THE USE OF VIRAL LOAD TESTING AND SECOND LINE SWITCHING OF ART TREATMENT IN HAITI

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ABSTRACT

The use of Viral Load Testing and Second Line Switching of ART Treatment in Haiti

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Objective: To describe time trends in Viral Load (VL) tests and results and time trends in use of second-line antiretroviral regimens for treatment of HIV/AIDS, and eventually to explore the association between VL test and second line regimen switching.

Study Design: We conducted a retrospective cohort study with over 80,000 patients drawn from 88 of 160 Haiti's national ART sites. Longitudinal data from the iSanté electronic data system was used to analyze time trends in the routine use of VL testing and switching to second-line ART treatments. We calculated the odds ratio of second-line regimen switching with 95% confidence intervals (CI) comparing patients never tested, patients tested with no VL failure and patients tested with VL failure, adjusted for individual characteristics.

Results: The number of viral load tests done annually increased from 11 in 2010 to 20585 in the first nine months of 2017, and the number of second-line regimen switches increased from 21 to 279 in this same period. Comparing patients never tested, patients who had VL testing with virologic suppression had VL tests had a 2.67times higher odds (95% CI for OR: 2.01-3.38; $p<0.001$) and those with a VL test showing treatment failure had a 6.67 times higher odds (95% CI for OR: 4.09-10.89; $p<0.001$) of switching to second-line regimen after adjustment for individual characteristics. Among patients with confirmatory VL failure, approximately half had weak adherence and half had strong adherence during the 90 days before the confirmatory test.

Conclusions: Haiti has significantly expanded access to VL testing since 2016. In order to promote timely switching to second-line regimens, it is essential for Haiti to continue broadening access to confirmatory VL testing, to support modification of HIV clinical management practices to embrace timely switching for patients with confirmed virologic failure despite strong ART adherence, and to expand evidence-based initiatives to promote strong ART adherence.

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INTRODUCTION

HIV is a life-threatening disease which if untreated, destroys the immune system, leaving those infected susceptible to opportunistic infection and early death. Antiretroviral therapy (ART) for the treatment of HIV has been adopted in most of the countries in the world including resource-limited countries, leading to highly successful clinical, immunologic, and virology outcomes. Therefore, the scale-up of ART treatment is essential in reversing the AIDS epidemic[1-2]. The Joint United Nations Program on HIV/AIDS (UNAIDS) and partners launched the 90–90–90 targets in 2014 to help end the AIDS epidemic. The aim is to achieve the 90-90-90 treatment targets by 2020: 90% of all people living with HIV know their HIV status, 90% of all people with HIV receive sustained ART and 90% of all people on ART have viral suppression[3].

World Health Organization (WHO) Standard ART consists of the combination of antiretroviral (ARV) drugs, which aims to suppress HIV replication and prevent the progression of HIV disease[4]. The initial treatment for most HIV patients is the first-line ART regimen, while either weak adherence or the presence of drug resistance can cause virologic failure. The number of patients who experience treatment failure and who need second-line therapy has increased[5-7]. Second-line treatments can be used to treat resistant forms of HIV successfully, but these regimens are more expensive than the first-line regimens. Therefore, there is a strong desire in resource-limited settings to optimize outcomes of first-line regimens so that the number of patients requiring second-line regimens is contained. For patients with resistant forms of HIV, switching to second-line regimens is appropriate, and delays in switching can result in excess morbidity and mortality.

To maximize the duration of the first-line regimen and switching patients resistant to their current regimen, monitoring patients on ART treatment is necessary. Since drug susceptibility and resistance testing is not widely available in many settings, the decision of switching to the second-line regimen is often based on the evidence of virologic failure,

immunologic failure, or clinical failure among patients with strong ART adherence. Among these methods, viral load (VL) testing is the gold standard to indicate treatment failure and is a vital element of evaluating the need for regimen switching in wealthy countries[8,9]. As a gold standard in HIV monitoring, viral load tests provide timely monitoring of treatment failure but is not able to differentiate between failure due to poor adherence or drug resistance. In resource-limited settings, clinician decisions to switch patients from the first-line regimen to second-line regimen mainly relied on WHO clinical and immunological criteria, which can result in delayed detection of treatment failure, and low switching rate to second-line ART regimen. Routine VL testing could improve the health outcome of HIV patients through timely detection treatment failure and is now recommended by the WHO for routine use in low and middle-income countries (LMICs)[10-12].

After sub-Saharan Africa, the Caribbean region has the second highest HIV prevalence globally[13], and Haiti constitutes the greatest burden of HIV infection of Caribbean region. In 1993, the prevalence of HIV among adults (ages 15- 49) was approximately 4%, and this level decreased to 2.5% among adult women and 1.7% among adult men by 2016 due to death, treatment, education and other prevention strategies[14-16]. Substantial progress has been made in all aspects of the HIV care continuum, including HIV testing, linkage to care, and treatment in Haiti. According to Haiti's 2018 Country Operation Plan (COP), 91,383 patients were receiving ART in 2017, representing over 62% of patients in need of treatment based on the national guidelines[17].

With this evidence and WHO recommendations to use VL test routinely and the support by the US President's Emergency Plan for AIDS Relief (PEPFAR) and other funding sources, Haiti and other resource-limited countries have taken steps to expand access to VL testing. In 2015-16, Haiti initiated the rollout of VL testing, to have VL testing after six months on ART and annually thereafter. In July 2016, Haiti adopted the Test and Start approach to ART initiation, to reach the goal that is improving patient health outcomes and reducing HIV incidence[18]. In 2018-19, Haiti plans to achieve 100% VL coverage for all

appropriate patients[17]. The aims of the present research study were: 1) to describe time trends in VL tests and results; 2) to describe time trends in use of second-line regimens; 3) to explore the association between these phenomena.

METHODS

Design and settings

This is a retrospective cohort study focusing on the routine use of VL testing and switching to second-line ART treatments. The study used longitudinal electronic medical record (EMR) data from the iSanté data system. iSanté is the largest of 3 EMRs in Haiti, which contains longitudinal medical records for approximately 70% of ART patients in Haiti. Secondary data routinely collected from iSanté EMR system is used for descriptive and exploratory analysis. Individual data was inputted in the local ART sites and then sent to a central data repository. The study cohort was drawn from 88 out of 160 national ART sites, with over 80, 000 patients[19]. All research in this study is overseen by Institutional Review Boards (IRB) of both Haiti's Comité National de Bioéthique and University of Washington.

Participants

ART sites were included in our study based on the timeliness of information uploading to the central data repository. Sites having less than 80% of patient visit forms saved to the iSanté central server within 90 days of the patient's visit were excluded from the analysis. Eligible patients were adults aged 16 and above who initiated on a standard first-line ART regimen between January 1st, 2010 and September 30th, 2017 and who completed at least 6 months on ART. The study excluded patients who initiated ART on a second-line regimen. In each calendar year, active patients were defined as picking up ART medication at least once that year. Patients were divided into annual ART cohort according to their year of ART initiation.

VL Test

Until 2015, the VL testing was not routinely used in Haiti. Since 2016, the Ministry of Public Health and Population (MSPP) of Haiti with the support of international partners has expanded access to HIV VL testing to improve monitoring of treatment outcomes. Haiti uses Genetic HIV VL Assay (Biometric Bandol France) to measure the Plasma VL22. The lower limits of detection are 300 copies / ml when 0.2ml plasma volumes are used for testing. VL suppression was defined as HIV RNA< 1000 copies/ml[20]. The possible VL testing outcomes include 1) no VL test, 2) VL suppressed (no virologic failure history), 3) initial virologic failure without follow-up test; 4) viral re-suppression, and 5) confirmed virologic failure (first failure followed by confirmed failure).

Second line ART regimen

The second-line regimen was defined as a two-nucleoside reverse-transcriptase inhibitors (NRTIs) + a ritonavir-boosted protease inhibitor (PI)[21]. The data of this study ranged from 2010 to 2017, and Haiti's national ART treatment guideline changed twice in this period. Second-line regimens were defined according to the national ART guidelines in place when the medication was picked up. ART medications picked up between Jan 1st, 2010 and Dec 31st, 2012 were defined according to Haiti's 2008 national guideline; ART medications picked up between Jan 1st, 2013 and Dec 31st, 2016 was defined according to Haiti's 2013 national guideline; medication picked up after Jan 1st, 2017 was defined according to Haiti's 2017 national guideline.

Measurements

According to WHO and Haiti national ART guidelines, patients who start with the first-line regimen should have the VL test six months after initiating ART treatment. The ART patients would keep the first-line regimen if the VL test were showing the viral suppressed. If they receive a detectable VL result upon their first VL test, patients should receive three

months' intense adherence counseling. Then, the patients should have a repeat VL testing six months after the prior VL failure. If the result indicates a second (confirmed) failure, the patients are eligible for switching to second line regimens. In this study, we define strong/weak adherence in the 180 days prior to the confirmed VL failure based upon medication possession ratio, or the percentage of days that patients had medication in their possession: If the rate was >=90%, the patients were considered as having strong adherence, and if the portion was <90%, the patients was considered as having weak adherence[22-27]. ART start year was defined as the year patients initiate ART treatment. The age of patients was categorized into five categories: 16 – 24, 25 – 34, 35-44, 45-54, >55; WHO stage status at ART initiation was used in this study.

Data Analysis

This research aims to describe time trends in VL tests and results, and to describe time trends in use of second-line regimens, and eventually to explore the association between VL test and second line regimen switching. To be more specific:

Aim1 VL Test

Aim1.1 The routine use of VL test by calendar year and by ART cohort.

Descriptive analysis was used to analyze VL testing among all eligible patients on ART treatment. The total number of VL tests, and the number and percentage of detectable tests, the number of total patients in care, the number and proportion of patients who had at least one VL test are described. The study shows the trend of routine by describing the prevalence of routine VL test of each ART cohort by calendar year, this aim also explored how access to routine VL testing among patients changed over time.

Aim 1.2 The outcome of the VL test.

Patients who have initiated ART treatment for at least 18 months were eligible. The proportion of patients is summarized by type of VL test outcome, as divided into three

categories first: 1) no VL test, 2) VL suppressed (no VL failure history), 3) initial VL failure. Patients who experienced an initial VL failure were divided into four sub-groups, namely: 1) initial virologic failure without follow-up test; 2) viral re-suppression; and 3) confirmed failure with good adherence, 4) confirmed failure with weak adherence.

Aim 2 Second line regimen switching

The participants involved in this aim are eligible patients who have initiated ART treatment for at least 18 months.

Aim 2.1 The overall second line regimen switching by calendar year and by ART cohort
The number and proportion of patients switching to the second line regimen by ART cohort and calendar year were described. Number and proportion of switching patients with VL failure were also calculated. Among those patients having VL failure, this study conducted a Kaplan Meier graph to observe the time of their second-line switching since VL failure.

Aim 2.2 VL testing outcome among second line switching patients
This aim described the use of VL test situation of each ART cohort among switching patients. Among switching patients with confirmed VL failure; the adherence status was described on a population basis.

Aim 3 Explore the relationship between VL outcome and second line regimen switching

We used a logistic regression model to assess the relationship between VL test and second line regimen switching. We explored the association between VL testing status (with categories of "No VL test," "VL test without failure," or "VL test with failure") and the outcome of switching to a second-line regimen of ART initiation. Then we explored the association after adjusting for the influence of ART start year, age, gender and WHO stage at ART initiation, and the interaction effect between VL condition and ART start year. We considered all VL tests and switches occurring prior to administrative censoring of the data,

meaning that patients had differing durations of follow up. We did not limit the analysis to switches occurring before the VL test.

RESULTS

Characteristic of ART Patients

At the data collection point (September 2017) a total of 126 sites were recorded in the iSanté system, there were 88 eligible sites with 67,361 patients. Figure 1 shows the data exclusion process. The median age for eligible patients at ART initiation was 36.0 years; 64.7% were female, 21.4% and 32.5 % were WHO stage III and stage IV respectively (Table 1).

Prevalence of VL Testing by Year

The number of ART patients active in care was 3,932 in 2010 and increased to 43,913 in 2016, with an average annual increase rate of 49.56% per year. The total number of active patients with at least one VL test also grew along with the number of active patients in this period. In 2010, only 11 (0.3%) patients had VL test, with a noticeable increase on both number and proportion from 2015 (840; 2.3%) to 2016 (16,754; 38.1%); this number reached 19,182 (47.3%) in the first three quarters of 2017. Until 2015, no more than 900 tests were conducted each year. The test number increased dramatically in 2016 (17,917) with a detectable rate of 40.6%, and this rate increase to 53.8% in 2017. (Table 2).

Prevalence of VL Testing of Each ART Cohort by Year

Among patients who are active in care, the proportion of patients with a VL test grew over time. For the 2010 ART cohort, 0.03% of patients had VL testing in their first year while the proportion is 59.6% in their seventh year (Table 3). This similar increase pattern also

happened in other ART cohorts, and each ART cohort reached the highest VL testing in their last year. Successive ART cohorts had a greater likelihood of receiving a VL test in the first year (Figure 2). Almost half patients who started ART treatment in 2016 had access to VL test while only 0.03 % patients of 2010 ART cohort had VL test in their first year (Table 3).

The Outcome of VL Test

Overall, 56% of patients never had VL test; 30% patients had VL test with the suppressed result; 14% of patients experienced an initial detectable viral load result. Among patients with detectable VL, 63% of patients did not have a follow-up test to confirm their VL status. For patients with VL failure who experienced a follow-up test, 35% had strong adherence prior to the confirmed failure, 46% had weak adherence, and 19% were re-suppressed. (Figure 3)

Patients who initiated earlier had a lower VL test proportion. For 2010 ART cohort 56.6% patients never had VL test, and this number decreased to 48.3% for 2016 ART cohort. The outcome of first VL test was similar within the seven ART cohorts (2010 ART cohort to 2016 ART cohort) that patients with VL suppressed were about twice more than patients with first VL failure. Patients who started ART earlier were more likely to have confirmed VL test after their initial VL failure. For the 2016 ART cohort, 64.5% patients did not have confirmatory test after experienced first failure, and this proportion for 2010 ART Cohort is 42%. The proportion of confirmed failure is higher among patients who initiated ART treatment earlier, with 36.5% for the 2010 ART Cohort but only 19.45% for the 2016 ART Cohort (Table 4).

Prevalence of Second-line Switching by Year

With the patients' growth of ART treatment in Haiti, the number of patients switching to second-line ART has increased as well. Twenty-one (0.5%) patients switched to second-

line ART in 2010. The number of switches increases to 373 in 2015 (1.0%), but after 2015 the absolute number of switches remained high while the proportion of eligible patients decreased. Patients switching to the second-line regimen with VL failure record(s) increased dramatically. Until 2012, there were no patients who had the record of a VL failure before switching, but by 2013 4.1% patients had VL failure before switching, and the rate reached 72.0% in 2017 (Table 5).

Figure 4 shows the proportion of patients switching to second-line regimens after VL failure by time to the switch, based upon the Kaplan Meier method. Before 2015, there were few cases of failures followed by switches and the overall proportion of patients who switched remained below 65% through 3 years following the observed failure. Only around 31% patients who experienced VL failure in 2015 and 53% patients in 2016 switched to second-line regimen within the 365 days of the observed VL failure, even though national ART guidelines advise repeat viral load testing within 3-6 months and switching thereafter. For patients with VL failure in 2015, about 38% of patients had been switched within 18 months (545 days) following the detectable test result, while for patients with a detectable VL result in 2016, an estimated 99% had been switched by this same time point (Table 6).

Prevalence of Switching to Second-line of Each ART Cohort by Year

The results show the peak of second-line regimen switching happened on the central time of the treating period for all the ART cohorts while the lowest switching rate occurred in the first year of the ART treatment (Figure 5). Patients who start ART treatment earlier had a higher peak. For 2010 ART cohort, the prevalence of switching in the first years is 0.9%, and the highest switching rate (3.4%) happened in the fourth year.

VL Test Outcome among Patients Switching to the Second-line Regimen

Among those switching patients, the proportion of patients switching to the second-line regimen without VL test became lower among later ART cohorts (Figure 6). For those

starting ART later, the proportion with confirmed failure prior to switching was higher. Only 16.5 % of patients were switched to the second line with confirmed VL failure for 2010 ART cohort while this number was 42.1% for 2016 ART cohort. In terms of ART adherence, more people with confirmed failure demonstrated weak adherence, except the 2010 ART cohort (Table 7).

Association between VL Testing and Second-line Regimen Switching

The analysis of the association between VL testing and regimen switching shows that patients who had VL showing virologic suppression had a 2.67 times higher odds and those with a VL test showing treatment failure had a 6.67 times higher odds of switching to a second line regimen compared to those with no VL test done, after adjustment for other factors. Patients who initiated ART treatment later had a lower likelihood of switching. The odds of switching within 18 months on treatment was only 0.15 times for the 2016 ART cohort compared with the 2010-2012 ART cohort (Table 8). The interaction between the outcome of VL test and cohort year was not statistically significant in this study. Being male, under 35 years old and higher WHO stage when starting ART treatment were also risk factors for switching, in the adjusted analysis.

DISCUSSION

From 2010 to 2017, in conjunction with the growth of the national ART program and the expansion of criteria for ART eligibility, Haiti dramatically increased the coverage of VL testing for ART patients. Meanwhile, the percentage of patients switching to second-line regimens increased a bit but then hit a plateau and even declined. The result demonstrates that patients who had VL tests, especially who had VL failure had a higher likelihood of switching to second-line ART regimen.

Regarding the outcome of the VL test, among patients having VL test, a majority had a suppressed VL result. Confirmatory testing after a first VL failure was often not done, as

directed in WHO and Haiti's national guidelines. Weak adherence to treatment is considerable concern and seems to explain just over half of the cases of confirmed VL failure. The meaningful subset of patients with good adherence but with a VL failure on confirmatory test suggests there is a resistance problem which is not being addressed[28]. While we cannot say for sure that those are cases of resistance, the finding is suggestive.

Concerning the association between VL test and second line regimen switching. Patients who had access to VL test, especially patients with VL failure record, were more likely to switch to second-line regimen compared with patients without access to VL test. This result indicates that the VL test is useful evidence on second line switching for healthcare workers. The scale-up of VL test could help more patients in need of switching to the second-line regimen, which could improve their health outcome by providing effective medication.

Before 2016, VL testing was not widely used as evidence for second line switching. But since 2016, VL test has become a guide for health caregivers to switch ART regimens. In 2017, over 70% of patients switching to second-line ART treatment had a VL failure history before switching. However, we can see the promising sign of more timely switching but still with overall low levels of switching and with a delay well past the timeframes described in the national ART guidelines for patient management. The delay of switching increased the risk of developing resistance to the current ART medication, and possibly transmitting a resistant form of HIV to others. The timeliness of switching of patients with strong adherence should be improved to prevent ART resistance.

Jean-Louis et al. (2017) conducted research assessing VL outcome among patients receiving antiretroviral therapy at five hospitals around Port-au-Prince, Haiti[20]. Among 7903 patients on ART for six months or longer between July 2013 and February 2015, 2,313(25.47%) patients received at least HIV-1 RNA (VL) test. The proportion of VL testing in our study ranged from 3.93% to 2.32% from 2013 to 2015, which is much lower compared with Louis' research. It is not surprising that Port-au-Prince, as the capital and the densest urban area of Haiti, would have had priority when Haiti began to increase the

access to VL testing. It seems to have taken additional time to expand VL testing beyond the capital city to a national level, and our results demonstrate that MSPP extended VL availability nationally after 2016. Regarding the outcome of the VL test, our results were similar to those of Jean-Louis et al. (2017), showing virologic suppression in around two-thirds of each ART cohort of patients. Our results demonstrated a pressing need for greater use of confirmatory VL testing and possible second-line regimen ART treatment among patients with an observed VL failure.

Our finding on the limited use of second-line regimens is consistent with findings from other resource-limited settings. In a cohort study involving patients from 16 sub-Saharan Africa countries from 2004 to 2013, 10,352 patients (3.5%) switched during 782,412 person-years of follow-up, for a rate of 1.3 switches per 100 person years[21]. A 2011 study from South Africa reported that 38.4% patients had access to VL test and 9.8% (9.1–10.5%) patients switched to the second-line ART treatment in the first three years.[29] The switching prevalence in our study was much lower than that reported in both these prior studies.

In theory, the broader use of VL test should result in optimized treatment with timely detection of VL failure and timely switching to the second-line ART regimen in cases where resistance is suspected. Our study found a mixed pattern where later ART cohorts did not necessarily have overall rates of switching which were consistently higher at comparable follow up periods compared to earlier cohorts, although switching following a detectable viral load test did seem to become more timely for later ART cohorts. Together these findings suggest that the pace of use of second-line regimens has not kept up with what might be expected given the greater access to viral load testing. The large proportion of patients without confirmatory testing may be an important reason for this result since Haiti has consistently had underused stocks of second-line regimens available at the national level[30]. It is necessary for Haiti to continue expanding access to confirmatory VL testing, which could help support modification of HIV clinical management practices to embrace timely switching for patients with confirmed virologic failure despite strong ART adherence, and expand evidence-based initiatives to promote strong ART adherence.

Limitations and Strengths

This study only included VL tests with results reported back to the iSanté EMR system and may have missed a meaningful portion of VL test done at one of the National Reference Laboratories, but without results yet returned to iSanté (reflecting a backlog of tests and results in the labs). Other monitoring methods in the ART treatment such as CD4 monitoring which is major monitoring approach before 2015 were not considered in this study. Another limitation is that the final exploratory model of associations between VL testing and regimen switching did not consider the timing and sequence of each event, future analyses could use time-to-event methods to address these limitations. Therefore, the results should not be interpreted as reflecting a causal relationship between the availability of viral load testing and the likelihood of second-line regimen switching. Also, our study was not able to track patients who transferred care between health facilities or detect cases where the same person may have been registered in the iSanté EMR using more than one patient identifier, meaning that our patient counts may have included duplicate records for the same person. Prior studies have estimated that the level of duplicate records within iSanté is approximately 8-10%[31,32].

This study is the first to describe the routine use of VL test and second line ART regimen switching on a national scale in Haiti. The study included 67361 patients from 88 sites, accounting for around half of Haiti's HIV patients, from all regions of the country, suggesting that our findings have broad representativeness in terms of the conclusions which can be drawn about the routine use of VL testing and second-line regimen switching within Haiti's national ART program. Our results could help Haiti's Ministry of Health to monitor and adjust the initiative of expanding viral load test. Also, this study involved almost eight-years of data and therefore reflects the implementation of the health policy of expanding access to VL testing. In addition, this is the first study focus on the association between VL test and second line regimen in Haiti. Moreover, this study considers the adherence factor when analyze switching patients with confirmed VL failure. Based on these strengths, this study can help policymakers and related stakeholders to figure out the

gaps remaining to reach the 90-90-90 goals for HIV epidemic control through understanding the level and results of VL testing scale-up.

CONCLUSION

In conclusion, this is the first study focus on the association between VL test and second line switching to second-line therapy at a wide scale in Haiti. The result elucidates the implementation of national and WHO guidelines on ART patient monitoring and trends in routine VL testing by year. Our findings show that expanded access to VL testing, especially since 2016, seems to have supported clinical decision making towards timely ART switching to some degree, but with progress still needed in order to achieve timely and appropriate use of second-line regimens in Haiti. There is still a way to go in broadening access to VL testing in ART treatment in Haiti, particularly timely confirmatory testing, which can guarantee patients are placed on appropriate medication in cases of likely HIV drug resistance. Our study suggests the lagging switching patients to second-line ART regimens remains a concern. To guarantee HIV patients are obtaining effective treatment and avoiding the resistance to medication, the healthcare givers should ensure confirmatory testing and take a faster action after confirmed viral load failure, so that Haiti's national ART monitoring guidelines move from theory to practice.

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TABLES AND FIGURES

TABLE 1 Patient Characteristics

Categories		Number	Proportion
	Total	67,361	100.0%
Age (Median age: 36.01)	16 - 24	8,404	12.5%
	25 - 34	22,845	33.9%
	35-44	19,158	28.4%
	45-54	10,947	16.3%
	>55	6,007	8.9%
Gender	female	43,591	64.7%
	male	23,732	35.2%
	missing	38	0.1%
Year of ART Initiation	year 2010	3,933	5.8%
	year 2011	5,865	8.7%
	year 2012	8,669	12.9%
	year 2013	10,938	16.2%
	year 2014	11,897	17.7%
	year 2015	10,740	15.9%
	year 2016	12,975	19.26%
	year 2017	2,344	3.5%
WHO stage	Stage 1	13,338	19.8%
	Stage 2	11,078	16.5%
	Stage 3	14,402	21.4%
	Stage 4	21,903	32.5%
	Missing	6,640	9.9%

TABLE 2 The Use of VL Test 2010-2017

	Year 2010	Year 2011	Year 2012	Year 2013	Year 2014	Year 2015	Year 2016	Year 2017
# of total test (column%)	11	9	84	971	829	865	17917	20585
# and % of detectable test	7 63.6%	4 44.4%	15 17.9%	409 42.1%	429 51.8%	307 35.5%	7278 40.6%	11083 53.8%
# of total patient active in care	3932	8950	16038	24251	31421	36245	43913	40521
# and % of active patients (with at least 1 test)	11 0.3%	9 0.1%	64 0.4%	952 3.9%	789 2.5%	840 2.3%	16745 38.1%	19182 47.3%

Note: Year 2017 includes three quarters.

TABLE 3: The Proportion of Routine Use of VL Testing of Each ART Cohort

	2010 ART Cohort	2011 ART Cohort	2012 ART Cohort	2013 ART Cohort	2014 ART Cohort	2015 ART Cohort	2016 ART Cohort
1st year	0.03%	0.1%	1.1%	2.7%	0.9%	15.4%	44.6%
2nd year	0.6%	2.7%	5.7%	2.4%	20.2%	48.2%	N.A.
3rd year	3.8%	8.1%	2.8%	19.6%	52.7%	N.A.	N.A.
4th year	7.8%	3.6%	23.5%	53.2%	N.A.	N.A.	N.A.
5th year	3.3%	24.1%	53.3%	N.A.	N.A.	N.A.	N.A.
6th year	28.7%	59.3%	N.A.	N.A.	N.A.	N.A.	N.A.
7th year	59.6%	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.

TABLE 4 The Outcome of VL Test by ART Cohort Year

	2010 ART Cohort	2011 ART Cohort	2012 ART Cohort	2013 ART Cohort	2014 ART Cohort	2015 ART Cohort	2016 ART Cohort
Total eligible patients	3933	5865	8669	10938	11897	10432	1887
Never Tested	56.6%	55.6%	57.5%	58.3%	54.7%	53.0%	48.3%
First VL: no failure	29.1%	29.8%	28.1%	27.9%	31.8%	32.6%	36.2%
First VL: failure	14.3%	14.6%	14.4%	13.9%	13.6%	14.5%	15.5%
Among those patients with first VL failure							
Total first VL failure patients	562	855	1244	1515	1615	1509	293
Followed by suppressed	6.8%	8.2%	7.0%	6.1%	7.3%	7.1%	5.1%
No confirmatory test done	56.8%	57.0%	61.9%	62.4%	63.8%	67.0%	75.4%
Confirmed VL Failure	36.5%	34.9%	31.1%	31.5%	28.9%	25.9%	19.5%
Among patients with confirmed failure							
Total confirmed VL failure patients	205	298	387	477	466	391	57
With strong adherence	48.8%	45.6%	47.0%	42.6%	41.2%	39.9%	43.9%
With weak adherence	51.2%	54.4%	53.0%	57.4%	58.8%	60.1%	56.1%

Note: 2016 ART Cohort only includes patients initiating ART treatment at first three months.

TABLE 5 The Prevalence Second Line Regimen Switching 2010-2017

	Year 2010	Year 2011	Year 2012	Year 2013	Year 2014	Year 2015	Year 2016	Year 2017
# of eligible patients	3,932	8,950	16,038	24,251	31,421	36,245	43,913	40,521
# and % of switching patients	21 0.5%	32 0.4%	59 0.4%	296 1.2%	306 1.0%	373 1.0%	344 0.8%	279 0.7%
# and % of switching patients with VL failure before switching	0 0.0%	0 0.0%	0 0.0%	12 4.1%	37 12.1%	68 18.2%	144 41.9%	201 72.0%

Note: Year 2017 includes first-three quarter data.

TABLE 6 Kaplan-Meier Estimates of the Proportion of Patients with VL Failure Who Switched to Second-line Regimens, by VL Failure Year

Time	Beg. Total	Fail	Survivor Function	Std. Error	[95% CI]
2010-2012					
180	9	1	0.89	0.10	[0.43, 0.98]
365	8	1	0.78	0.14	[0.36, 0.94]
545	7	1	0.67	0.16	[0.28, 0.88]
2013					
180	245	45	0.84	0.02	[0.80, 0.88]
365	207	36	0.72	0.03	[0.66, 0.77]
545	170	36	0.59	0.03	[0.53, 0.65]
2014					
180	198	27	0.88	0.02	[0.83, 0.92]
365	172	23	0.78	0.03	[0.72, 0.83]
545	152	20	0.69	0.03	[0.62, 0.74]
2015					
180	114	34	0.77	0.03	[0.69, 0.83]
365	103	11	0.69	0.04	[0.61, 0.76]
545	91	11	0.62	0.04	[0.54, 0.69]
2016					
180	4122	679	0.86	0.01	[0.85, 0.87]
365	2206	1874	0.47	0.01	[0.45, 0.48]
545	42	2087	0.01	0.00	[0.01, 0.01]

TABLE 7 VL Testing among Patients Switching to the Second-line Regimen

	2010 ART cohort	2011 ART cohort	2012 ART cohort	2013 ART cohort	2014 ART cohort	2015 ART cohort	2016 ART cohort
# of total switching	243	340	398	317	225	168	19
# and % with no VL test	69 28.4%	89 26.2%	103 25.9%	87 27.4%	61 27.1%	40 23.8%	4 21.1%
# and % with no failure	85 35.0%	114 33.5%	132 33.2%	82 25.9%	46 20.4%	39 23.2%	2 10.5%
# and % with single failure	49 20.2%	78 22.9%	96 24.1%	80 25.2%	61 27.1%	31 18.5%	5 26.3%
# and % with confirmed failure	40 16.5%	59 17.4%	67 16.8%	68 21.5%	57 25.3%	58 34.5%	8 42.1%
With strong adherence	23 57.5%	28 47.5%	33 49.3%	25 36.8%	20 35.1%	26 44.8%	3 37.5%
With weak adherence	17 42.5%	31 52.5%	34 50.7%	43 63.2%	37 64.9%	32 55.2%	5 62.5%

Note: Cohort 2016only includes patients initiating ART treatment at first three months

TABLE 8 Association between VL Test and Second-line Regimen Switching

		Odds Ratio	p value	95% Confidence Interval
VL Test	No Test	1	Reference	Reference
	No VL Failure	2.61	<0.001	(2.01, 3.38)
	VL Failure	6.67	<0.001	(4.09, 10.89)
Cohort Year	Cohort 2010-2012	1	Reference	Reference
	Cohort 2013	0.55	0.001	(0.39, 0.78)
	Cohort 2014	0.40	0.001	(0.24, 0.68)
	Cohort 2015	0.30	0.010	(0.12, 0.76)
	Cohort 2016	0.15	0.014	(0.03, 0.67)
Gender	Female	1	Reference	Reference
	Male	1.39	<0.001	(1.24, 1.56)
Age Group	16~24	1	Reference	Reference
	25~34	1.05	0.565	(0.88, 1.25)
	35~44	0.96	0.689	(0.79, 1.16)
	45~54	0.86	0.105	(0.73, 1.03)
	>55	0.74	0.024	(0.56, 0.96)
WHO Stage	1	1	Reference	Reference
	2	1.43	0.015	(1.07, 1.92)
	3	1.98	<0.001	(1.49, 2.64)
	4	3.18	<0.001	(2.55, 3.98)

FIGURE 1 Data Exclusion Process

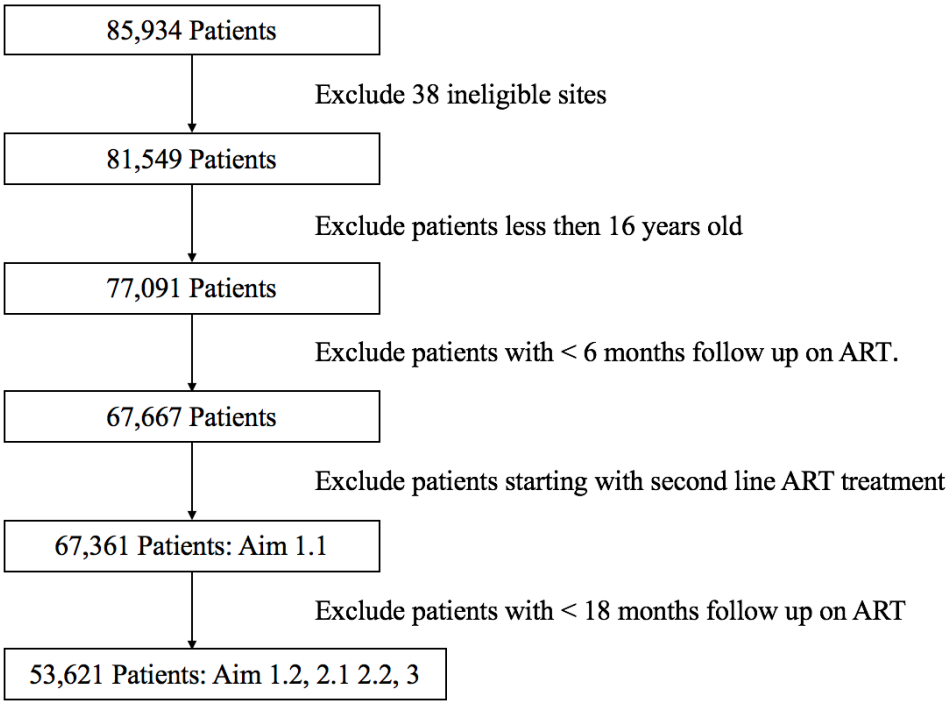


FIGURE 2 The Proportion of Routine Use of VL Testing of Each ART Cohort

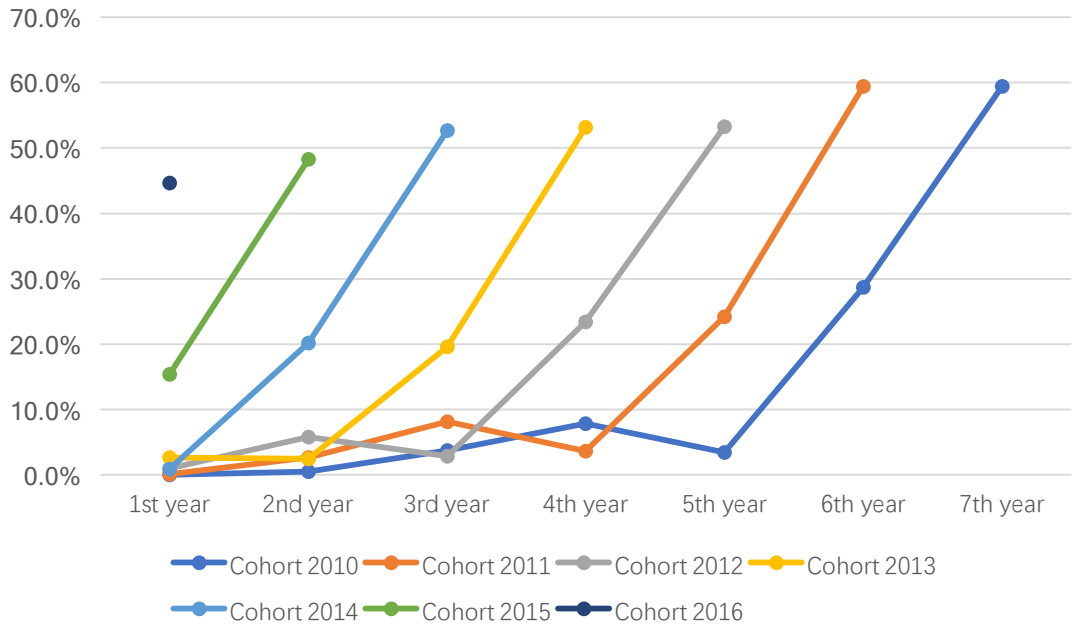


FIGURE 3 The Overall Outcome of VL Testing, All ART Cohorts (2010-2016)

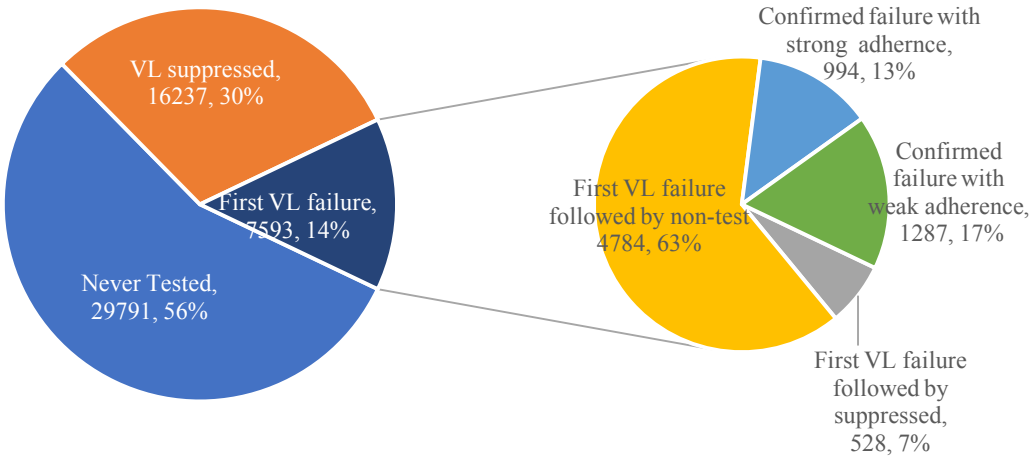


FIGURE 4: Kaplan-Meier Estimates of the Proportion of Patients with VL Failure Who Switched to Second-line Regimens, by VL Failure Year

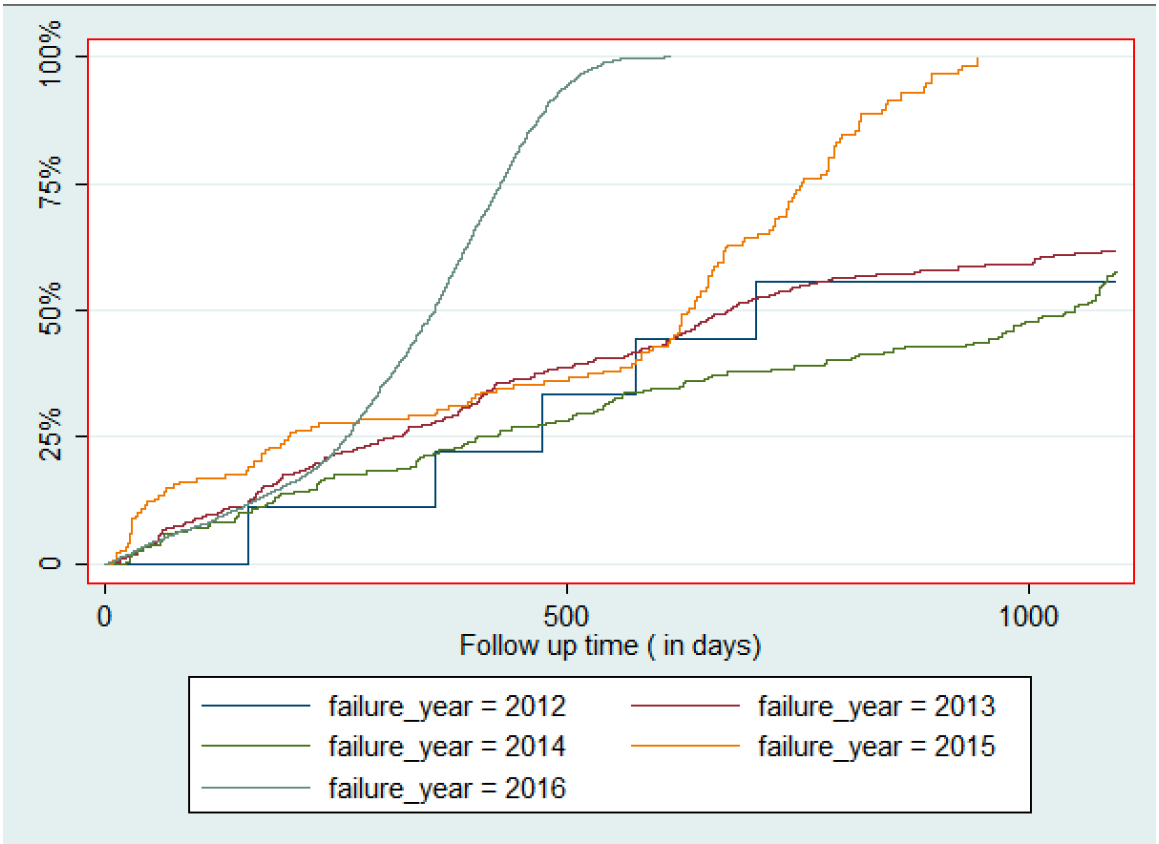
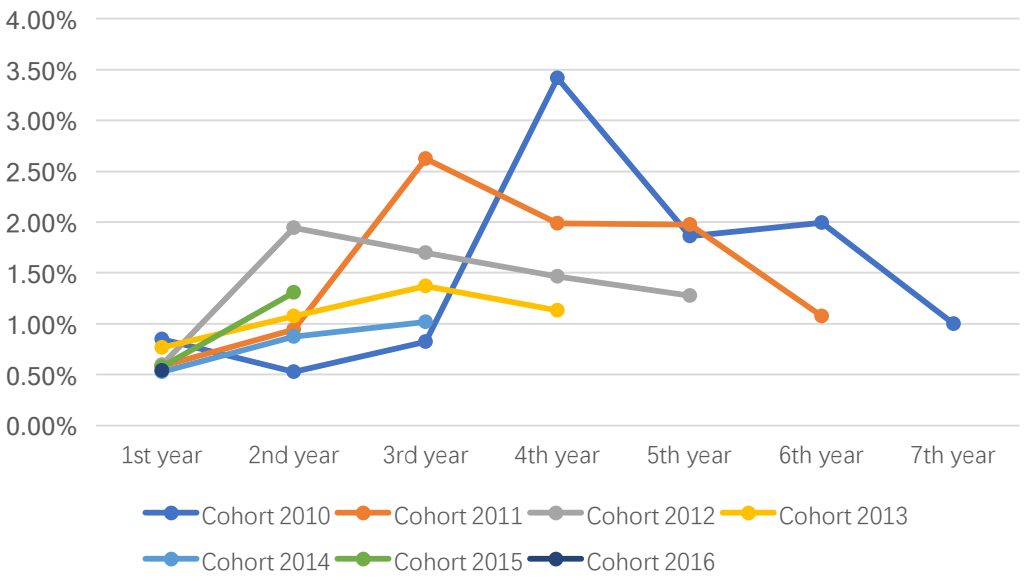


FIGURE 5 The Prevalence of Second Line Regimen Switching in ART Treatment of Each ART Cohort



Note: 2016 ART cohort only includes patients initiating ART treatment during January – March 2016.

FIGURE 6 The Distribution of VL Outcome among Patients Switching to Second-line Regimen