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Beating HIV from day 1: strengthening same-day antiretroviral therapy in South Africa: challenges, realities, and the path forward

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Abstract

Same-day initiation of antiretroviral therapy (ART), known as same-day ART, has been endorsed by the World Health Organization since 2017 as a strategy to improve treatment coverage, reduce HIV transmission, and increase the survival of people living with HIV. This approach aims to minimize loss to follow-up (LTFU) and strengthen engagement in care, particularly in high-prevalence settings such as South Africa. This review aims to synthesize available data on the benefits, challenges, and impacts of same-day ART, with a particular focus on resource-limited settings. A literature review was conducted on published studies that addressed the effectiveness, adherence, retention in care, and clinical outcomes associated with same-day ART. The studies indicate that same-day ART is associated with a significant improvement in treatment initiation and reduced delays in therapy. However, its success depends on several factors, including patient acceptability, healthcare system capacity, and the quality of psychosocial support. Increased risks of long-term LTFU have also been reported among certain vulnerable populations. Same-day ART represents a major advancement in the fight against HIV, but its implementation requires a contextualized approach, adequate training of healthcare providers, and strengthened psychosocial support to ensure long-term retention in care.

Keywords: *HIV infection. Same-day antiretroviral therapy. Health system situation and challenges. South Africa.*

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Introduction

To tackle ongoing challenges related to the initiation of ART, the National Department of Health (NdoH) introduced same-day initiation (SDI), which entails beginning ART on the day an individual receives a human immunodeficiency virus (HIV) diagnosis[1]. In August 2017, a circular from the NDoH was issued, urging all public health facilities to enhance ART initiation for every individual infected with HIV, aligning with universal test and treat (UTT) guidelines, and specifically aiming to offer SDI to those recently diagnosed with HIV who are both clinically and psychologically ready for lifelong ART[1,2]. Clinical readiness involves screening for symptoms of tuberculosis (TB) and Cryptococcal meningitis, as it is important to postpone the initiation of antiretroviral therapy (ART) for clients with these conditions to reduce complications such as immune reconstitution inflammatory syndrome (IRIS)[2]. When effectively executed, streamlined delivery of care (SDI) can help prevent the dropout of ART-eligible clients from pre-ART services before treatment starts, which has been an issue in various sub-Saharan African regions, including South Africa[3,4]. Multiple randomized trials have demonstrated that rapid ART initiation offers several advantages compared to delayed ART start, such as enhanced ART engagement by 6 months, improved retention in care after 6 months, higher viral suppression rates at 6 months, and reduced mortality risk[5,6]. Despite efforts to enhance treatment outcomes through SDI, adverse treatment results have still been observed in sub-Saharan Africa. Consequently, there is a lack of developed and tested tools in the literature that can monitor and provide close support for newly diagnosed individuals living with HIV, which is essential for strengthening the implementation of SDI. This literature review, therefore, aims to explore the benefits and limitations of SDI in South Africa, with a focus on addressing the central research question: What are the key factors limiting the effectiveness and sustainability of same-day ART initiation in the South African context?

Same-day initiation of ART

Rationale and global evidence for same-day ART

Starting ART on the same day an individual is diagnosed with HIV has emerged as a critical strategy in the global response to the HIV epidemic. This approach aims to improve treatment uptake and patient outcomes by minimizing delays between diagnosis and treatment initiation. Studies have shown that same-day ART enhances engagement in care and promotes better health outcomes for people living with HIV (PLHIV)[7,8]. Notably, these studies reported no significant adverse effects associated with rapid ART initiation in both randomized controlled trials (RCTs) conducted in low- and middle-income countries and observational cohorts in high-income settings.

According to Günthard et al., Bovinton et al., and Ford et al.[9-11] same-day ART plays two essential roles. First, it helps control the HIV epidemic by supporting the principle that an undetectable viral load eliminates the risk of HIV transmission (U = U). Second, it contributes to improved individual health outcomes by enabling early treatment. In low-resource settings, where laboratory and baseline assessments may be limited, same-day ART typically refers to initiating treatment on the very day of diagnosis[12]. A pivotal study by Koenig et al.[13] in Haiti developed an operational framework for implementing same-day ART. This approach, outlined in Fig. 1, demonstrated positive clinical outcomes and served as a model for rapid ART initiation protocols in similar contexts.

Regional experiences and implementation in Sub-Saharan Africa

Evidence from sub-Saharan Africa provides further insight into the benefits and limitations of same-day ART. For instance[14], evaluated the implementation of the "Treat All" strategy in Nigeria. Their findings revealed that patients offered same-day HIV testing and ART initiation were less likely to attend follow-up visits regularly compared to those who were already aware of their HIV status before initiating ART. Only 45% of the patients in their study attended a clinic visit in each of the four quarters during their 1st year of treatment[12], examining ART uptake across sub-Saharan Africa, highlighted that while many individuals are eligible for ART under the "treat-all" strategy, a significant proportion either refuse testing or choose not to engage in care despite knowing their status. Thus, although same-day ART increases eligibility, it does not automatically translate into successful long-term engagement.

In the SADC region[15], researchers reported that a fast-track, clinic-based ART initiation model in Lesotho significantly improved linkage to care and viral suppression outcomes shortly after diagnosis. These findings

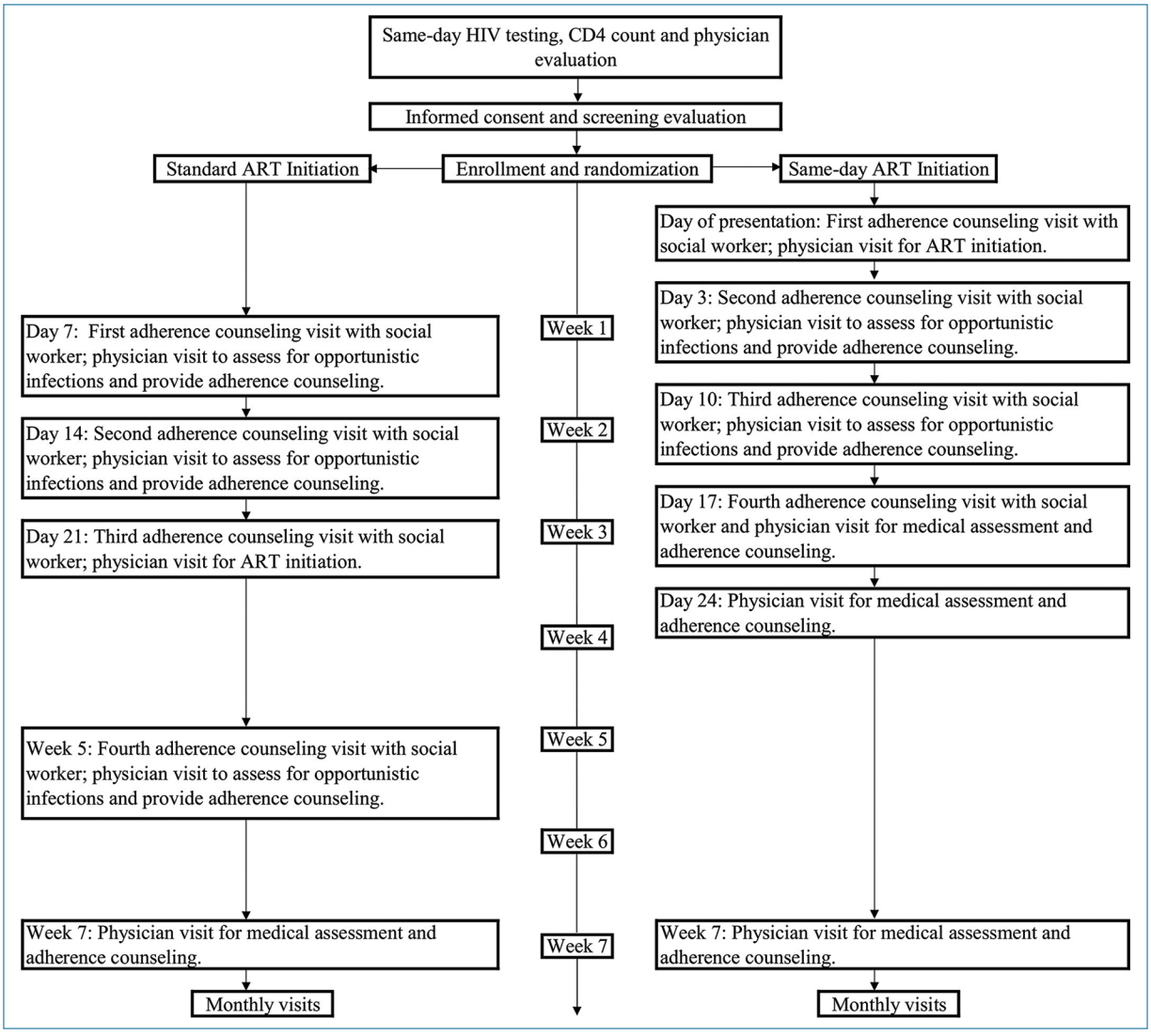

Figure 1. Research interventions for standard antiretroviral therapy (ART) and same-day ART groups[13].

reinforce the potential of same-day ART when implemented under well-structured protocols. In South Africa, same-day ART eligibility is currently guided by WHO clinical staging. Patients presenting signs or symptoms consistent with WHO Stage 3 or 4 conditions (such as TB or Cryptococcal meningitis) are excluded from immediate ART initiation to avoid complications such as IRIS. The current national eligibility framework is illustrated in Fig. 2.

Historical context of ART initiation protocols

The initial reports of acquired immunodeficiency syndrome (AIDS) emerged in 1981. Since that time, HIV infections have expanded globally, with an estimated 74.9 million individuals infected and 32 million suffering from AIDS-related conditions[16]. World Health Organization (WHO)[17] stated that for the first 15 years, no treatments were effective in managing or slowing the virus's spread. Over the last two decades, the guidelines set by the WHO regarding ART initiation have undergone significant changes[17]. The initial guidelines, released in 2002/2003, recommended starting ART for patients with AIDS-related conditions or a CD4 count of ≤ 200 cells/mm (Fig. 3). At that time, available treatments were both costly and risky[18].

As noted by Govere and Chimbari[19], delaying ART until a CD4 count fell below 200 cells/mm^3 was intended to minimize adverse effects. However, persistent AIDS-related deaths and ART effectiveness prompted

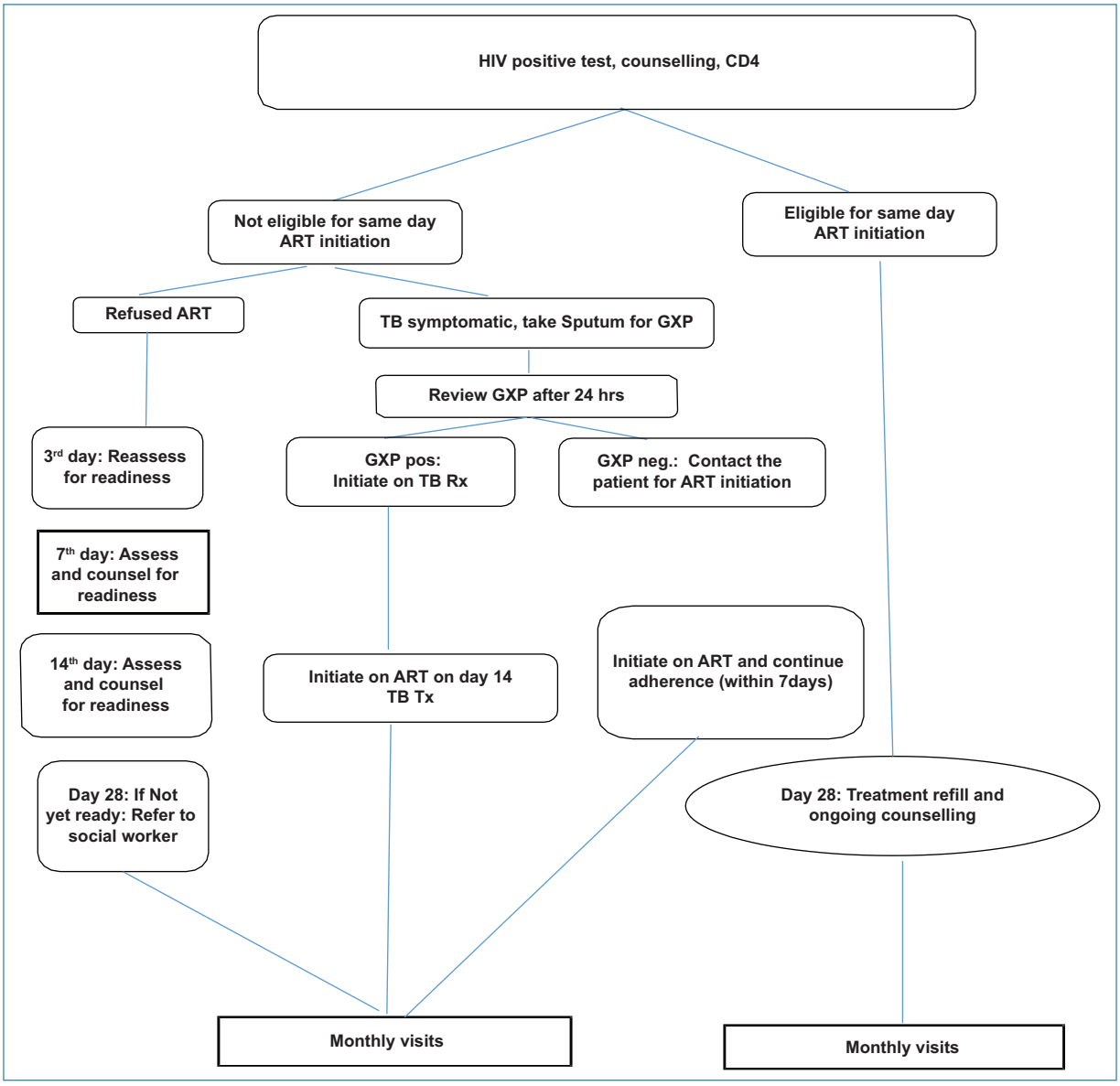

Figure 2. Same-day antiretroviral therapy initiation eligibility criteria in South Africa.

an increase in the CD4 threshold to 350 cells/mm^3 in 2006. In 2010, the limit was further raised to CD4 < 350 cells/mm^3, irrespective of the clinical stage. Then in June 2013, the standard was adjusted to CD4 < 500 cells/mm^3 for all individuals over the age of 5 and adults, regardless of clinical conditions or symptoms[20] (Fig. 3). By 2015, the WHO and various international organizations did away with the CD4 threshold, suggesting that ART should be given to everyone, irrespective of CD4 count or clinical stage[21]. This change resulted in the implementation of the UTT policy by all major international organizations, including the WHO. As reported by the WHO, adopting these guidelines on a global scale could avert 21 million deaths and result in 28 million fewer new infections by 2030[22] (Fig. 3).

Despite the progress made in HIV treatment and prevention, there remain considerable disparities in the global HIV crisis, with inequalities fueling the epidemic worldwide, particularly in low- and middle-income countries[23]. In their study, they further claim that since 2019, ART guidelines recommend that patients should be enrolled in treatment on the same day of their HIV status to optimize early linkage to care and subsequently achieve positive treatment outcomes such as retention in care and early viral load suppression (Fig. 4).

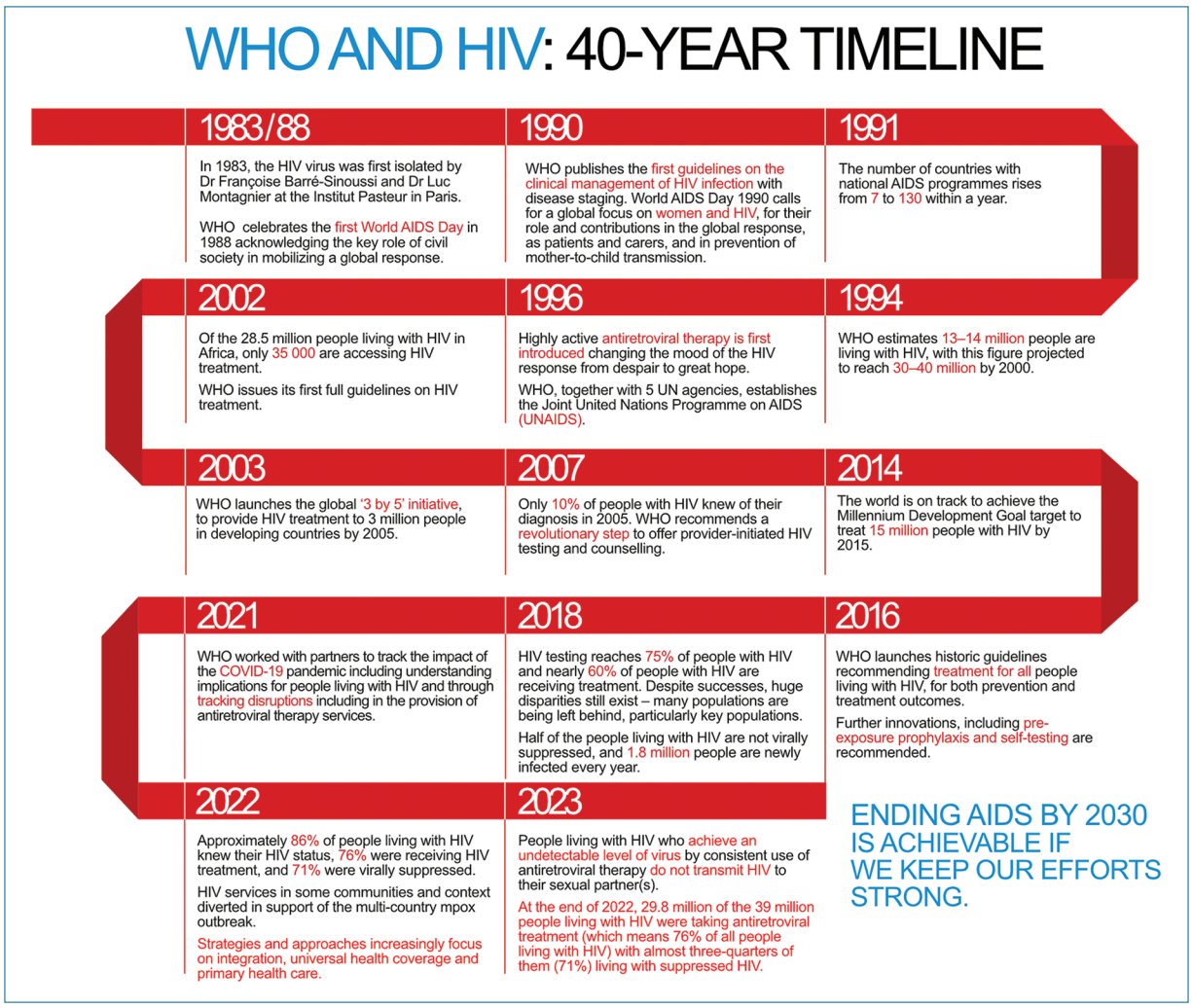

Figure 3. History of HIV in the 40-year timeline[24].

Current guidelines and recommendations for ART initiation

Current recommendations regarding the initiation of ART highlight the importance of starting treatment as soon as an individual is diagnosed with HIV, as this approach is crucial for enhancing the health and life expectancy of HIV patients, as well as for preventing the transmission of the virus to sexual partners, injection drug users, and infants. Research by Pathela et al. and Huhn et al.[25,26] indicates that rapid initiation of ART (within 7 days of diagnosis), which may include initiating treatment on the same day as diagnosis or during the first clinic visit, significantly increases the chances of patients engaging with HIV care and sustaining viral suppression over time. Based on existing evidence, ART should be commenced within 7 days of diagnosis, including on the actual day of diagnosis or at the initial clinic appointment, provided that the patient is prepared and there are no co-occurring opportunistic infections that could affect the timing of treatment initiation[23]. Since 2019, the recommended initial ART regimens for patients with HIV have included dolutegravir (DTG) due to its effectiveness, tolerability, safety, high resistance barrier, minimal pill burden, and low risk of drug–drug interactions[23]. According to Saag et al. and García-Ruiz de Morales et al.[27,28], a fixed dose of tenofovir disoproxil fumarate/lamivudine (3TC)/DTG is recommended for starting ART. According to their findings, abacavir is no longer recommended as the first-line treatment for the majority of HIV patients due to concerns about its link to cardiovascular disease, the risk of abacavir hypersensitivity, and the cost of HLA B*5701 testing.

When laboratory results are not available, it is recommended to begin early ART with DTG/3TC/TAF[29]. For individuals with an opportunistic infection, ART should

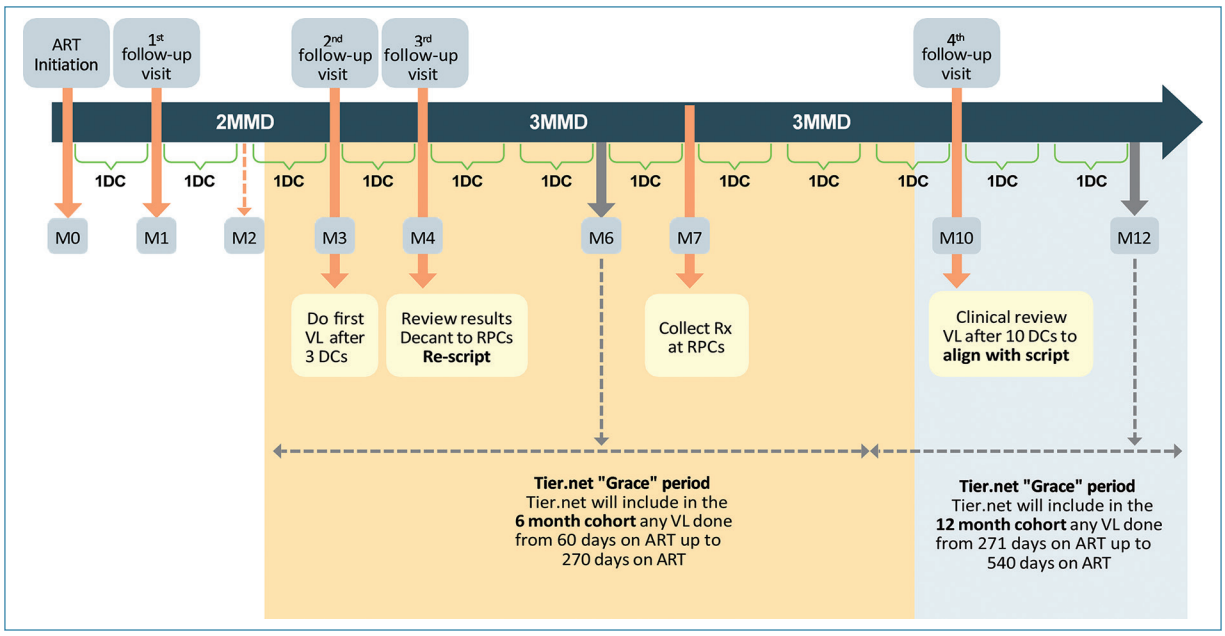

Figure 4. Diagram presenting the 2023 same-day antiretroviral therapy initiation guideline.

ideally start within 2 weeks of initiating treatment for the infection unless there is evidence indicating that delaying ART could pose a higher risk of morbidity or mortality due to IRIS[23].

The research suggests that individuals diagnosed with active TB should commence ART within 2 weeks of starting their treatment, particularly if their CD4 cell count falls below 50/μL[30]. Furthermore, advise that individuals with tuberculous meningitis receive high-dose steroids alongside their TB treatment, with ART initiation occurring within 2 weeks. In addition, individuals with Cryptococcal meningitis who have access to close monitoring and supportive care for potential side effects should start ART between 2 and 4 weeks after beginning antifungal therapy[23].

Benefits and challenges of same-day ART initiation

The provision of antiretroviral medication (ART) to persons infected with HIV has led to a better prognosis of sickness, a higher quality of life, and a reduction in HIV transmission[31]. HIV-positive people who begin ART on the same day as their HIV diagnosis, stick to treatment, and remain in care can reduce the HIV viral load in their serum to undetectable levels, removing the risk of spreading HIV to others[32,33]. The main advantage of starting ART on the same day, highlighted in studies from South Africa and Kenya, is an increase in prompt ART uptake[34]. Nevertheless, despite improved access to HIV testing and treatment services, the issue of individuals discontinuing antiretroviral medication (ART) remains a significant challenge for ART programs in low-income countries[35]. Their report also emphasizes that since the same day "test and treat" strategy is relatively new in developing nations, there exists limited evidence regarding the effectiveness of initiating ART on the same day as an HIV diagnosis.

The outcomes from published RCTs on same-day ART initiation in Haiti[13] and Lesotho[15] are challenging to apply to ART facilities with scarce resources for routine service delivery. Recent observational research assessing the nationwide implementation of "test and treat" in South Africa[36] and Haiti[37] revealed that although a larger proportion of PLHIV began ART on the same day as their diagnosis, those who started ART that day were less likely to remain engaged in care 6 months after initiating treatment in the 1st year of "test and treat" implementation. Individuals who began ART on the same day as their diagnosis had nearly 3 times the risk of loss to follow-up (LTFU) at 6 months in comparison to those who started ART more than 7 days prior[35]. In addition, another study also reported that individuals who initiated ART on the same day had higher odds of LTFU compared to those who began treatment more than 1 day later at the end of the 6-month follow-up period[36].

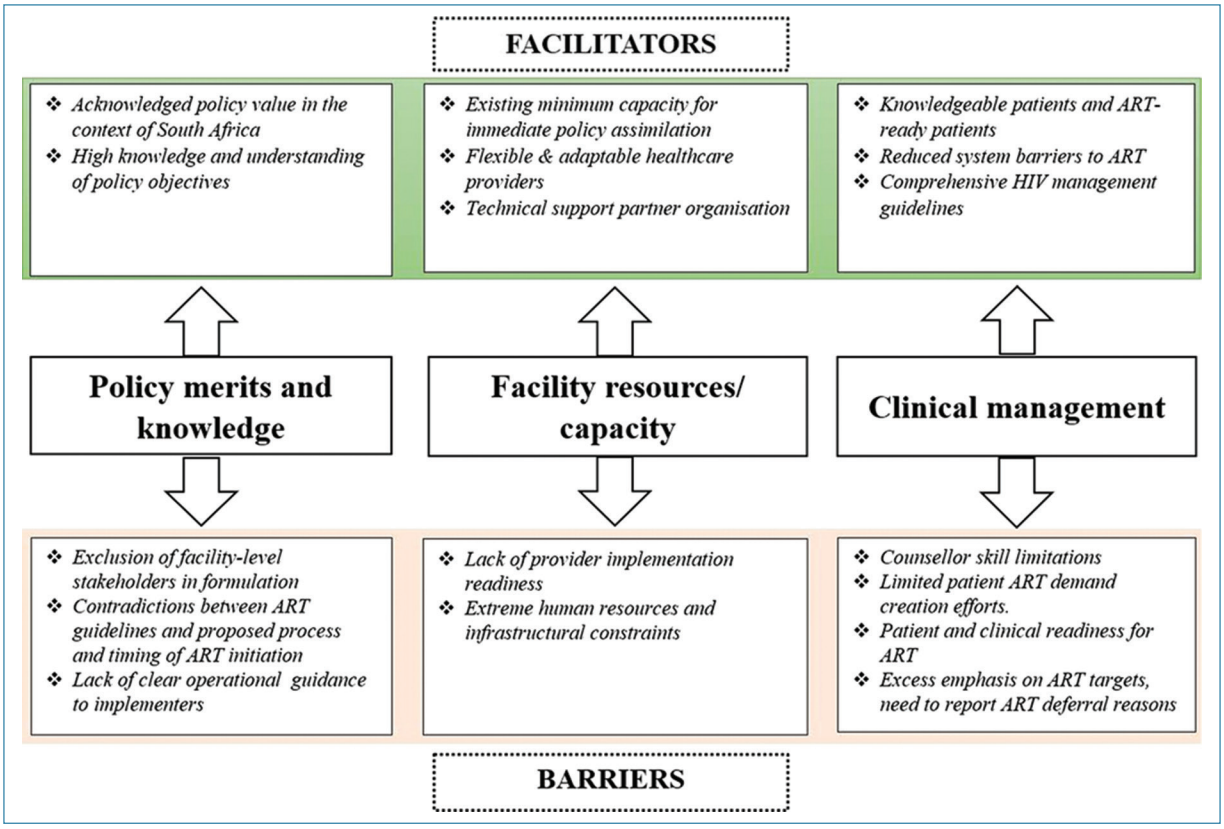

Figure 5. A summary of the hurdles and facilitators to same-day antiretroviral therapy policy implementation at basic healthcare institutions in South Africa[38].

Healthcare providers' perspectives and experiences with same-day ART initiation

In South Africa, a health provider's perspective on the implementation of SDI policy was investigated, where the facilitators of the policy were compared against the barriers to implementing the policy[38]. In their analysis, they discovered that healthcare practitioners were aware of the policy changes and appreciated the importance of initiating ART early, not only to improve clinical results but also to avoid transmission to HIV-negative partners. They further assert that healthcare providers also enjoyed the support they got from partners or non-government organizations that supported the facilities with the training and mentoring of the staff on the implementation of the same-day ART policy. However, barriers that were reported to hinder the implementation of the same-day ART policy, including, among others, health system resource and capacity challenges in South Africa, were discovered[38]. As noted by some studies, key challenges faced by healthcare providers include an increased workload coupled with limited healthcare infrastructure and inadequate health personnel[39,40]. Furthermore, other research indicates that while non-governmental organizations have contributed to the implementation of policies in South Africa and Sub-Saharan Africa, they frequently encounter difficulties in addressing long-term infrastructural challenges[41]. In addition, highlight that healthcare providers expressed uncertainty regarding strategies for evaluating ART readiness obstacles, as well as ways to keep patients engaged in the healthcare system who opt to postpone ART until they feel prepared to initiate treatment[38]. Moreover, other providers have pointed out that issues related to patient implementation, along with the pressure on clinicians to meet ART initiation targets, may unintentionally hinder attention to patient-specific factors influencing ART readiness[42].

Another healthcare professional involved in the research mentioned that patients who are unprepared and compelled to begin ART might withdraw from care, diminishing the potential advantages of the SDI policy provision[38]. Through interviews with healthcare providers, counseling is essential in helping patients accept their HIV-positive status and get ready for lifelong ART,

especially among those diagnosed while relatively healthy and who may not recognize the immediate benefits of starting ART early[11,43]. Fig. 5 illustrates the schematic representation of the findings from[38].

Standard operating procedure (SOP) for same-day ART initiation in South Africa

Several studies have developed SOPs for ART initiation in South Africa, highlighting the importance of standardized protocols in ensuring consistent quality care[13,38]. A review of existing SOPs reveals that while they provide valuable guidance on ART initiation, they often lack specific details on same-day initiation[44]. Although the fast-track initiation and counseling SOP aims at rapidly linking patients to HIV treatment after the diagnosis, same-day ART initiation is not explicitly described. The monitoring of these patients through patient navigation and out-of-the-facility psychosocial support is not clearly stated.

Comparison of existing SOPs

A comparison of SOPs developed in South Africa reveals that they often focus on general ART initiation protocols, with limited attention to same-day initiation[14,15]. For example, the National Department of Health's guidelines provide a framework for ART initiation, but do not specifically address same-day initiation[44]. Other studies have developed SOPs for specific contexts, such as primary care facilities or community-based programs[36,37].

Limitations of existing SOPs

Existing SOPs in South Africa have the following limitations: lack of specificity for same-day ART introduction[35], insufficient focus on patient preparation and psychosocial support[38], and inadequate guidelines for managing difficult cases or comorbidities[23].

Development of a new SOP for same-day ART Initiation

Given the limitations of the existing SOPs stated above, a new SOP explicitly addressing same-day ART commencement in South Africa is required[26]. This SOP should consider the specific constraints and potential of same-day commencement, such as patient preparation, healthcare system capacity, and psychosocial support[13]. By designing a personalized SOP, healthcare professionals may ensure that same-day ART commencement is carried out successfully and securely, eventually increasing treatment results and lowering transmission rates.

Key recommendation for new SOP

The new SOP for same-day ART introduction in South Africa should contain instructions for patient preparation and psychosocial assistance[38]. Further, the specific protocols for dealing with difficult situations or comorbidities[23] should also be outlined. In addition, guidelines for healthcare system capacity and resource allocation[37] must be developed. Finally, a focus on patient-centered treatment and confidentiality[29] should be prioritized. South Africa can improve the effectiveness and safety of its HIV treatment programs by establishing and implementing a tailored SOP for same-day ART commencement, resulting in better health outcomes and lower transmission rates[32].

Recommendations and future directions

In the future, it will be essential to step up qualitative research to better understand the psychological barriers to immediate treatment initiation and to adapt care models to patients' needs and preferences. Integrating community-based approaches, such as the use of peer coaches, could improve adherence and retention in care. In addition, particular attention will need to be paid to assessing the long-term effects of same-day ART, particularly in terms of sustained viral suppression, resistance to antiretrovirals, and quality of life. Finally, healthcare policies will need to support this strategy through ongoing training of staff and better allocation of resources in primary care facilities.

Conclusion

The strategy of initiating antiretroviral treatment on the same day as diagnosis represents a turning point in the management of HIV, particularly in high-prevalence countries such as South Africa. Available data confirms its effectiveness in reducing the time taken to start treatment and improving public health indicators. However, the approach is not suitable for all patients, and its implementation raises logistical, human, and ethical challenges. Individualized patient assessment, combined with a robust psychosocial support system,

is essential to ensure the long-term success of this strategy.

Author contributions

S. Nontamo designed the research, S. Nontamo, G. Tchuente-Kamsu, N. Agrinette-Madolo, and E.J. Ndebia operated the literature retrieval and data extraction, and wrote the paper. All authors read and approved the final manuscript.

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Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The study does not involve patient personal data nor requires ethical approval. The SAGER guidelines do not apply.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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