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Survival of Patients on ART in the Test-and-Treat Era: A Retrospective Cohort Study in Maputo, Mozambique

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Abstract

Introduction: As the 2030 global target for ending AIDS approaches, Mozambique continues to face significant challenges in HIV response. Although the test-and-treat strategy (TTS) has been in place for nearly a decade, survival outcomes remain suboptimal in many settings. We estimated the effect of TTS on survival among ART patients and identified associated factors in Maputo. **Method:** We conducted a retrospective cohort study with two arms—BTT (2013-2016) and ATT (2017-2020)—using routinely collected data from ART patients aged 15 - 49 years across 12 health facilities, in Maputo. Data were extracted from the electronic patient tracking system (ePTS/Open MRS). Survival was estimated using Kaplan-Meier methods; predictors of death were identified via Cox proportional regression, and population attributable fraction (PAF) was calculated to assess the impact of TTS. **Results:** Among 16,968 patients on ART (9036 BTT; 7932 ATT), 6258 HIV-related deaths occurred over 236,754 person-years follow-up. Mortality rate was lower in the ART arm (24.5 per 1000 person-year), with longer median survival time (50.6 months), than in the BTT arm (28.1 per 1000 person-year) in 43.1 months. Test-and-treat strategy had a protective effect against mortality (HR = 0.84%), with an adjusted PAF for the exposure of 7.3%. Increased hazard of death was consistently associated with older age, male sex, suburban residence, second-line ART, HIV-TB co-infection, advanced WHO stage, and low BMI. **Conclusions:** Test-and-treat strategy improved survival among ART patients in Maputo, strengthening its relevance for Mozambique and other low-income, high-HIV-burden countries. Future studies should examine its effects on subgroups, undocumented mortality and self-transfer.

Keywords

HIV, Antiretroviral Therapy, Test-and-Treat Strategy, Survival, Mozambique

1. Introduction

HIV remains a critical public health challenge [1] [2], especially in sub-Saharan Africa region, which accounts for nearly two-thirds of the global burden [3]. Since 1981, an estimated 85.6 million people have been infected and 40.4 million have died, ranking HIV among the deadliest pandemics in human history [4]. Mozambique has one of the highest HIV prevalence rates in the region, with 12.5% among adults and higher levels in urban areas, such as Maputo [5]. Over the past decade, substantial progress in ART scale-up has been made, followed by national policy reforms to improve access, retention, and survival of people living with HIV (PLHIV) [6] [7]. The 2015 introduction of the World Health Organization (WHO) Test-and-treat strategy (TTS) marked a paradigm shift in HIV care.

Evidence from observational studies and randomized trials across resource-limited settings consistently shows that early ART initiation improves clinical outcomes, reduces HIV incidence and decreases HIV-related morbidity and mortality [8]-[10]. However, social epidemiology underscores the importance of contextual factors in shaping the effectiveness of public health interventions such as TTS [11]-[13]. Despite notable progress following TTS implementation, major challenges persist, with adherence to ART, retention in care, and survival outcomes remaining suboptimal in many settings [14]-[16].

Studies from across sub-Saharan African (SSA) countries indicate that although the TTS has improved the overall survival, a substantial proportion of patients still experience early mortality, particularly within the first year of treatment [17]-[19]. Poor outcomes have been consistently associated with advanced clinical stage at treatment initiation, late presentation to care, male sex, and comorbidities such as tuberculosis [20] [21]. In Mozambique, this may also be the case; however, evidence remains limited, and little is known about survival among patients initiating ART under TTS, highlighting the opportunity to evaluate treatment outcomes in routine programmatic settings. Understanding survival outcomes and their predictors is essential for optimizing HIV programs, guiding resource allocation, and informing interventions to reduce preventable deaths. This study assessed survival among HIV-positive patients initiating ART under TTS and identified factors associated to survival, in Maputo.

2. Method

2.1. Study Design

We conducted a retrospective cohort study with two arms (cohorts) for comparative purpose: 1) BTT comprised ART patients not exposed to the TTS, selected from routinely collected data before its introduction (2013-2016); and 2) ATT included TTS-exposed patients on ART, selected from data after its introduction (2017-2020) (**Figure 1**). HIV diagnosis was confirmed through rapid test performed according to Ministry of Health (MoH) testing guidelines or by laboratory testing using the Enzyme-Linked Immunosorbent Assay (ELISA) technique [22].

Follow-up for each cohort began on the date of diagnosis and ended at death, loss to follow-up (no contact for >90 consecutive days), transfer out, or administrative censoring (June 30, 2016 for BTT; December 31, 2020 for ATT).

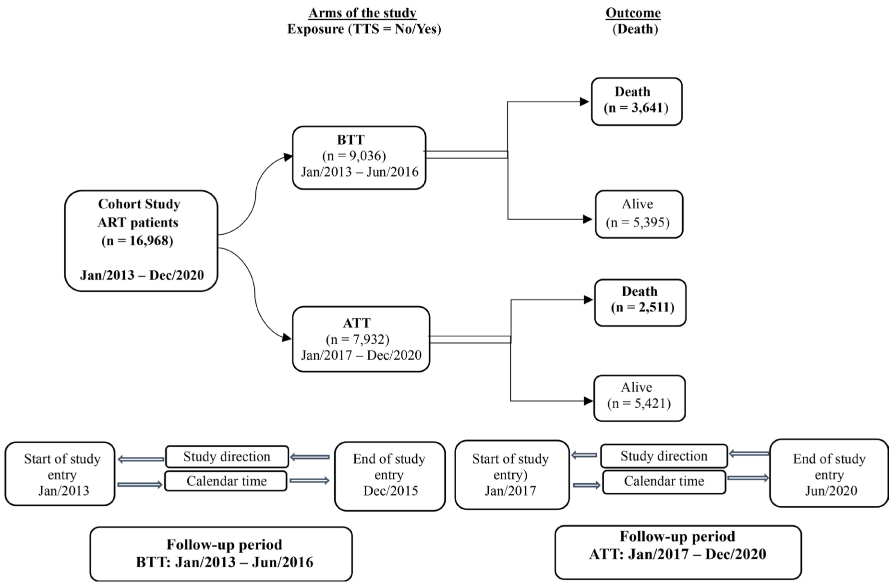

Figure 1. Follow-up of ART patients in BTT and ATT cohorts: exposures and outcomes. Maputo, 2013-2020.

2.2. Study Site

The study was conducted in Maputo, the capital city of Mozambique, which occupies an area of 347.69 km^2 and an estimated population of 1,120,867 (52% women) in 2017. Maputo is a high HIV-burden setting, where ART has been provided free of charge as part of the national HIV response. Data were collected in 12 health facilities delivering comprehensive HIV care across urban and peri-urban areas. This study is part of a larger project entitled "HIV & AIDS Challenges in a Low-Income Country: Survival and Retention of ART Patients in the Test-and-Treat Era in Maputo, Mozambique" (local institutional review board Ref.: 260/CNBS/20).

2.3. Data Source

Data were extracted from the national electronic patient tracking system (ePTS) – OpenMRS – which records living patients, those lost to follow-up, and HIV-related deaths. Causes of death are classified using clinical records and facility registers, with deaths from opportunistic infections, AIDS-defining illnesses, or advanced HIV coded as HIV-related. The ePTS also integrates sociodemographic, clinical, programmatic, pharmacy, and treatment-related information for people living with HIV enrolled in care.

2.4. Formation of Study Arms

The study population comprised HIV-positive adults aged 15 - 49 years diagnosed during 2013-2016 (BTT) or 2017-2020 (ATT), the latter corresponding to the nationwide introduction of the TTS in Mozambique. The analysis was restricted to patients aged 15 - 49 years to focus on the age group with the highest HIV prevalence and mortality burden in Mozambique, thereby ensuring comparability with national surveillance indicators. Patients were excluded if at diagnosis they had age out of the range; had incomplete baseline demographic data; were transfer-in cases from other HFs without a recorded diagnosis date. Also were excluded patients with events ≤ 30 days post-diagnosis and those with CD4 < 50 cells/mm^3 at the time of diagnosis, to minimize confounding from advanced disease and early mortality, which are unlikely to be influenced by time-to-switch (TTS) (**Figure 2**).

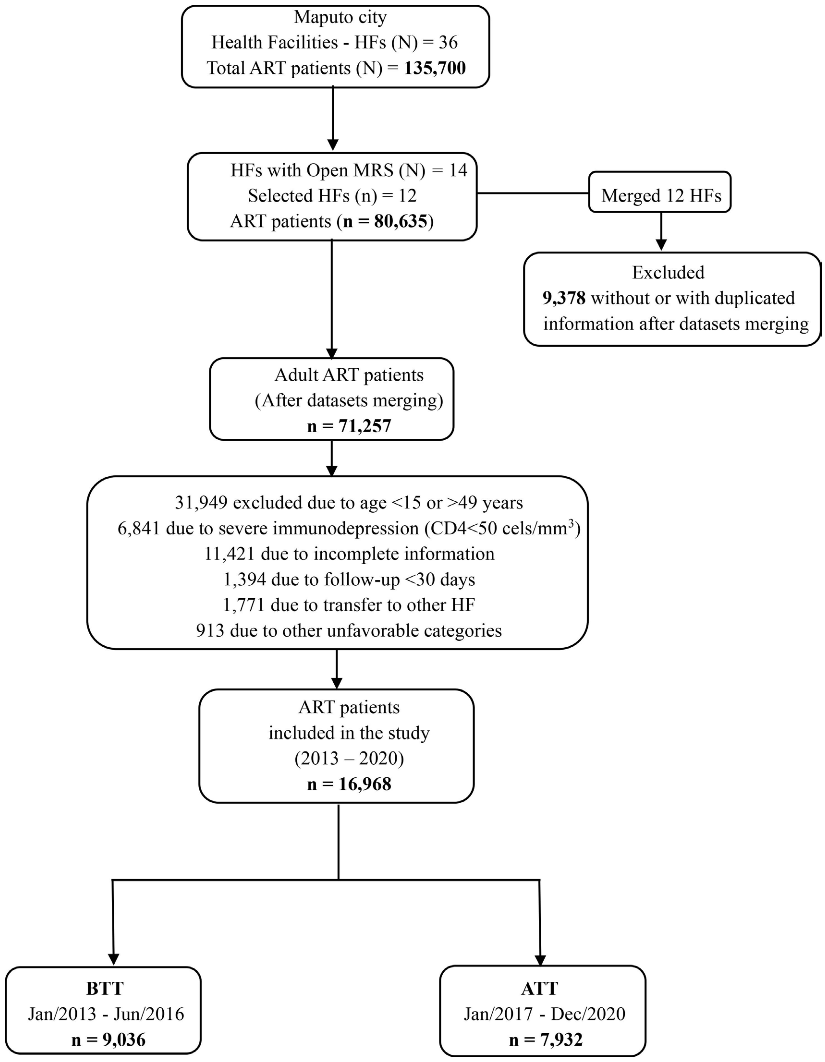

Figure 2. Exclusion criteria and formation of study arms for ART patients (BTT vs. ATT) aged 15 - 49 years. Maputo, 2013-2020.

2.5. Study Variables and Categorization

Covariates were grouped into three domains. Sociodemographic variables included sex (female = 0, male = 1), age (15 - 24 = 1; 25 - 39 = 2; 40 - 49 = 3), education (university = 0; 8th-12th grade = 1; 1st-7th grade = 2; none = 3), and region of residence (urban = 0; suburban = 1). Clinical variables included date of HIV diagnosis, WHO stage (I = 0; II = 1; III = 2; IV = 3), CD4 count (>350 cells/mm^3 = 0; 200 - 350 = 1; <200 = 2), viral load (<400 copies/ml = 0; ≥400 = 1), treatment regimen (first-line = 0; second-line = 1), HIV/TB co-infection (no = 0; yes = 1), and body mass index (normal [18.5 - 24.9 kg/m^2] = 0; overweight [>25] = 1; thinness [<18.5] = 2). Programmatic variables included test-and-treat (yes = 0; no = 1) and community ART group (CAG) membership (yes = 0; no = 1). For all covariates, category "0" was the reference. In both study arms, the outcome of interest was death and the exposure was TTS.

2.6. Data Analyses

Data analysis was performed separately for the BTT and ATT cohorts. Quantitative variables (age, CD4 count, viral load, and body mass index) were categorized. Baseline sociodemographic, clinical, and programmatic characteristics were summarized using descriptive statistics.

Kaplan-Meier methods were applied to estimate cumulative survival probabilities, and survival curves were compared using the log-rank test; for comparisons involving more than two groups, the log-rank test for trend was used [23]. Survival time was defined as the interval in months from HIV diagnosis to death (event) or censoring. The proportional hazards assumption was assessed both graphically and statistically. Censoring was applied in the following situations: 1) administrative, at study closure for patients alive; 2) non-HIV-related death; 3) date of last visit or antiretroviral (ARV) pickup for patients lost to follow-up; and 4) date of transfer to another facility. Mortality rates were calculated as the number of deaths divided by total person-time at risk [24].

Cox proportional hazards regression was used to identify factors associated with survival time, with results presented as hazard ratios (HRs) and 95% confidence intervals (CIs). Variables with $p < 0.20$ in bivariate analyses, along with those deemed biologically plausible, were included in the multivariable model. The final model was built using stepwise forward selection, while viral load was excluded from the inferential analysis due to incomplete data. Adjusted population attributable fraction ($PAF_{adj.}$) for the TTS-exposed group (ATT cohort) was calculated to estimate the impact of the strategy at populational-level, using the formula: $PAF_{adj.} = p_1(aHR - 1)/aHR$, where p_1 is the proportion of patients exposed to the risk factor; *aHR* is the adjusted hazard ratio for the risk factor [24] [25]. Data were analysed using R (version 3.6.1; R Foundation for Statistical Computing, Vienna, Austria) and Stata (version 14; Stata Corp, College Station, TX, USA).

2.7. Ethical Aspects

This study used de-identified routinely collected secondary data, ensuring strict patient confidentiality. Ethical approval was obtained from the National Committee for Bioethics in Health (CNBS) – Mozambique's IRB – under the Ref:

260/CNBS/20. Data access was authorized by the Maputo City Health Services and the Ministry of Health.

3. Results

The study was conducted between 2013-2020, during which a total of 16,968 ART patients were included, established in two cohorts: 9036 (53.3%) enrolled before TTS introduction (BTT) and 7932 (46.7%) after TTS introduction (ATT). Baseline characteristics were generally comparable between cohorts, except for sex distribution, with fewer females in the ATT cohort (41%) than in the BTT cohort (65%), likely due to temporal enrolment patterns. The distribution of other characteristics was generally comparable between both cohorts (**Table 1**). Kaplan–Meier curves indicated higher survival among patients in the ATT cohort compared with those in the BTT cohort (**Figure 3**).

Table 1. Baseline sociodemographic, clinical, and programmatic characteristics of ART patients by study arm (BTT vs. ATT). Maputo, 2013-2020.

Characteristics	BTT	ATT
	Total (n = 9036) N (%)	Total (n = 7932) N (%)
Sex		
Female	5903 (65)	3277 (41)
Male	3132 (35)	4655 (59)
Age range		
15 - 24	1203 (13)	952 (12)
25 - 39	4894 (54)	4189 (53)
40 - 49	2939 (33)	2791 (35)
Education		
>12 years (university)	2037 (22)	1796 (23)
8˚ - 12˚ year	3140 (35)	2760 (34)
1˚ - 7˚ year	2111 (23)	1888 (24)
None	1748 (20)	1488 (19)
Region of residence		
Urban	2504 (28)	3232 (41)
Suburban	6532 (72)	4700 (59)
HIV/TB co-infection		
No	5181 (57)	5687 (72)
Yes	3855 (43)	2245 (28)
WHO stage		
I	3812 (42)	3399 (43)
II	2874 (32)	2579 (32)

Continued

III	2026 (22)	1741 (22)
IV	324 (4)	213 (3)
ART regimen		
Line I	5242 (58)	5254 (66)
Line II	3794 (42)	2678 (34)
CD4 count* **		
>350 Cels/mm^3	6459 (71)	5601 (71)
200 - 350 Cels/mm^3	2146 (24)	1894 (24)
<200 Cels/mm^3	431 (5)	437 (5)
Loss to follow-up		
No	4384 (48)	4143 (48)
Yes	4652 (52)	3789 (52)
CAG# membership		
Yes	1571 (17)	2022 (25)
No	7465 (83)	5910 (75)
Body mass index (BMI)		
Thinness (<18.5 Kg/m^2)	964 (11)	858 (11)
Normal (18.5 - 24.9 Kg/m^2)	5316 (59)	4725 (60)
Overweight (>25 Kg/m^2)	2756 (30)	2349 (29)
Viral load		
Undetectable (<400 copies/ml)	1278 (14)	1306 (16)
≥400 copies/ml	4885 (54)	4027 (51)

BTT (Jan/2013-June/2016); **ATT (Jan/2017-Dec/2019); ***First CD4 count after diagnosis; #Community ART groups; n = simple size.

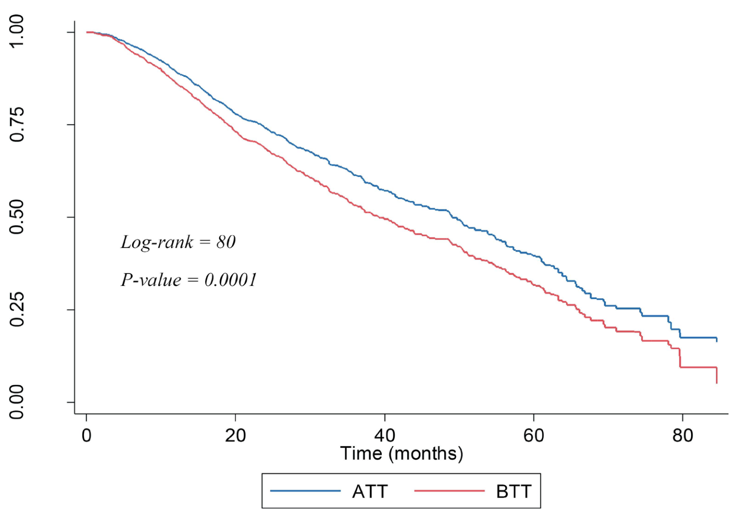

Figure 3. Comparison of ART patients' survival across study arms (BTT vs. ATT). Maputo, 2013-2020.

3.1. Mortality Rate

Among the 16,968 patients included in the study, 236,754 person-years of follow-up were accumulated, during which 6258 HIV-related deaths were recorded. In the BTT cohort, 9036 patients were included, contributing 125,910 person-years with 3542 HIV-related deaths. The ATT cohort comprised 7932 patients with 110,844 person-years of follow-up and 2716 deaths. The mean mortality rate was higher in the BTT cohort (28.1 per 1000 person-years) than in the ATT cohort (24.5 per 1000 person-years). Median survival time was also longer in the ATT cohort (50.6 months) compared to the BTT cohort (43.1 months).

3.2. Cumulative Survival Probability

Cumulative survival probabilities (CSP) in the BTT cohort were 95.2%, 89.9%, 77.9%, 70.0%, and 55.4% at 6, 12, 18, 24, and 36 months, respectively, with a median survival time (MST) of 43.1 months (3.6 years). In the ATT cohort, CSPs were 96.4%, 88.9%, 80.6%, 73.6%, and 60.6% at the same time points, with an MST of 50.6 months (4.2 years). Overall, MST and CSP were higher in the ATT cohort, indicating improvements in survival compared with the BTT cohort (Table 2).

Table 2. Median survival time (MST) of ART patients in the two cohorts (BTT vs. ATT) by sociodemographic, clinical, and programmatic characteristics (months). Maputo, 2013-2020.

Characteristics	Patients on ART	MST (Months)		*P value*[(£)]
	N	BTT*	ATT**	
Sex				<0.0001
Female	9181	49.0	56.3	
Male	7787	30.4	45.0	
Age range				<0.0001
15-24	2155	50.3	67.7	
25-39	9083	40.9	61.1	
40-49	5730	35.1	33.8	
Education				<0.0001
>12 years (university)	3833	38.3	50.2	
8˚ - 12˚ year	5900	39.9	50.5	
1˚ - 7˚ year	3999	39.1	46.0	
None	3236	40.6	48.8	
Regions of residence				<0.0001
Urban	5736	51.1	61.1	
Suburban	11232	35.8	41.8	
WHO stage				<0.0001
I	7211	43.9	51.1	

Continued

II	5453	41.5	49.0	
III	3767	35.4	48.7	
IV	537	26.4	32.9	
ART regimen				<0.0001
Line I	10496	48.6	50.6	
Line II	6472	33.8	44.0	
CD4 count* **				<0.0001
>350 Cels/mm^3	12060	39.3	49.8	
200 - 350 Cels/mm^3	4040	39.0	50.6	
<200 Cels/mm^3	868	39.3	34.7	
Loss to follow-up				<0.0001
No	8441	43.9	59.1	
Yes	8527	36.4	39.1	
CAG[($)] membership				<0.0001
Yes	13375	45.7	52.1	
No	3593	38.3	48.8	
Body mass index (BMI)				<0.0001
Normal (18.5 - 24.9 Kg/m^2)	10041	38.4	48.7	
Overweight (>25 Kg/m^2)	5105	45.0	56.4	
Thinness (<18.5 Kg/m^2)	1822	33.9	38.1	

[(£)]Likelihood ratio test; *BTT (Jan/2013-June/2016); **ATT (Jan/2017-Dec/2019); ***First CD4 count after diagnosis; [($)]Community ART groups; N = simple size.

The TTS was protective, reducing the hazard of death by 84%, independent of other predictors. The adjusted PAF for the exposure was 7.3%, indicating that the exposure was associated with a 7% reduction in the hazard of deaths at the population level. Factors associated with increased deaths included: non-exposure to TTS (HR = 1.16; 95% CI 1.10 - 1.22), age 25 - 39 (HR = 1.52; 95% CI 1.37 - 1.69) and 40 - 49 (HR = 2.16; 95% CI 1.94 - 2.41), suburban residence (HR = 1.45; 95% CI 1.36 - 1.54), male sex (HR = 1.41; 95% CI 1.33 - 1.49), second-line ART (HR = 1.19; 95% CI 1.13 - 1.26), HIV/TB co-infection (HR = 1.16; 95% CI 1.10 - 1.23), WHO stage IV (HR = 1.93; 95% CI 1.70 - 2.17), and BMI <18.5 kg/m^2 (HR = 1.18; 95% CI 1.07 - 1.29) (Table 3).

4. Discussion

To our knowledge, this is the first cohort study in Mozambique to estimate the effect of the TTS on survival among patients receiving ART in public HFs. Using survival analysis, we compared survival probabilities and mortality rates among patients initiating ART before and after the implementation of TTS in Maputo.

Table 3. Bivariate and multivariate analysis of factors associated with survival time among ART patients. Maputo, 2013-2020.

Characteristics	Bivariate HR. (IC95%)	Multivariate aHR. (IC95%)
Sex		
Female	1	1
Male	1.46 (1.38 - 1.53)	1.41 (1.33 - 1.49)
Age range		
15 - 24	1	1
25 - 39	1.61 (1.46 - 1.79)	1.52 (1.37 - 1.69)
40 - 49	2.40 (2.17 - 2.66)	2.16 (1.94 - 2.41)
Education		
>12 years (university)	1	---
8˚ - 12˚ year	0.98 (0.92 - 1.05)	---
1˚ - 7˚ year	1.00 (0.93 - 1.08)	---
None	0.98 (0.90 - 1.06)	---
Region of residence		
Urban	1	1
Suburban	1.50 (1.42 - 1.59)	1.45 (1.36 - 1.54)
HIV/TB co-infection		
No	1	1
Yes	1.33 (1.27 - 1.40)	1.16 (1.10 - 1.23)
WHO stage		
I	1	1
II	1.00 (0.95 - 1.07)	0.98 (0.92 - 1.04)
III	1.13 (1.06 - 1.21)	1.07 (1.00 - 1.14)
IV	1.72 (1.53 - 1.94)	1.93 (1.70 - 2.17)
ART regimen		
Line I	1	1
Line II	1.38 (1.32 - 1.46)	1.19 (1.13 - 1.26)
CD4b count		
>350 Cels/mm^3	1	---
200 - 350 Cels/mm^3	0.99 (0.93 - 1.05)	---
<200 Cels/mm^3	1.20 (1.08 - 1.33)	---
Loss to follow-up		
No	1	---
Yes	1.39 (1.32 - 1.47)	---
CAG membership		

Continued

Yes	1	---
No	1.19 (1.11 - 1.27)	---
Body mass index (BMI)		
Normal (18.5 - 24.9 Kg/m^2)	1	1
Overweight (>25 Kg/m^2)	1.26 (1.18 - 1.33)	1.04 (0.97 - 1.10)
Thinness (<18.5 Kg/m^2)	1.52 (1.40 - 1.66)	1.18 (1.07 - 1.29)
Test-and-treat strategy		
Yes	1	1
No	1.16 (1.10 - 1.22)	1.16 (1.09 - 1.22)

HR = crude hazard ratio; aHR = adjusted hazard ratio; ART = antiretroviral therapy; [b]First CD4 count after diagnosis.

In this study, patients exposed to TTS demonstrated higher median survival time and greater survival probabilities at 6, 12, 18, 24, and 36 months compared with those not exposed. The mortality rate was also lower in the post-TTS cohort (24.5 per 1000 person-years) than in the pre-TTS cohort (28.1 per 1000 person-years), corresponding to a 12.8% reduction following implementation. These findings are consistent with evidence from other settings. For example, a study in southern Ethiopia reported higher survival probabilities and lower mortality (2.4 per 100 person-years) among TTS-exposed patients, compared to 3.8 per 100 person-years among non-exposed patients [14]. Similarly, in Addis Ababa, mortality rates were 81.8 versus 92.4 per 1000 person-years among TTS-exposed and non-exposed patients, respectively [26]. Comparable trends have been observed in Eastern Uganda [27] and in Chengdu, China, where the study focused on men who have sex with men (MSM) [28]. Furthermore, a cluster-randomized community trial in KwaZulu-Natal, South Africa, demonstrated a 31.6% reduction in mortality, from 17.1 to 11.7 per 1000 person-years between the control and intervention groups [29].

Analysis of associated factors indicated that survival decreased with increasing age in both cohorts, with older patients experiencing a higher hazard of death compared to those aged 15 - 24 years. Notably, age-related differences in mortality narrowed following the introduction of TTS. These findings have important clinical and programmatic implications, underscoring the need for tailored interventions for older patients who remain at elevated risk. Similar age-related survival patterns have been documented in Ethiopia [30] and Brazil [31]. Disparities by region of residence were also evident, with higher mortality among patients living in suburban areas, consistent with observations from Gurage, Ethiopia [14].

HIV/TB co-infection was another significant predictor of survival, with co-infected patients experiencing a higher hazard of death than those without TB; nevertheless, the risk decreased following TTS implementation. These findings align with evidence from a systematic review and meta-analysis, as well as studies from southern Zambia and northwest Ethiopia [32]-[34]. Membership in CAGs was also associated with improved survival, highlighting the protective role of differentiated service delivery models and corroborating findings from Mozambique, Nigeria, and Uganda [35]-[37].

A key contribution of this study is the estimation of the adjusted PAF for the exposure. The PAF of 7.3% indicates that a modest but meaningful proportion of deaths in the study population were attributable to the absence of TTS. Although the impact on mortality was relatively smaller, these findings highlight the survival benefits of TTS among ART patients in Maputo. Overall, the findings suggest that widespread TTS implementation substantially improved survival in this study population. To date, no other cohort study in Mozambique has reported comparable findings. From a public health perspective, these results underscore the potential of TTS to improve ART outcomes and offer valuable evidence to guide policymakers and HIV program implementers in Mozambique.

This study is significant in three main areas: 1) it is among the first to evaluate the impact of TTS on survival among ART patients in Mozambique, providing evidence to inform the National HIV & AIDS Control Program; 2) it confirmed survival predictors identified in other sub-Saharan African contexts, reinforcing their relevance to the Mozambican setting; and 3) it highlighted the importance of monitoring undocumented mortality and patient self-transfer, which continue to challenge ART program success.

The study has several limitations. First, it relied on secondary data from public health service databases, which are often incomplete and may not fully represent individuals from higher socioeconomic backgrounds. Second, undocumented mortality and self-transfer could have led to overestimation of hazard ratios. Finally, the relatively short follow-up period for each cohort may have limited the ability to capture longer-term effects of TTS implementation

5. Conclusion

Test-and-treat strategy improved survival and reduced mortality among ART patients in Maputo, highlighting its relevance for Mozambique and other resource-limited, HIV high-burden settings. Future research should examine its effect on specific subgroups, undocumented mortality and self-transfer.

Contribution of Each Author

The study was fully designed, conducted, and reported by the primary author, with the co-author providing substantial contributions to the review process as required.

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Conflicts of Interest

The authors declare no conflicts of interest related to this study.

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Abbreviations

ARV	Antiretroviral
IRB	Institutional review board
ePTS	Electronic patient tracking system
Open MRS	Open medical record system
SSA	Sub-Saharan African
BTT	Before the introduction of test-and-treat
ATT	After the introduction of test-and-treat
TTS	Test-and-treat strategy
PAF	Population-attributable fraction
CAG	Community ART group
DSDM	Differentiated service delivery models
MoH	Ministry of Health
MST	Median survival time
PLHIV	People living with HIV
NHS	National health system
PS	Public service
MCHS	Maputo City Health Services
ART	Antiretroviral therapy
HF	Health facility