priority and to inform strategies capable of reducing avoidable mortality among the most vulnerable people living with HIV.

2. Literature Review and Evidence Synthesis

2.1. Epidemiology of Advanced HIV Disease in the Universal ART Era

Despite more than a decade of widespread implementation of universal antiretroviral therapy, advanced HIV disease remains a common clinical presentation globally. Across low- and middle-income countries, a substantial proportion of individuals newly diagnosed with HIV continue to present with severe immunosuppression, often defined by CD4 cell counts below 200 cells per microliter or by advanced clinical staging. Large cohort analyses from sub-Saharan Africa and Asia consistently demonstrate that between one quarter and one third of adults entering HIV care meet criteria for advanced disease, even in settings with long-standing ART programs [5]. These figures underscore the persistence of late diagnosis and delayed linkage to care, despite expanded testing strategies.

Trends over time suggest only modest declines in the prevalence of advanced HIV disease at presentation since the introduction of Treat All policies. While overall ART coverage and viral suppression rates have improved substantially at the population level, these gains have not translated into proportional reductions in advanced disease. In many settings, the epidemiology of advanced HIV disease has evolved rather than diminished. Increasingly, cases are observed among individuals with prior ART exposure who have disengaged from care or experienced prolonged treatment interruptions [6]. This shift reflects ongoing challenges related to retention, adherence, and continuity of care, particularly in overstretched health systems.

Certain populations remain disproportionately affected. Men consistently present later to care than women and experience higher mortality, a pattern attributed to gender norms, lower health-seeking behavior, and weaker engagement with routine services. Older adults are another high-risk group, often diagnosed late due to low perceived risk and limited testing coverage. Mobile populations, including migrants and informal workers, face structural barriers to sustained engagement in care, while individuals with prior ART interruption frequently re-enter care with advanced disease [7]. Together, these patterns highlight that advanced HIV disease in the universal ART era is driven not by lack of treatment availability, but by persistent gaps in access, engagement, and long-term retention.

2.2. Pathways to Preventable Mortality in Advanced HIV Disease

The high mortality observed among individuals with advanced HIV disease arises from a convergence of biological vulnerability and systemic delay. Severe immune suppression creates a permissive environment for opportunistic pathogens, many of which progress rapidly and present atypically. High pathogen burden at the time of clinical presentation is common, particularly for tuberculosis and cryptococcal infection, and is strongly associated with early mortality. Once advanced disease is established, even short delays in diagnosis or treatment initiation can be fatal [8].

Delayed presentation to care remains a central pathway to preventable death. Many individuals with advanced HIV disease have experienced prolonged periods of untreated infection or disengagement from services, often due to structural barriers, stigma, or competing socioeconomic priorities. When care is finally accessed, symptoms may be non-specific, and health systems frequently lack the diagnostic capacity to rapidly identify life-threatening opportunistic infections. As a result, diagnostic delays compound biological vulnerability, allowing disease to progress unchecked [9].

Mortality risk is particularly concentrated in the first weeks after presentation or ART initiation. Early deaths often occur before diagnostic evaluations are completed or before prophylactic and therapeutic interventions can take effect. This narrow window of extreme vulnerability exposes weaknesses in clinical triage, inpatient management, and linkage between diagnostic and treatment services. Importantly, these deaths are rarely unavoidable. Rather, they reflect failures to anticipate risk, rapidly deploy available tools, and deliver integrated care tailored to the needs of severely immunocompromised patients [10].

2.3. Opportunistic Infections as Leading Causes of Preventable Death

Opportunistic infections remain the dominant causes of mortality among individuals with advanced HIV disease, accounting for the majority of deaths in both ART-naïve and ART-experienced populations. Among these, tuberculosis continues to be the single most important contributor to mortality worldwide. HIV-associated tuberculosis frequently presents with atypical or extrapulmonary manifestations, making diagnosis challenging, particularly in resource-limited settings. Conventional diagnostic approaches, reliant on sputum-based testing, often fail in patients with advanced immunosuppression. The introduction of urine-based lipoarabinomannan testing has represented a major advance, particularly for hospitalized patients with low CD4 counts. However, uptake of this tool remains inconsistent, and many eligible patients are not tested, resulting in missed or delayed diagnoses [11].

In addition to diagnostic gaps, preventive strategies for tuberculosis are underutilized among people with advanced HIV disease. Delays in initiating TB treatment, lack of systematic screening, and inconsistent use of preventive therapy all contribute to avoidable mortality. These failures reflect both logistical constraints and fragmented service delivery, particularly where HIV and TB programs operate in parallel rather than in an integrated manner [12].

Cryptococcal disease is another major driver of preventable death, particularly in sub-Saharan Africa. Cryptococcal meningitis carries a high case fatality rate, even with treatment, but outcomes are substantially improved when infection is detected early. Robust evidence supports routine cryptococcal antigen screening for individuals with low CD4 counts, followed by pre-emptive antifungal therapy for those who test positive. Despite clear recommendations and demonstrated mortality benefit, implementation of cryptococcal screening remains incomplete in many high-burden settings. Limited access to diagnostics, delays in laboratory processing, and inconsistent availability of antifungal medications continue to undermine effective prevention [13].

Other opportunistic infections, including *Pneumocystis jirovecii pneumonia*, severe bacterial infections, and *toxoplasmosis*, also contribute significantly to early mortality. These conditions often present with non-specific symptoms and require a high index of clinical suspicion. Cotrimoxazole prophylaxis has been shown to reduce morbidity and mortality across a range of infections, yet gaps in coverage persist, particularly among individuals re-entering care. Collectively, these infections illustrate that preventable mortality in advanced HIV disease is driven not by lack of effective interventions, but by failures in timely identification and comprehensive preventive care [14].

2.4. Non-AIDS Conditions and Competing Causes of Death

As people living with HIV survive longer on ART, non-AIDS conditions have emerged as important contributors to mortality. However, among individuals with advanced HIV disease, these conditions often intersect with severe immunosuppression in complex ways. HIV-associated malignancies, chronic liver disease related to viral hepatitis, and cardiovascular complications may be accelerated by immune dysfunction and chronic inflammation. In advanced disease, these conditions are frequently under-recognized or diagnosed late, as clinical attention is focused primarily on opportunistic infections.

Diagnostic overshadowing is common in this context. Symptoms such as weight loss, fever, or neurological impairment are often attributed to opportunistic infections, delaying recognition of malignancy or other non-infectious conditions. Limited diagnostic capacity further constrains timely identification. While non-AIDS conditions account for a smaller proportion of deaths than opportunistic infections in advanced HIV disease, they contribute to overall mortality and reflect the need for more comprehensive and integrated clinical evaluation [15].

2.5. ART Initiation, Immune Reconstitution, and Early Mortality

Rapid initiation of antiretroviral therapy is a cornerstone of contemporary HIV treatment and has clear benefits for long-term outcomes. In the context of advanced HIV disease, however, the timing of ART initiation requires careful clinical judgment. Early ART reduces viral replication and supports immune recovery, but it may also precipitate immune reconstitution inflammatory syndrome, particularly in the presence of untreated opportunistic infections. IRIS can be severe and, in some cases, fatal, especially when it involves the central nervous system.

Balancing the urgency of ART initiation with optimal management of opportunistic infections remains a clinical challenge. Evidence suggests that short delays in ART initiation for specific conditions, such as cryptococcal meningitis, can improve survival by reducing the risk of severe IRIS. In practice, however, such nuanced approaches are difficult to implement in overstretched health systems with limited specialist support. As a result, patients may either experience harmful delays in ART initiation or be started on treatment without adequate screening and prophylaxis, both of which contribute to early mortality [16].

2.6. Health System and Programmatic Drivers of Preventable Mortality

Beyond clinical factors, health system weaknesses play a central role in sustaining preventable mortality among individuals with advanced HIV disease. Fragmentation between HIV and TB services remains a major barrier to comprehensive care, leading to missed diagnoses and delayed treatment. Referral pathways are often weak, particularly between inpatient and outpatient settings, resulting in loss to follow-up during critical periods.

Supply chain failures, including stock-outs of essential diagnostics and medicines, further undermine effective care. Even where guidelines recommend routine screening and prophylaxis, implementation is constrained by inconsistent availability of tests and treatments. Workforce limitations, high patient volumes, and insufficient training contribute to gaps in clinical decision-making, particularly in recognizing and managing advanced disease. These systemic failures disproportionately affect the sickest patients, for whom delays and omissions carry the highest risk of death [17].

2.7. Structural and Social Determinants

Preventable mortality in advanced HIV disease is also shaped by broader structural and social determinants. Poverty limits access to timely testing, transport to health facilities, and sustained engagement in care. Stigma and discrimination continue to discourage early health-seeking

behavior and contribute to treatment interruption. Gender norms influence patterns of care-seeking, particularly among men, who are more likely to present late and experience poor outcomes.

Criminalization and marginalization of key populations further exacerbate these challenges by restricting access to services and undermining trust in health systems. These factors operate upstream of clinical care, shaping who presents with advanced disease and who survives. Addressing preventable mortality in advanced HIV disease therefore requires not only clinical and programmatic interventions, but also sustained efforts to reduce structural barriers and promote equitable access to care [18].

3. Methodological Approach of the Review

This article was conducted as a narrative, non-systematic review examining preventable mortality among individuals with advanced HIV disease in the era of universal antiretroviral therapy. A narrative approach was deliberately selected to enable integration of clinical evidence, programmatic experience, and health system analyses, including policy documents and implementation guidance that are not easily captured through systematic review methodologies. The aim was to generate interpretive and policy-relevant insights rather than an exhaustive or quantitative synthesis of the literature.

A targeted literature search was undertaken across major biomedical and public health databases, including PubMed, Embase, and Web of Science. The search focused on publications released between January 2010 and December 2025, corresponding to the period following the global adoption of Treat All and universal ART policies. Search terms combined concepts related to advanced HIV disease, preventable mortality, opportunistic infections, immune suppression, antiretroviral therapy initiation, and health system delivery. Database searches were complemented by manual screening of reference lists from key publications to identify additional relevant studies.

In addition to peer-reviewed articles, the review incorporated global normative guidance, technical reports, and policy documents from the World Health Organization and other international health agencies. Evidence was prioritized based on relevance to advanced HIV disease, mortality outcomes, and the delivery or implementation of recommended preventive and clinical interventions. Particular emphasis was placed on landmark studies, large cohort analyses, randomized trials informing clinical practice, and recent implementation studies reflecting real-world care in the universal ART era. Formal inclusion or exclusion criteria were not applied, consistent with the narrative review design.

The synthesis followed a thematic analytical framework centered on the concept of preventability. Evidence was organized across three interconnected domains: (1) biological and clinical drivers of early mortality, including opportunistic infections and immune reconstitution; (2) health system and programmatic factors influencing diagnosis, triage, and continuity of care; and (3) structural and social determinants shaping access to services and sustained engagement in care. Findings were interpreted through integration of clinical outcomes data with health system and implementation perspectives, with particular attention to areas where effective interventions exist but are inconsistently applied.

Overall, this narrative synthesis drew on approximately 120–150 peer-reviewed articles, global guidelines, and technical reports identified through database searches and reference screening. Given the global distribution of advanced HIV disease and HIV-related mortality, particular emphasis was placed on evidence from high-burden low- and middle-income countries, especially sub-Saharan Africa, while incorporating relevant data from other regions where available.

This methodological approach was intended to highlight critical implementation gaps, contextualize preventable mortality within broader health system failures, and identify policy-relevant opportunities to improve survival among individuals with advanced HIV disease.

4. Discussion

4.1. Why Preventable Mortality Persists in the Universal ART Era

The persistence of preventable mortality among individuals with advanced HIV disease in the era of universal antiretroviral therapy reflects a fundamental disjunction between scientific progress and service delivery. Over the past two decades, the HIV field has generated a robust arsenal of effective tools, including potent antiretroviral regimens, rapid diagnostics, and evidence-based prophylactic strategies. However, these advances have not been translated into consistent, high-quality care for those presenting with severe immunosuppression. Mortality in advanced HIV disease is therefore less a consequence of therapeutic inadequacy than of systemic failure to deploy available interventions at the point of greatest need [19].

A contributing factor has been the dominant focus on population-level treatment indicators, particularly ART coverage and viral suppression. While these metrics are essential for monitoring epidemic control, they obscure the experiences of individuals at the margins of care. Patients with advanced HIV disease represent a relatively small but high-risk group whose outcomes are not adequately captured by aggregate indicators. As programs have shifted toward simplified, high-throughput models of care, the complexity of managing advanced disease has often been deprioritized, leaving frontline providers ill-equipped to identify and manage severe illness in a timely manner [20].

4.2. Implementation Gaps in the WHO Advanced HIV Disease Package of Care

The World Health Organization has issued clear recommendations for a comprehensive package of care for advanced HIV disease, encompassing rapid ART initiation alongside targeted screening and prophylaxis for opportunistic infections. When implemented as intended, this package reduces mortality. Yet, evidence from multiple settings indicates that uptake remains incomplete. Diagnostic tools such as urine lipoarabinomannan testing and cryptococcal antigen screening are underutilized, even where they are available, and prophylactic interventions are inconsistently prescribed [21].

These gaps reflect weaknesses in accountability and monitoring. Advanced HIV disease indicators are rarely tracked with the same rigor as ART initiation or viral suppression, limiting programmatic visibility of high-risk patients. In the absence of routine reporting and performance benchmarks, implementation of advanced disease care is often left to individual clinicians rather than embedded within health system processes. This variability undermines the potential impact of existing guidelines and perpetuates preventable mortality. Rather than reflecting gaps in biomedical knowledge, mortality in advanced HIV disease is best understood as the product of systemic failures across the

care continuum [22]. Table 1 presents a conceptual mapping of these failures, illustrating where existing health system processes fall short and where targeted interventions could substantially reduce preventable deaths.

Table 1: Advanced HIV Disease as a Health System Failure: Points of Breakdown Across the Care Continuum

Stage Care Continuum	Optimal Care Standard	Current Practice Gap	Patient Impact	System-Level Solution
HIV diagnosis and linkage	Early HIV testing with rapid linkage to care	Late diagnosis or delayed linkage	Presentation with severe immunosuppression	Expanded targeted testing and same-day linkage
Clinical triage at presentation	Identification of advanced disease and urgent risk stratification	Advanced disease not recognized or deprioritized	Delayed investigation and initiation of treatment	Routine AHD screening and standardized triage protocols
Diagnostic evaluation	Rapid screening for TB, cryptococcal disease, and severe bacterial infection	Limited or delayed access to diagnostics	Missed or late diagnosis of life-threatening infections	Point-of-care diagnostics and reflex testing
ART initiation	Timely ART with appropriate management of opportunistic infections	ART delayed or initiated without adequate screening	Increased risk of early mortality or severe IRIS	Condition-specific ART timing algorithms
Inpatient management	Integrated, care multidisciplinary care	Fragmented care across services	Incomplete treatment and inadequate monitoring	Integrated HIV–TB inpatient care models
Transition to outpatient care	Structured discharge planning and close follow-up	Loss to follow-up after hospitalization	Preventable post-discharge deaths	Strengthened referral and follow-up systems
Program monitoring	Routine tracking of AHD outcomes and mortality	Focus limited to ART coverage and viral suppression	High-risk population remains invisible	Inclusion of AHD indicators in national reporting

This table synthesizes key stages in the HIV care continuum where health system and programmatic failures contribute to preventable mortality among individuals with advanced HIV disease. Rather than reiterating clinical causes of death, the table highlights mismatches between recommended care and routine practice, illustrating how cumulative breakdowns in diagnosis, triage, service integration, and follow-up amplify mortality risk. The framework emphasizes actionable opportunities for system-level intervention to improve survival in the era of universal antiretroviral therapy.

4.3. Reframing Advanced HIV Disease as a Health System Emergency

To frame advanced HIV disease as a health system emergency rather than a clinical inevitability, Figure 1 presents a conceptual overview of how failures across the care continuum converge to drive preventable mortality despite the availability of effective interventions. Addressing preventable mortality in advanced HIV disease requires a conceptual shift in how such patients are prioritized within health systems. Advanced disease should be treated as a clinical emergency requiring rapid, coordinated, and resource-intensive care. Standard outpatient models designed for stable patients on long-term ART are poorly suited to the needs of individuals with severe immunosuppression, who often require immediate diagnostics, inpatient management, and close follow-up during the early weeks of treatment [23].

Differentiated care models that explicitly account for disease severity are urgently needed. Integration of inpatient and outpatient HIV services is particularly critical, as transitions between these settings represent periods of high risk for loss to follow-up and missed interventions. Strengthening clinical triage, ensuring continuity of care after hospitalization, and aligning service delivery around patient acuity rather than treatment status would represent important steps toward reducing early mortality [24].

This conceptual framework illustrates how preventable mortality in advanced HIV disease arises from the interaction between structural and social determinants, health system and programmatic gaps, and severe biological vulnerability. Delayed diagnosis, fragmented services, and limited access to timely diagnostics and integrated care contribute to late presentation with advanced disease and high early mortality. The figure highlights key intervention points where comprehensive implementation of WHO-recommended advanced HIV disease care, integrated inpatient–outpatient services, and differentiated, high-intensity follow-up could interrupt progression to avoidable death.

4.4. Implications for Policy and Practice

From a policy perspective, advanced HIV disease must be elevated within national HIV strategies as a priority population requiring targeted investment. This includes dedicated funding for diagnostics, essential medicines, and training focused on advanced disease management. Task-shifting and decentralization of services, when accompanied by adequate support and supervision, can expand access to life-saving interventions, particularly in resource-limited settings.

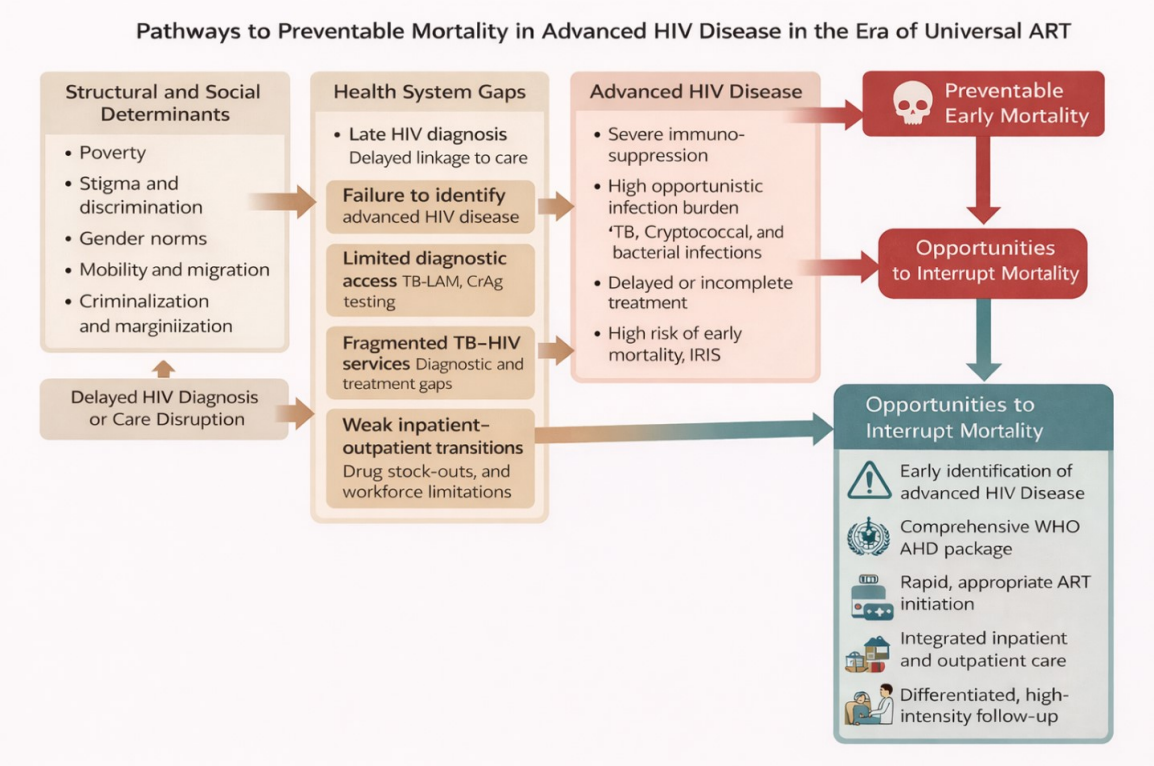

Figure 1: Pathways to Preventable Mortality in Advanced HIV Disease in the Era of Universal Antiretroviral Therapy

Point-of-care diagnostics offer a critical opportunity to shorten time to diagnosis and treatment, especially in facilities with limited laboratory infrastructure. Equally important is the development of robust strategies to re-engage ART-experienced individuals who return to care with advanced disease. These patients often fall outside standard care pathways and require tailored approaches that address both clinical complexity and the social drivers of disengagement [25].

4.5. Research and Programmatic Priorities

Future research should prioritize implementation science approaches that evaluate how best to deliver comprehensive advanced HIV disease care in real-world settings. Operational studies examining service integration, workforce models, and diagnostic algorithms are needed to inform scalable solutions. Mortality audits and real-time use of routine data can help identify avoidable deaths and guide quality improvement efforts.

Innovations in community-based and differentiated service delivery also warrant further exploration. While advanced HIV disease often necessitates facility-based care, community interventions may play a role in early identification, linkage to care, and post-discharge follow-up. Understanding how these models can be effectively integrated into existing health systems is essential [26].

4.6. Strengths and Limitations of This Review

This review synthesizes a broad range of clinical and programmatic evidence to provide an integrated perspective on preventable mortality in advanced HIV disease. By focusing on implementation gaps and health system dynamics, it offers policy-relevant insights that extend beyond clinical outcomes alone. However, the narrative and non-systematic nature of the review introduces the possibility of selection bias, and findings should be interpreted as illustrative rather than exhaustive. Despite these limitations, the convergence of evidence across settings supports the central conclusion that most deaths associated with advanced HIV disease are preventable with existing tools. As a narrative review, study selection was inherently interpretive and may be subject to selection bias; however, the convergence of findings across diverse settings and study designs supports the robustness of the conclusions.

5. Conclusion

Advanced HIV disease remains a persistent and lethal condition in the era of universal antiretroviral therapy. Despite major global gains in treatment access and viral suppression, a substantial share of HIV-related deaths continues to occur among individuals who present with, or return to care with, severe immunosuppression. Mortality in this population is concentrated in the early weeks of clinical contact and is driven predominantly by opportunistic infections and complications that are well characterized and, in many cases, preventable. The persistence of these deaths underscores a critical disconnect between scientific capability and routine health system delivery.

Evidence synthesized in this review demonstrates that the majority of deaths associated with advanced HIV disease could be averted through timely diagnosis, systematic screening for opportunistic infections, appropriate prophylaxis, and integrated clinical management. Rapid diagnostic tools, effective antifungal and antibacterial therapies, and optimized antiretroviral regimens are widely available and supported by strong clinical evidence. However, their impact has been undermined by inconsistent implementation, fragmented service delivery, and the continued marginalization of advanced disease within HIV programs. Consequently, those at highest risk of death are often

least likely to receive comprehensive, life-saving care.

These findings highlight the limitations of relying on universal ART coverage alone as a marker of programmatic success. While treatment scale-up remains essential, it is insufficient to eliminate HIV-related mortality without parallel investments in the quality, intensity, and coordination of care for individuals with advanced disease. Health systems must move beyond simplified, one-size-fits-all models and adopt differentiated approaches that recognize advanced HIV disease as a medical emergency requiring rapid, coordinated, and resource-intensive intervention. Full implementation of comprehensive packages of care for advanced disease should be treated as a core function of national HIV strategies rather than an optional add-on.

Preventable mortality in advanced HIV disease represents a failure of delivery rather than a failure of discovery. The knowledge and tools required to save lives already exist. Translating evidence into survival gains will require urgent action in four priority areas: scaling up access to point-of-care diagnostics for tuberculosis and cryptococcal disease, particularly in inpatient and high-volume settings; integrating inpatient and outpatient HIV services to ensure continuity of care during periods of highest mortality risk; incorporating advanced HIV disease indicators, including early mortality, into routine program monitoring to strengthen accountability; and explicitly prioritizing advanced HIV disease within national strategies and funding frameworks. Without these targeted investments and system-level reforms, preventable mortality will persist, and the promise of universal antiretroviral therapy will remain unrealized for those who need it most.

Article Information

Disclaimer (Artificial Intelligence): The author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.), and text-to-image generators have been used during writing or editing of manuscripts.

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