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Toward Universal HIV Treatment in Haiti: Time Trends in ART Retention Following Expanded ART Eligibility in a National Cohort from 2011-17

Nancy Puttkammer, MPH, PhD,
International Training and Education Center for Health (I-TECH), Department of Global Health, University of Washington, Seattle, WA

Canada Parrish, MPH, PhD(cand),
International Training and Education Center for Health (I-TECH) and Department of Health Services Research, University of Washington, Seattle, WA

Yrvel Desir, BA,
National Association of State and Territorial AIDS Directors (NASTAD), Port-au-Prince, Haiti

Nathaelf Hyppolite, MD, MSHI,
Independent Consultant, formerly with Centre Haitien de Renforcement du Système Sanitaire (CHARESS), Port-au-Prince, Haiti

Bradley Wagenaar, PhD,
Department of Global Health, University of Washington, Seattle, WA

Nadjy Joseph, MD, MBA,
National Association of State and Territorial AIDS Directors (NASTAD), Port-au-Prince, Haiti

Lara Hall, MD, MPH,
US Centers for Disease Control and Prevention, Port-au-Prince, Haiti

Jean Guy Honoré, MD, MPH,
Centre Haitien de Renforcement du Système Sanitaire (CHARESS), Port-au-Prince, Haiti

Ermane Robin, MD, MPH,
Programme National de Lutte contre le VIH/SIDA (PNLS), Ministère de Santé Publique et de la Population (MSSP), Port-au-Prince, Haiti

Georges Perrin, MD, MPH,
US Centers for Disease Control and Prevention, Port-au-Prince, Haiti

Kesner François, MD, MPH

Corresponding Author: Nancy Puttkammer, MPH, PhD, 325 Ninth Ave, Box # 359932, Seattle, WA 98104, Tel: +1 (206) 616-5139, FAX: +1 (206) 221-4945.

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Programme National de Lutte contre le VIH/SIDA (PNLS), Ministère de Santé Publique et de la Population (MSSP), Port-au-Prince, Haiti

Abstract

Background—The World Health Organization (WHO) recommends universal antiretroviral therapy (ART) for people living with HIV (PLWH), but evidence about effects of expanded ART access on ART retention in low-resource settings is limited.

Setting—Haiti's Ministry of Health endorsed universal ART for pregnant women in March 2013 (Option B+) and for all PLWH in July 2016. This study included 51,579 ART patients from 2011–17 at 94 hospitals and clinics in Haiti.

Methods—This observational, retrospective cohort study described time trends in 6-month ART retention using secondary data, and compared results during three time periods using an interrupted time series (ITS) model: pre-Option B+ (period 1: 1/11–2/13), Option B+ (period 2: 3/13–6/16), and Test and Start (T&S, period 3: 7/16–9/17).

Results—From the pre-Option B+ to the T&S period, the monthly count of new ART patients increased from 366/month to 877/month, and the proportion with same-day ART increased from 6.3% to 42.1% ($p<0.001$). The proportion retained on ART after 6 months declined from 78.4% to 75.0% ($p<0.001$). In the ITS model, ART retention improved by a rate of 1.4% per quarter during the T&S period after adjusting for patient characteristics (Adjusted Incidence Rate Ratio [aIRR]=1.014; 95% confidence interval [CI]: 1.002–1.026, $p<0.001$). However, patients with same-day ART were 14% less likely to be retained compared to those starting ART >30 days after HIV diagnosis (aIRR=0.86; 95% CI: 0.84–0.89, $p<0.001$).

Conclusion—Achieving targets for HIV epidemic control will require increasing ART retention and reducing the disparity in retention for those with same-day ART.

Keywords

antiretroviral therapy (ART); Haiti; universal treatment; same-day treatment; ART retention; implementation science

Background

In September 2015 the World Health Organization (WHO) recommended universal antiretroviral therapy (ART) for all persons living with HIV (PLWH), regardless of level of HIV disease progression.[1] This recommendation was based on studies showing improved levels of viral suppression and reduced morbidity and mortality with ART, even for patients with high CD4 counts, [2–4] as well as modeling studies demonstrating that universal ART could reduce onward HIV transmission. Subsequent clinical trials on same-day and rapid ART[5–7] contributed to additional WHO recommendations in July 2016 that patients without evidence of opportunistic infections (OIs) should initiate ART within 7 days, or on the same day of HIV diagnosis with demonstrated ART readiness, and that symptomatic patients should initiate ART within 2–8 weeks in conjunction with clinical management of co-occurring opportunistic infections.[8]

Evaluating universal ART implemented at scale in resource-limited settings is important in order to identify policy successes and outstanding gaps.[9,10] Several countries have contributed evidence on ART retention and other health outcomes following adoption of universal ART among pregnant women (Option B+)[11–16] and evidence timely uptake of treatment under universal ART for all PLWH,[17–19] but there is less evidence on health outcomes following national-scale adoption of universal ART policies.[20]

Haiti has a national HIV prevalence rate of 2.0% among adults,[21] representing the largest absolute burden of HIV in the Caribbean region. The Haiti Ministère de la Santé Publique et de la Population (MSPP, or Ministry of Health) endorsed universal treatment for pregnant and postpartum women in March 2013 (Option B+) and extended universal ART (known in Haiti as “Test and Start”, or T&S) to all PLWH in July 2016. Our study’s objectives were to 1) describe trends in timing of ART initiation, patient characteristics, and ART retention in Haiti; and 2) explore the association between rapid ART initiation and ART retention as national guidelines for ART eligibility changed.

Methods

Study Setting and Patient Population

This retrospective cohort study covered PLWH who initiated ART at 94 out of approximately 160 health ART facilities in Haiti from January 2011 – September 2017. Health facilities in the study used the iSanté electronic medical record (EMR) system.

Haiti’s National ART Guidelines

Before March 2013, ART was recommended for adult patients with CD4 counts of below 350 cells/mm3; the preferred first line regimen consisted of two nucleoside reverse transcriptase inhibitors and one non-nucleoside reverse transcriptase inhibitor, generally tenofovir plus emtricitabine plus efavirenz or nevirapine.[22] In March 2013, ART eligibility was expanded to adult patients with CD4 counts < 500 cells/mm3 and to all pregnant and postpartum women regardless of CD4 count (Option B+), and the preferred first line regimen was tenofovir plus lamivudine plus efavirenz.[23] The July 2016 national ART guidelines expanded ART eligibility to all PLWH, but did not change the preferred first and second-line ART regimens.

Data Source

The study’s two data sources were: 1) *iSanté* EMR, which is operated by the MSPP and covers approximately 70% of all ART patients in Haiti[12,24,25]; and 2) *Suivi Actif Longitudinal du VIH/SIDA en Haiti* (SALVH) database, a national, longitudinal HIV case surveillance database.[26,27] SALVH receives names-based HIV case reports via automated monthly data extracts from Haiti’s three EMRs (including iSanté) as well as from the Monitoring Evaluation et Surveillance Intégrée (MESI, http://mesi.ht/) system, a web-based case reporting data system covering all HIV testing sites in the country. SALVH contains de-duplicated data on all patients diagnosed with HIV since 2004 in Haiti. It is estimated that 74.8% of all people living with HIV in Haiti have been diagnosed with HIV,[28] and all of these individuals have records in SALVH. We matched iSanté records to unique identifiers

from SALVH, then identified the first-ever date and location of HIV diagnosis for each iSanté patient. We used iSanté data saved to a central national data repository through March 2018 or an earlier date through which the health facility's data was considered current. This method enabled us to take advantage of the gold-standard record linkage from SALVH as well as the rich set of clinical data on ART patients from iSanté.

Measures

Time Period—We divided dates of ART initiation into periods based on changes in national guidelines on ART eligibility: period 1 (pre-Option B+, 1/11 – 2/13); period 2 (Option B+, 3/13 – 6/16); and period 3 (T&S, 7/16 – 9/17).

ART Retention—The outcome of interest, 6-month ART retention, was based on being not more than 30 days late in picking up ART medication as of the date 183 days after starting ART. We also examined the outcome of failing to return for any follow-up ART pickup within 6 months of the initial ART dispense. We were unable to assess HIV viral suppression because HIV viral load results were available for only 48.8% of patients diagnosed before July 2016 and 25.3% of patients diagnosed after July 2016.

Timeliness of ART Initiation—We calculated the number of days between the first-ever HIV diagnosis date, from SALVH, and the ART start date, calling this the "pre-ART interval." We explored ART retention by distribution of pre-ART interval, and categorized pre-ART interval based on cut-points where meaningful differences in retention levels were observed: same-day ART, ART within 1–30 days after HIV diagnosis, and ART > 30 days after diagnosis.

Covariates—Covariates included socio-demographic factors, clinical status measures, and use of HIV-related health services. Socio-demographic characteristics were assessed at HIV diagnosis, and included sex, age (grouped as <15, 15–24, 25–34, 35–49, 50+ years, and missing), marital status (grouped as married/cohabiting, widowed/divorced, single, or missing), Department of residence, and Department of the health facility where the patient started ART. We also considered whether the patient was diagnosed with HIV and initiated ART in the same health facility, and whether they had received HIV-related services in more than one facility before initiating ART. Among women, we determined pregnancy and lactation status at ART initiation using EMR data from clinical assessments, obstetrical consultations, and labor and delivery records, using methods described elsewhere.[12] We considered initial ART regimen, grouped as first-line regimen of tenofovir, lamivudine and efavirenz (TDF+3TC+EFV), alternative first-line regimen not containing protease inhibitors (PI), or PI-based regimen. Clinical characteristics included WHO stage of HIV disease progression and body mass index (BMI), and were based on values observed in the 90 days before ART start up until 7 days after ART start. Binary covariates for HIV-related health services were: receipt of ART adherence counseling before starting ART; use of Cotrimoxazole for prevention of opportunistic infections; use of isoniazid prophylaxis for latent tuberculosis; and use of treatment for tuberculosis (TB).

Analysis Methods

We restricted the dataset to patients first diagnosed with HIV starting in January 2004, when the iSanté EMR began. We excluded PLWH first diagnosed at a site outside of the iSanté network of 94 sites, since we could not definitively determine their pre-ART interval; this exclusion represented approximately 3% of all unique patients in the dataset. Finally, we restricted the dataset to ART patients with at least 183 days of follow up time within our dataset.

We used descriptive statistics to characterize the cohort and ART retention levels across time periods. We compared pre-ART interval, other patient covariates, and ART retention across time using the Chi-2 test of equality of proportions, Wilcoxan rank sum test, and Students t-test. We graphed the time trend in proportion of patients with ART retention at 6 months by period and calendar month, by pre-ART interval group. We assessed for seasonality of the outcomes by visual inspection for a cyclical pattern in ART retention by calendar month.

Next, we used an uncontrolled interrupted time series (ITS) model to evaluate the association between pre-ART interval and ART retention outcomes and the three periods of policy change on ART eligibility. ITS is a useful quasi-experimental method for leveraging routine data sources to infer the effects of large-scale policy changes, when investigator-controlled, experimental methods are not feasible.[29–31] Our ITS model used the form:

$$Y_{ret=1} = \beta_0 + \beta_{m1-26} + \beta_{m27-66} + \beta_{m67-81} + \sum_{m=2}^{12} \beta_m + \beta_{pre-ARTinterval} + \beta_{covars}$$

The model grouped patient-level binary ART retention outcomes by calendar month over the 81 months of the study and estimated rates of change, or slopes during each of three periods (β_{m1-26} , β_{m27-66} , β_{m67-81}). The model allowed for a change in slope at the start of each policy period but no immediate discontinuous level effects, since the official adoption of guidelines did not necessarily represent a moment of sudden practice change. The model included individual month fixed-effects (β_m), to address seasonality of the outcome. The model adjusted for pre-ART interval ($\beta_{pre-ARTinterval}$)with ART >30 days after diagnosis as the reference category) and other patient covariates (β_{covars}), to control for the changing profile of ART patients over time. Covariates were included in the final multivariable model based upon statistical significance at the $p<0.05$ level in separate ITS models which included the outcome, time components, and each single covariate. In a sensitivity analysis, we used an ITS model which included discontinuous level effects and which allowed for interaction of pre-ART interval and time, as well as discontinuous levels by period.

The ITS model used generalized estimating equations (GEE) with Poisson family and log link, in order to estimate a measure of relative risk rather than an odds ratio for the binary outcome. The model treated patient observations as correlated at the health facility level, and used an exchangeable correlation structure and robust variances to address correlation of data by health facility.[32,33] Last, we assessed the marginal predicted probability of ART retention at the start and end of each period, by pre-ART interval category, to obtain the

post-estimation probability of the outcome among individuals with different pre-ART interval categories but like profiles in all other characteristics. We used Stata 15.1 (StataCorp, College Station, TX) for all analyses.

Ethical review

The study received scientific and ethical review and approval from the US Centers for Disease Control and Prevention and the Haiti National Committee on Bioethics, and was exempted from human subjects review by University of Washington.

Results

Patient characteristics

There were 51,729 new ART patients in the study, 9,515 (or 366/month) during period 1, 29,053 (or 745/month) during period 2, and 13,161 (or 877/month) during period 3 (Table 1). Women made up 63.0% of ART patients, and 46.9% of women were pregnant or postpartum at ART start. Median age was 34 years, and about half of all patients (50.5%) were married or cohabitating. Nearly one-third (30.6%) were residents in the West Department. Most patients (98.6%) started ART in the same clinic where they received their first HIV diagnosis, and only 0.5% of patients had prior history of HIV care in an alternative ART clinic before starting ART. About half had a normal BMI (50.5%), and a small fraction (<3%) were being treated for active TB at ART initiation.

While all sociodemographic and clinical covariates had statistically significant changes in distribution across the three periods ($p<0.001$ for all comparisons of all categorical variables across periods), several meaningful changes in the patient profile over time bear noting. The share who started ART at a clinic in the West Department declined from 41.6% in period 1 to 36.0% in period 3. The proportion using TDF+3TC+EFV increased from 29.5% in period 1 to 90.0% in period 3. Among patients with a documented WHO stage level at ART initiation, the proportion with Stage 1 or Stage 2 increased from 25.9% in period 1 to 74.5% in period 3. Fewer than one third of patients had ART adherence counseling or an HIV treatment buddy at ART start, and levels decreased with time. The proportion who received Cotrimoxazole prophylaxis started high in period 1 and increased to a nearly universal level in period 3, while the proportion who received isoniazid (INH) prophylaxis for latent TB increased from 24.2% to 55.9% from period 1 to period 3.

Timing of ART: pre-ART intervals over time

The median pre-ART interval decreased from 51 to 3 days from period 1 to period 3 ($p<0.001$ for Wilcoxan rank sum test) (Table 1). The proportion of patients with same day ART increased from 6.3% to 42.1% from period 1 to period 3. The sociodemographic and clinical characteristics of same-day ART patients, by year of ART initiation, are described in Supplemental Table 1. Among same day ART patients with documented WHO stage, the proportion with WHO stage 1 or 2 increased from 55.6% in 2011 to 80.1% in 2017.

Time Trends in ART Retention Outcomes

From period 1 to period 3, the proportion of patients retained on ART at 6 months declined from 78.4% to 75.0% (p<0.001) (Table 2). The largest change was the increase from 56.7% vs. 71.6% among the same-day ART group (p<0.001) (Table 2 and Figure 1). The proportion of ART patients with no return ART pickup increased from 12.7% to 17.3% (p<0.001) from period 1 to period 3, and the largest change was the decline observed in the same day ART group (33.0% vs. 20.1%, p<0.001) (Table 2).

Adjusted Analysis of Time Trend and Association between Pre-ART Interval and 6-Month ART Retention

ART regimen, Department of health facility at ART initiation, and linkage to ART in the same health facility as HIV diagnosis were not associated with ART retention in single covariable ITS models, and were excluded from the final multivariable ITS model. During period 1, the time trend or slope for ART retention was not significantly different from the null value of 1.0, and there was no significant difference in slope from period 1 to period 2 (Table 3). During period 3, ART retention was estimated to increase by 1.4% per quarter compared to period 1 (adjusted incidence rate ratio [aIRR]=1.014; 95% confidence interval [CI]: 1.002–1.026, p=0.02).

Compared to those who started ART >30 days after diagnosis, same day ART patients were 14% less likely (aIRR=0.86; 95% CI: 0.84–0.89, p<0.001), and those who started ART 1–30 days after diagnosis were 4% less likely (aIRR=0.96; 95% CI: 0.94–0.98, p<0.001) to be retained on ART at 6 months, after adjustment for time and other patient-level factors (Table 3).

Independent positive predictors of ART retention included being a pregnant/lactating female or being male (compared to the reference category of non-pregnant/lactating female), being a pediatric patient or a patient >34 years (compared to 25–34 years), residing in the Central Department (compared to the West Department), having had prior HIV care at a different clinic, being overweight or obese (compared to normal BMI), having WHO Stage 2 (compared to WHO Stage 1), and having any additional HIV-related health services at ART baseline (Table 3). Independent predictors for reduced likelihood of ART retention included being an adolescent or young adult aged 15–24, residing in the Artibonite or North-west Departments, and being underweight.

The adjusted marginal predicted probabilities of ART retention by pre-ART interval at the start of each period are shown in Table 2. After taking into account patient characteristics, the marginal probability of ART retention increased from July 2011 to March 2018 across all pre-ART interval groups. By March 2018, compared to patients with ART >30 days after diagnosis, the probability of ART retention was 12.0 percentage points lower in the same day ART group and 3.9% percentage points lower in the group with ART 1–30 days after diagnosis.

The alternative ITS model demonstrated an increase of 7% in the level of 6 month ART retention with the start of period 3 compared to period 1 (aIRR=1.07; 95% CI: 1.01–1.13, p=0.02). The model estimated same day ART to have 22% lower retention on average

compared to ART >30 days after diagnosis, a marginally significant difference (aIRR=0.78; 95% CI: 0.60–1.02, p=0.07), and no significant differences in rates of change in the outcome by pre-ART interval group (Supplemental Table 2).

Discussion

Universal ART is a critical pillar of efforts to achieve the 95–95–95 targets for HIV epidemic control. Our study of a large cohort of ART patients from 94 clinics in Haiti demonstrated a 2.4 fold increase in monthly enrollment of new ART patients from the pre-Option B+ period before March 2013 to the T&S period after July 2016. The share of new ART patients with WHO Stage 1 or 2 nearly tripled over this time frame, reflecting the success of the policy changes in ensuring earlier treatment initiation for PLWH.

Six-month ART retention declined from 78.4% to 75.0% in Haiti over the three periods in our study, and fell short of targets for HIV epidemic control. This could reflect the challenges of extending treatment to hard-to-reach patients as well as to asymptomatic patients with less motivation to remain on treatment. The level of 71.6% among same-day ART patients also fell short of the 12-month retention level of 80% reported in an earlier randomized controlled clinical trial of same-day ART set in Port-au-Prince, Haiti.[5] It can be challenging to translate results of clinical trials in real-world conditions. The results from Haiti echo the experience with scaled up universal treatment in Nigeria, where high loss to follow up (LTFU) of 34% at 12 months was reported following adoption of universal treatment.[20]

On the other hand, after taking into account the changing sociodemographic and clinical profile of ART patients over the time frame of our study, we found evidence of a favorable time trend in ART retention after adoption of T&S, estimated at a 1.4% increase per quarter during period 3. This result could reflect normalization of universal treatment in the eyes of patients and providers, as well as improvements in program procedures like post-test counseling, linkage to care services, and other clinical practices.

A discouraging finding was the disparity in ART retention among same-day ART patients, estimated to be 14% less likely to be retained on ART at 6 months, compared to those starting ART >30 days after diagnosis. Indeed, one in five same-day ART patients failed to return to pick up ART following their initial dispense during the T&S period. In Haiti as in other low-resource settings, starting and being retained on treatment are modifiable outcomes shaped by individual, social, and health system factors.[9] The process of diagnosis and ART initiation must help patients accept their diagnosis, understand the process of treatment, develop behavioral skills for ART adherence, and build social support for long-term ART retention. Strategies for enhancing patient-centeredness of care services at the time of HIV diagnosis and ART initiation, and for intensifying early support for patients newly initiating ART, especially same-day ART patients, are needed in Haiti. More evidence is needed from other resource-limited settings to identify similarities and differences in patterns of ART retention following scale-up of universal treatment.

Strengths and Limitations

A key strength of this study was our ability to link records for patients who were multiply registered or who transferred care between health facilities. The inability to establish valid values for date of initial HIV diagnosis and for ART retention based on unique records has bedeviled many observational studies using secondary data sources.[34] While some patients in our study may have silently transferred care to sites outside of the iSanté network, leading us to underestimate ART retention, we believe this minimally affected our estimates given the low rates of transfer of care between the 94 iSanté clinics.

There are several limitations to our study. First, we could not differentiate mortality from LTFU. Further understanding of the role of mortality versus LFTU is important in identifying interventions to improve overall ART retention and reduce the disparity in outcomes for same-day ART patients. Second, the changes in ART eligibility occurred in tandem with other changes in the national ART program. In the early days of Haiti's ART program, donor funding was used to support a robust model of ancillary services for ART patients, including psychosocial support, food assistance, transportation subsidies, microenterprise development, and even school fees for children. As donor's focus shifted to expanded ART access and HIV care cascade targets, the robust model of "social advantages" was pared back. However, our study was not able to separately estimate effects of changes in ART eligibility guidelines versus other types of ART program changes. Third, our study was not able to take into account certain patient-, provider- and facility-level factors which influence ART retention, such as socio-economic status, food security, travel distance to the clinic and access to transportation, knowledge and motivation about treatment, level of social support for treatment, clinic wait times, perceived technical competence or friendliness of health providers, or availability of ancillary services. Finally, measurement of covariates was imperfect, with high levels of missingness and potential misclassification of variables like ART adherence counseling (which may have been offered but not documented), introducing bias in our estimates in unknown directions. Additional research on these topics would be helpful.

Conclusion

Observational studies play an important role in setting global guidelines and in demonstrating the feasibility, acceptability, and effectiveness of strategies like T&S.[10] This large-scale study demonstrated expanded access to ART and a narrowing of the disparity in ART retention between patients with same day ART compared to delayed ART. Further observational and pragmatic intervention studies are needed in order to refine guidelines for the process of rapid ART initiation and to optimize ART retention under universal treatment.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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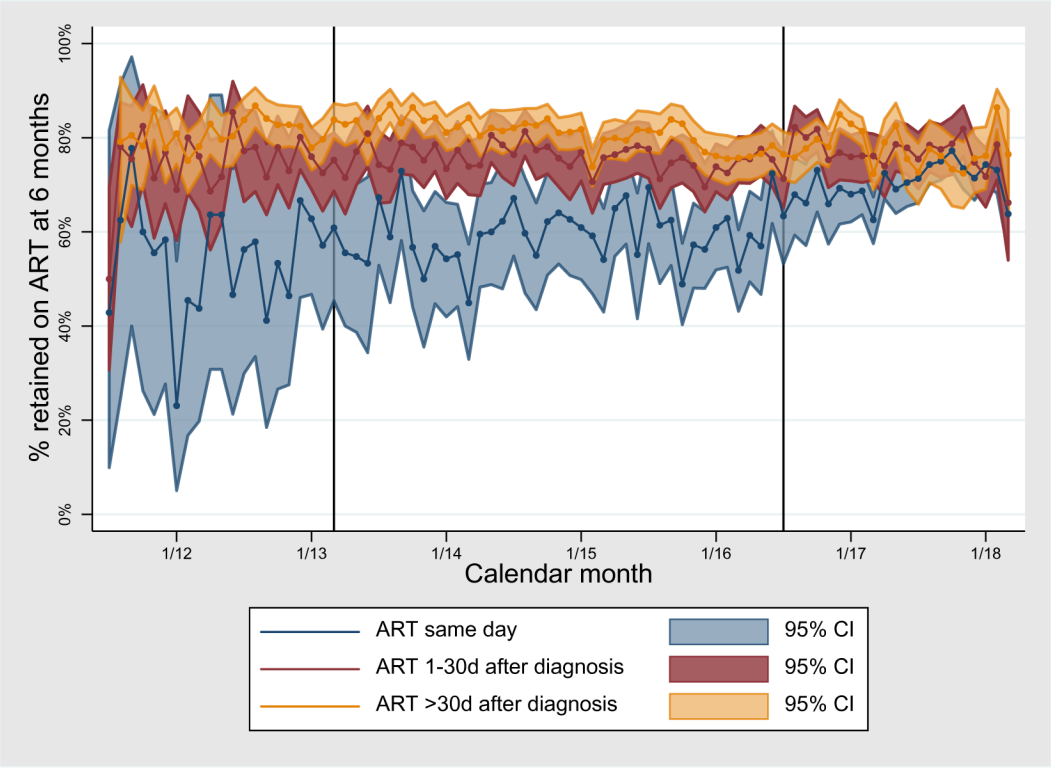

Figure 1:

Proportion of ART patients retained on ART at 6 months, by calendar month and pre-ART interval (July 2011-March 2018)[†]

[†]Monthly estimated values by pre-ART interval, with exact binomial 95% confidence interval (CI)

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Table 1:

Characteristics of ART patients

	Period	Period 1 Pre-Option B+ (1/11–2/13)	Period 2 Option B+ (3/13–6/16)	Period 3 Test & Start (7/16–9/17)	All periods (1/11–7/17)
Characteristic		**N (%)**	**N (%)**	**N (%)**	**N (%)**
	All ART	9,515 (18.4%)	29,053 (56.2%)	13,161 (25.4%)	51,729 (100%)
Pre-ART interval *	Days (median, IQR)	51 (18, 139)	35 (8, 216)	3 (0, 129)	30 (4, 176)
	Same Day	600 (6.3%)	3,751 (12.9%)	5,539 (42.1%)	9,890 (19.1%)
	1–30 days	2,912 (30.6%)	9,806 (33.8%)	3,343 (25.4%)	16,061 (31.0%)
	>30 days	6,003 (63.1%)	15,496 (53.3%)	4,279 (32.5%)	25,778 (49.8%)
Sex *	Female	6,053 (63.6%)	18,377(63.3%)	8,154 (62.0%)	32,584 (63.0%)
	Pregnant/lactating **	2,993 (49.4%)	9,004 (49.0%)	3,287 (40.3%)	15,284 (46.9%)
	Male	3,460 (36.4%)	10,637 (36.6%)	4,951 (37.6%)	19,048 (36.8%)
	Missing	2 (<0.1%)	39 (0.1%)	56 (0.4%)	97 (0.2%)
Age at HIV diagnosis * (years)	Years (median, IQR)	35 (27, 43)	34 (27, 44)	34 (27, 43)	34 (27, 44)
	0–14	532 (5.6%)	1,228 (4.2%)	668 (5.1%)	2,428 (4.7%)
	15–24	1,083 (11.4%)	3,834 (13.2%)	1,744 (13.3%)	6,661 (12.9%)
	25–34	3,035 (31.9%)	9,533 (32.8%)	4,289 (32.6%)	16,857 (32.6%)
	35–49	3,440 (36.2%)	9,709 (33.4%)	4,584 (34.8%)	17,733 (34.3%)
	50+	1,403 (14.7%)	4,689 (16.1%)	1,813 (13.8%)	7,905 (15.3%)
	Missing	22 (0.2%)	60 (0.2%)	63 (0.5%)	145 (0.3%)
Marital status *	Married/cohabiting	4,652 (48.9%)	14,846 (51.1%)	6,613 (50.2%)	26,111 (50.5%)
	Widow/divorce	1,154 (12.1%)	3,479 (12.0%)	1,467 (11.1%)	6,100 (11.8%)
	Single	1,691 (17.8%)	5,452 (18.8%)	2,715 (20.6%)	9,858 (19.1%)
	Missing	2,018 (21.2%)	5,276 (18.2%)	2,366 (18.0%)	9,660 (18.7%)
Department of residence *	West	2,931 (30.8%)	9,041 (31.1%)	3,873 (29.4%)	15,845 (30.6%)
	North	1,670 (17.6%)	5,776 (19.9%)	2,438 (18.5%)	9,884 (19.1%)
	Artibonite	936 (9.8%)	3,630 (12.5%)	1,824 (13.9%)	6,390 (12.4%)
	South	841 (8.8%)	2,280 (7.8%)	919 (7.0%)	4,040 (7.8%)
	North-east	438 (4.6%)	1,581 (5.4%)	777 (5.9%)	2,796 (5.4%)

	Period	Period 1 Pre-Option B+ (1/11–2/13)	Period 2 Option B+ (3/13–6/16)	Period 3 Test & Start (7/16–9/17)	All periods (1/11–7/17)
Characteristic		**N (%)**	**N (%)**	**N (%)**	**N (%)**
	North-west	463 (4.9%)	1,405 (4.8%)	835 (6.3%)	2,703 (4.2%)
	South-east	369 (3.9%)	897 (3.1%)	431 (3.3%)	1,697 (3.3%)
	Grand Anse	350 (3.7%)	792 (2.7%)	444 (3.4%)	1,586 (2.1%)
	Nippes	251 (2.6%)	713 (2.5%)	298 (2.3%)	1,262 (2.4%)
	Center	15 (0.2%)	48 (0.2%)	128 (1.0%)	191 (0.4%)
	Missing	1,251 (13.1%)	2,890 (9.9%)	1,194 (9.1%)	5,335 (9.3%)
Department of health facility where started ART *	West	3,957 (41.6%)	11,286 (38.8%)	4,737 (36.0%)	19,980 (38.6%)
	North	1,782 (18.7%)	6,198 (21.3%)	2,638 (20.0%)	10,618 (20.5%)
	Artibonite	988 (10.4%)	3,605 (12.4%)	1,716 (13.0%)	6,309 (12.2%)
	South	856 (9.0%)	2,469 (8.5%)	1,093 (8.3%)	4,418 (8.5%)
	North-west	456 (4.8%)	1,417 (4.9%)	925 (7.0%)	2,798 (5.4%)
	North-east	399 (4.2%)	1,439 (5.0%)	712 (5.4%)	2,550 (4.9%)
	Nippes	380 (4.0%)	1,037 (3.6%)	454 (3.4%)	1,871 (3.6%)
	Grand-Anse	351 (3.7%)	767 (2.6%)	444 (3.4%)	1,562 (3.0%)
	South-east	346 (3.6%)	835 (2.9%)	442 (3.4%)	1,623 (3.1%)
Linkage *	ART at same dx site	9,266 (97.4%)	28,764 (99.0%)	12,949 (98.4%)	50,979 (98.6%)
Mobility *	Prior HIV care at >1 clinic at ART start	75 (0.8%)	190 (0.7%)	18 (0.1%)	283 (0.5%)
ART Regimen *	TDF+3TC+EFV	2,810 (29.5%)	24,530 (84.4%)	11,842 (90.0%)	39,182 (75.7%)
	Other first line	6,595 (69.3%)	4,379 (15.1%)	1,158 (8.8%)	12,132 (23.5%)
	PI regimen	110 (1.2%)	144 (0.5%)	161 (1.2%)	415 (0.8%)
Body mass index (BMI) *	<18.5	1,499 (15.8%)	4,822 (16.6%)	2,074 (15.8%)	8,395 (16.2%)
	normal 18.5-<25	4,802 (50.5%)	15,055 (51.8%)	6,292 (47.8%)	26,149 (50.5%)
	overweight 25-<30	990 (10.4%)	3,327 (11.5%)	1,518 (11.5%)	5,835 (11.3%)
	obese >=30	283 (3.0%)	1,022 (3.5%)	544 (4.1%)	1,849 (3.6%)
	Missing	1,941 (20.4%)	4,827 (16.6%)	2,733 (20.8%)	9,501 (18.4%)
WHO stage *	Stage 1	1,289 (13.5%)	5,888 (20.3%)	5,285 (40.2%)	12,462 (24.1%)
	Stage 2	993 (10.4%)	4,899 (16.9%)	3,296 (25.0%)	9,188 (17.8%)

	Period	Period 1 Pre-Option B+ (1/11–2/13)	Period 2 Option B+ (3/13–6/16)	Period 3 Test & Start (7/16–9/17)	All periods (1/11–7/17)
Characteristic		**N (%)**	**N (%)**	**N (%)**	**N (%)**
	Stage 3	2,202 (23.1%)	5,968 (20.5%)	1,847 (14.0%)	10,017 (19.4%)
	Stage 4	4,341 (45.6%)	10,321 (35.5%)	1,093 (8.3%)	15,755 (30.5%)
	Missing	690 (7.3%)	1,977 (6.8%)	1,640 (12.5%)	4,307 (8.3%)
HIV related services *	Adherence counseling	2,936 (30.9%)	8,315 (28.6%)	1,822 (13.8%)	13,073 (25.3%)
	Buddy named	2,491 (26.2%)	7,301 (25.1%)	2,686 (20.4%)	12,478 (24.1%)
	Cotrimoxazole	8,369 (88.0%)	27,404 (94.3%)	12,783 (97.1%)	48,556 (93.9%)
	INH prophylaxis	2,303 (24.2%)	15,168 (52.2%)	7,355 (55.9%)	24,826 (48.0%)
	TB treatment	250 (2.6%)	850 (2.9%)	174 (1.3%)	1,274 (2.5%)

*All categorical variables had distributions which significantly varied across time periods at p<0.001 level, based upon Chi-2 test for equality of proportions.

**Pregnancy / postpartum status at time of ART initiation, among all women.

Table 2:

Proportion of patients retained on ART, by pre-ART interval and time

Observed proportions (unadjusted % with 95% CI)				
	Period 1 Pre-Option B+	**Period 2 Option B+**	**Period 3 Test & Start**	**p-value***
6 month ART retention				
All ART	78.4% (77.6, 79.2)	76.6% (76.1, 77.1)	75.0% (74.3, 75.7)	p<0.001
ART same day	56.7% (52.6, 60.7)	61.1% (59.5, 62.6)	71.6% (70.4, 72.8)	p<0.001
ART 1–30d	75.4% (73.8, 77.0)	76.2% (73.3, 77.0)	76.5% (75.0, 77.9)	P=0.52
ART >30d	82.1% (81.1, 83.0)	80.7% (80.1, 81.3)	78.2% (77.0, 79.4)	p<0.001
No return ART pick-up				
All ART	12.7% (12.1, 13.4)	14.3% (13.9, 14.7)	17.3% (16.6, 17.9%)	p<0.001
ART same day	33.0% (29.2, 36.9)	28.6% (27.2, 30.1)	20.1% (19.0, 21.1%)	p<0.001
ART 1–30d	13.8% (12.5, 15.1)	13.4% (12.7, 14.0)	14.4% (13.2, 15.6%)	P=0.32
ART >30d	10.2% (9.4, 11.0)	11.4% (10.9, 11.9)	15.9% (14.8, 17.0%)	p<0.001
Marginal probability of 6 month ART retention (adjusted estimates, with 95% CI)**				
	Start Period 1 Jul-2011	**Start Period 2 Sep-2013**	**Start Period 3 Jan-2017**	**End Period 3 Mar-2018**
ART same day	69.8% (64.3, 74.5)	69.1% (64.4, 74.5)	69.8% (66.1, 74.5)	75.2% (70.4, 74.5)
ART 1–30d	77.4% (71.4, 83.4)	76.6% (71.8, 81.3)	77.4% (73.5, 81.3)	83.3% (78.0, 88.7)
ART >30d	81.0% (74.9, 87.1)	80.1% (75.6, 84.7)	81.0% (76.8, 85.2)	87.2% (81.3, 93.1)

* p-value for equality of proportions across time period (Chi-2 test).

* Marginal probability at each time point given pre-ART interval, age 25–34, female sex (non pregnant / postpartum), residence in West department, married/cohabiting, has not had prior care at another ART clinic, normal body mass index, WHO stage 1, did not have ART adherence counseling, did not name ART treatment buddy, received Cotrimoxazole and isoniazid prophylaxis, not on TB treatment.

Table 3:

Interrupted time series model for 6 month ART retention †

Variable	Category	aIRR	(95% CI)	*p*-value
Rate of change per 3 month period (ref = slope for Period 1)	Slope for Period 1 (pre-Option B+)	1.002	(0.994, 1.010)	0.66 ††
	Period 2 (Option B+)	0.997	(0.987, 1.006)	0.50
	Period 3 (T&S)	1.014	(1.002, 1.026)	0.02
Pre-ART interval (ref = ART >30d after diagnosis)	ART same day	0.86	(0.84, 0.89)	<0.001
	ART 1–30d after diagnosis	0.96	(0.94, 0.98)	<0.001
Sex (ref = female non-pregnant)	Female pregnant	1.06	(1.05, 1.08)	<0.001
	Male	1.02	(1.01, 1.04)	<0.001
	Missing	1.12	(0.91, 1.37)	0.27
Age at HIV diagnosis (ref = 25–34 years)	0–14	1.22	(1.16, 0.29)	<0.001
	15–24	0.94	(0.92, 0.96)	<0.001
	35–49	1.04	(1.03, 1.05)	<0.001
	50+	1.07	(1.05, 1.09)	<0.001
	missing	1.02	(0.87, 1.19)	0.85
Marital status (ref = Married/cohabitating)	Widow/divorce	1.00	(0.99, 1.02)	0.59
	Single	1.01	(1.00, 1.02)	0.21
	Missing	0.97	(0.95, 0.99)	<0.01
Department of residence (ref = West)	North	0.99	(0.94, 1.05)	0.83
	Artibonite	0.95	(0.91, 0.99)	0.03
	South	1.00	(0.96, 1.04)	0.97
	North-east	1.03	(0.98, 1.08)	0.22
	North-west	0.93	(0.88, 0.98)	0.01
	South-east	1.03	(0.98, 1.08)	0.23
	Grand Anse	0.95	(0.90, 1.00)	0.07
	Nippes	0.98	(0.94, 1.02)	0.29
	Central	1.09	(1.04, 1.15)	<0.01
	Missing	0.97	(0.94, 0.99)	0.01

Variable	Category	aIRR	(95% CI)	*p*-value
Mobility	Prior HIV care at >1 site at ART start	1.08	(1.02, 1.14)	<0.01
BMI at ART baseline (ref = normal 18.5-<25)	underweight <18.5	0.96	(0.94, 0.97)	<0.001
	overweight 25-<30	1.04	(1.02, 1.05)	<0.001
	obese >=30	1.04	(1.02, 1.07)	<0.01
	Missing	0.83	(0.80, 0.86)	<0.001
WHO stage at ART baseline (ref = Stage 1)	Stage 2	1.02	(1.00, 1.04)	0.04
	Stage 3	1.00	(0.98, 1.02)	0.99
	Stage 4	0.99	(0.98, 1.01)	0.53
	Missing	0.95	(0.91, 0.98)	<0.01
HIV related services (ref = No)	Adherence counseling	1.07	(1.05, 1.09)	<0.001
	Buddy named	1.03	(1.01, 1.04)	<0.01
	Cotrimoxazole prophylaxis	1.11	(1.07, 1.16)	<0.001
	INH prophylaxis	1.02	(1.00, 1.03)	0.04
	TB treatment	1.04	(1.01, 1.06)	<0.01

aIRR = adjusted Incidence Rate Ratio; BMI = body mass index; WHO = World Health Organization; TB = tuberculosis.

† Model adjusted for fixed effects for calendar month.

†† p-value for comparison to null value of slope=1.0.