Impact of Provider Initiated Testing and Counseling optimization on Care Recipient's' Clinical, Immunologic, and Virologic status at time of presentation into care

FINAL REPORT

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Abstract

Introduction

Similar to other countries with a generalized HIV epidemic, Mozambique is moving closer to reaching the first UNAIDS goal of having 95% of all persons with HIV (PWH) knowing their status (i.e., HIV infections diagnosed). The strengthening and scaling up of routine opt-out and efficient HIV testing in high-yield settings to maximize the identification of persons with unknown status coupled with their timely linkage to antiretroviral therapy (ART) services is a critically important strategy to accelerate progress towards the first lofty UNAIDS 95-95-95 goal by 2025. . This report describes the impact of a Provider Initiated Testing and Counseling (PITC) optimization strategy on trends in clinical, immunologic and virologic status among patients newly identified as being HIV-positive through PITC services, in the district of Quelimane City between October 2017 and September 2018.

Methods

A retrospective cohort evaluation using routine data was done. Data on all patients enrolled in HIV care who were tested in 14 selected health facilities in the district of Quelimane City from October 2017 to September 2018 were included. Descriptive analyses were done and presented as frequencies, means and standard deviations, as well as medians and interquartile ranges (IQR). A mixed effect logistic regression model was used with early retention in care as the outcome, and site (i.e., health facility) as a random effect.

Results

A total of 13,803 persons with HIV (PWH) who were identified through PITC were included in the analysis. Four percent (n=500) of the identified patients were children less than 5 years of age, with 6% (n=365) being between 5 and 14 years of age. Overall, 38% of patients were diagnosed as being HIV-positive via PITC services, 29% via voluntary counseling and testing (VCT) services, 19% within maternal and child health (MCH) services, and 6% outside of VCT, MCH or PITC services. Data were not available for the other 8% of patients. Over this 12-month evaluation period, there was no significant increase seen in the number of persons newly diagnosed with HIV and registered across all testing domains. There was an increase from 37% to 43% in the proportion of patients diagnosed with HIV via PITC (of all tested), with the largest increase in the proportion of persons being newly diagnosed via PICT being seen in the final quarter of this evaluation period.

The median CD4 cell count at first visit (defined as a treatment follow-up visit within the first month following registration into HIV care services) was 340 cells/mm^3 across all evaluation sites. When combining all patients entering HIV care from all possible entry points, the median CD4 cell count among adults changed from 357 cells/mm^3 to 310 cells/mm^3 from the start to the end of evaluation period , namely from October 2017 to September 2018. The median CD4 cell count

among children 5 to 14 years of age from all HIV entry points combined and computed across the evaluation period and sites was equal to 389 cells/mm^3; these median CD4 cell counts trended from 382 cells/mm^3 during the first month of the evaluation (October 2018) to 260 cells/mm^3 during the last month of the evaluation period (June 2019). The median CD4 percentage was equal to 20% across the evaluation period, with a change from 17% to 14% from start to end of the evaluation period, among children under five years of age. Among patients who attended PITC, the median CD4 cell count value changed from 333 cells/mm^3 to 282 cells/mm^3 among adults, from 476 cells/mm^3 to 314 cells/mm^3 among children 5 to 14 years of age, and from 17% to 21% among children under five years of age. The median CD4 cell count among those greater than or equal to 15 years of age was in general lower for those tested in PITC (305 cells/mm^3, versus 330 cells/mm^3 [VCT], 394 cells/mm^3 [MCH], and 375 cells/mm^3 [Other sectors]). For children 5-14 years of age, the median CD4 cell count was 384 cells/mm^3 for PITC, 546 cells/mm^3 for VCT, 341 cells/mm^3 for MCH, and 497 cells/mm^3 for the Other sector(s). Among children less than five years of age, the median CD4 cell count percentage was 20% for PITC, 20% for VCT, and 22% for MCH.

The probability of adult patients in this cohort to be retained in care at three months post ART initiation increased almost linearly with immunologic status for CD4 cell count values up to approximately 500 cells/mm^3, however, the probability for adult retention at three months stabilized, or even waned slightly with CD4 cell count values greater than 500 cells/mm^3. Among children, the probability of early retention in care generally increased with increasing CD4 cell counts, however, no significant association was seen.

A total of 935 (7%) of the 13,803 ART-treated patients were eligible for viral load (VL) analysis and had one done. Eighty-two percent of the patients who were enrolled into care in October 2017 had an undetectable viral load, while in March 2018, the viral suppression rate was 76%.

Conclusions

The evaluation showed that during the evaluation period for the implementation of the PITC optimization strategy, there was an increase in proportion of patients diagnosed through PITC. Patients newly identified as HIV-positive through PITC had more advanced immunosuppression within the first month of being registered into HIV services when compared to persons being newly identified as being HIV-positive via free-standing VCT services.

1. Project Background

When considering the Joint United Nations Programme on HIV/AIDS (UNAIDS)'s 2020 HIV performance 90-90-90 goals) and the updated95-95-95 top-line targets to be achieved by 2025, one of the most critical step in the human immunodeficiency virus (HIV) treatment cascade appears to be the identification of new positive cases, the first of the three UNAIDS target elements. In 2020, 84% of persons with HIV (PWH) knew their HIV status. Among people who knew their status, 87% were accessing treatment, and among people accessing treatment, 90% were virally suppressed [1]. In Mozambique in 2020, these numbers were 82%, 68% and 56% for the three respective indicators [2].

During the past five years, Mozambique, like other countries in southern Africa, has mainly focused on the second 95:95:95 goal, the provision of combination antiretroviral therapy (ART) to eligible HIV-positive adults and children. Significant progress has certainly been made in terms of ART coverage, with coverage improving from 55% in 2018 to 68% in 2020 among adults, and 42% in 2018 to 64% in 2020 among children [2, 3]. The MOH introduced PITC guidelines in 2015, as a way of increasing the identification of people living with HIV and ensure immediate initiation of antiretroviral therapy[4]. An ongoing challenge is the identification of PWH; which, in order to be addressed, requires more innovative and efficient high yield testing strategies.

In addition, performance towards the second 95:95:95 goal (which now applies to all newly identified PWH given the nationwide implementation of the Test-and-Start strategy, i.e., the initiation of ART in all HIV-positive persons regardless of immune status) is critically linked to performance in the first 95-95-95 goal. If significant numbers of new PWH are not continually identified, the numbers of persons newly enrolled into ART will lag and epidemic control efforts will suffer.

In terms of Mozambique-specific data, the 2015 population-based evaluation, titled *Inquérito de Indicadores de Imunização, Malária e HIV/SIDA em Moçambique* (IMASIDA, Immunization Indicators Survey, Malaria and HIV/AIDS in Mozambique, in English) showed that significant proportions of reproductive-aged (15-59 years of age) men (58%) and women (38%) had never been tested for HIV [5]; representing a significant gap in the first 95 UNAIDS target. More recent estimates from data generated through the Spectrum Software (developed with UNAIDS support)[1], estimate that approximately 2.1 million people are living with HIV in Mozambique (2020) [1], underscoring the importance of reaching and/or surpassing the goal for at least 95% of these persons to know their status and initiate care.

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[1] UNAIDS and partners helped develop the AIDS Impact Module using Spectrum Software to support countries in monitoring their HIV epidemic, using HIV surveillance, survey, demographic and program data. Retrieved from: https://www.unaids.org/en/dataanalysis/datatools/spectrum-epp.

In Mozambique during 2020, approximately 7.9 million people were tested for HIV, an increase of 38% since 2014, when about 5.7 million were tested. The overall HIV seropositivity rate for those tested (2020) was 4.4% [2]. Among all tests completed, 9.6% were carried out within a health facility (HF)-based voluntary counseling and testing (VCT) context, 52% within maternal and child health (MCH) services, 35% as provider-initiated testing and counseling (PITC) (including all PITC service delivery points except MCH), and 2% as part of community-based VCT initiatives. However, by 2020, the country of Mozambique as a whole was still only reaching 82% of its target in terms of numbers of people HIV tested and counseled [2]. With an increasing number of supported HF in Zambézia province districts with varying HIV disease burdens (i.e., a widely varying population densities and HIV prevalence), there is a significant need to more efficiently provide HIV testing services (HTS) and HIV testing and counseling (HTC) service delivery points in the highest yield geographic settings in order to maintain excellent performance in the identification of new HIV-positive individuals (and prompt linkage to ART services).

Friends in Global Health (FGH), a wholly owned subsidiary of Vanderbilt University Medical Center (VUMC), has been operating as a Mozambican Ministry of Health (MOH) implementing partner in Zambézia province since 2006. Over the past 10 years, FGH's *Avante* program, funded by the U.S. President's Emergency Plan for AIDS Relief (PEPFAR), has expanded dramatically, now supporting the provision of comprehensive HIV/AIDS services (including potentially life-saving ART) in 199 health facilities across 17 districts within Zambézia. As of February 2021, FGH staff supported 144 Zambézia-based facilities across 18 districts. Analyzing Joint Underperformance and Determining Assistance (AJUDA) Phase 1 thru 3 health facilities offering HIV Care, Treatment & Prevention Services into Primary Care.

VUMC/FGH has led the way among clinical implementing partners in the development and scale-up of targeted provider-initiated counseling and testing (PITC), referred to as the PITC Optimization Strategy, within service delivery points (e.g., emergency room and outpatient clinic) where additionally allocated and trained counselors applied a Ministry of Health (MoH) approved HIV risk-based screening (signs and symptoms) tool to adults presenting for care in these high HIV test positivity yield settings. During the 2017 Country Operational Plan (COP17), FGH implemented its "PITC optimization" strategy to maximize HIV testing yield in its high-volume supported HF (initially in the provincial capital district of Quelimane City).

The FGH team prioritized sectors within each of these HF with the highest proportion of ill patients (and those most likely to have underlying immunosuppression) present, such as the emergency ward, adult and pediatric triage wards, and inpatient medical wards. Generally speaking, "PITC optimization" describes a set of intervention activities implemented by PEPFAR clinical implementation partners, identified, and monitored in partnership with the MOH, and aimed to result in a significant increase of patients identified through PITC. For FGH, this included partnership with the Provincial Health Directorate of Zambézia (DPS-Z) to implement a strategy which included the following activities:

- Training of health care providers on PITC;
- Allocation of checklists for signs and symptoms of HIV to facilitate screening in adults and children;
- Allocation of furniture, and/or rehabilitation space for PITC in the Adult Screening and Emergency Room (ER) clinic;
- Support for human resources;
- Performing biweekly joint technical support with DPS-Z for selected HF.

The assumption was that prior to the PITC optimization strategy, patients may have been visiting a HF and receiving care (e.g., for opportunistic infections [OI], etc.) but may not have been HIV tested until after a number of visits, when HIV disease was perhaps more advanced. As such, it was suspected that patients tested and diagnosed as HIV-positive via PITC had more advanced immunosuppression at the time of HTC when compared to those diagnosed within HF-based VCT services. In the routine monitoring of our program, we found that the implementation of the PITC optimization strategy showed an increase in the number of persons tested coupled with an overall decrease in HIV seropositivity rates among those tested. We hypothesized that since the advent of this strategy of PITC optimization (i.e., with greater numbers of patients tested and diagnosed via PITC), persons newly identified as being HIV-positive via PITC would have less advanced immunosuppression compared to those diagnosed pre-PITC optimization.

To better inform program decision-making and to assist in the design of tailored interventions aimed at improving performance in the first 90 (or 95) UNAIDS target of "knowing one's status," we aimed to determine if the sociodemographic, laboratory, and clinical characteristics (including the level of immune suppression at the time of presentation into HIV care) differed or changed over time among persons newly identified as being HIV-positive within the context of an optimized PITC strategy.

2. Evaluation Purpose and Questions

The major question sought to be answered by this evaluation was: by increasing the number of people identified as HIV-positive through PITC (i.e., through PITC optimization), would it be possible to enroll HIV-positive patients with less advanced immunosuppression into care compared to persons newly identified as being HIV-positive prior to the implementation of the PICT optimization strategy.

The general objective was to evaluate the effect of the PITC optimization strategy on trends in clinical (i.e., World Health Organization [WHO] clinical stage), immunologic (i.e., CD4 cell count) and virologic (i.e., viral load suppression [VLS]) status among patients newly identified as

being HIV-positive through PITC services, in the district of Quelimane City between October 2017 and October 2018.

Specific objectives were:

1) To evaluate the trends in clinical, immunologic, and virologic status of newly identified HIV-positive persons at their time of presentation into care by whether they underwent HTC in a VCT versus a PITC setting;

2) To evaluate the association of the level of immunosuppression at the time of presentation into HIV care with the timeliness of ART initiation; and

3) To evaluate the association of the level of immunosuppression at the time of presentation into HIV care with early retention in care rates among persons initiated on ART.

3. Evaluation Design/ Methods/ Limitations

1. *Evaluation type*

We conducted an internal outcomes evaluation, in which programmatic data were analyzed to evaluate the outcomes of interest.

2. *Evaluation design*

A retrospective cohort study was performed. We conducted a secondary data analysis on aggregated individual- and health facility-level data routinely collected by district and provincial teams for programmatic monitoring and reporting purposes.

3. *Sampling strategy*

All data available from the electronic patient database OpenMRS were included in the analysis. Routinely collected, de-identified data were extracted from OpenMRS for this retrospective cohort analysis.

4. *Methods*

We included data from all HIV-positive patients (children and adults of all ages) who were identified at HTC services at any entry point and were enrolled in HIV services at the selected HF,

from the period of October 2017 through September 2018 in all FGH-supported HF in the district of Quelimane City. There were no specific exclusion criteria.

Description of key terms

For the purposes of this evaluation, *early retention in care* was defined as three-month retention, with at least three ART pick-ups within the first 99 days following ART initiation. For *immunodeficiency status* (at time of enrollment into care), a CD4 cell count (cells/mm^3) measured within the 30 days after enrollment to HIV care was considered (as a CD4 cell count result more than one month after enrollment may be influenced by initiation of ART). The CD4 cell counts are presented as absolute values for children $\geq$ 5 years of age and adults, while the immunodeficiency status among children under the age of five are presented as percentages, due to the age-related differences in lymphocyte counts, with very young children (i.e., less than 5 years of age) having significant higher total lymphocyte counts. *Time of presentation into care* was defined by the period of 30 days after enrollment in HIV services. *Timeliness of ART initiation* was defined as initiation of ART within 15 days of being diagnosed via a positive HIV test. The *HIV entry points* were defined as VCT, MCH, PITC and other, where "Other" includes any entry point that is not PITC, MCH or VCT (including services/sectors for Tuberculosis [TB], gender based violence [GBV], community testing, referred from another HF, adolescent, and young adult friendly services [SAAJ], private clinics, etc.). *Early (3-month) retention* was defined as having at least three ART pick-ups within 99 days from ART initiation date.

5. *Analysis plan*

The analysis was descriptive, and data are presented as totals/numbers, per health facility, by sector where HTC took place for those patients who initiated ART. The analysis was done using frequencies, means and standard deviation (sd), as well as medians and interquartile ranges (IQR) provided. A mixed effect logistic regression model was used with early retention in care as the outcome, and site (i.e., health facility) as a random effect. All statistical analyses were conducted with the support of software programs STATA/SE 15.1 (Statacorp LLC, Tx, US) and R version 4.0.5 [6].

6. *Limitations of design*

There were several limitations within the realization of this evaluation. The evaluation included data only from the health facilities in the more urban district of Quelimane City and, as such, results may not be generalizable for PWH patient populations living in rural areas in the province of Zambézia. The evaluation period was one year, but the inclusion year was measured in the period of October 2017 to June 2018 to allow analysis for retention to care and uptake of CD4 cell count analysis, which could limit the interpretability of these findings, specifically related to a limitation in detecting any significant trends during the short period, and a limitation in applying these results to a subsequent longer programmatic period.

As routine data were used, these results/findings are subject to the quality and completeness of data registry and entry into the OpenMRS electronic patient tracking system. Data from people who were diagnosed with HIV at the selected HF but did not enroll into HIV care were not included in the analysis.

Additionally, while WHO clinical stage data were available, there are questions regarding the reliability of this data, as these results were found to be the same across all patients included in the analysis (i.e., all had same documented WHO clinical stage). As no trend could be assessed based on these homogeneous data, this analysis was not performed as planned.

7. *Ethical considerations*

This secondary data analysis is covered under the blanket protocol "*Quality Improvement for HIV Care and Treatment in Zambézia province of the Republic of Mozambique under the President´s Emergency Plan for AIDS Relief (PEPFAR)*." The data use and evaluation plan were approved the VUMC Institutional Review Board (IRB) (#201887), the Institutional Research Ethics Committee for Health of Zambézia Province (*Comité Institucional de Bioética para Saúde – Zambézia*; CIBS-Z-20), and was reviewed in accordance with the Centers for Disease Control and Prevention (CDC) human research protection procedures and was determined to be research, but CDC investigators did not interact with human subjects or have access to identifiable data or specimens for research purposes.

All data included in this analysis were de-identified programmatic data and aggregated data. The electronic databases outlined in the *Methods* section were stored on password protected and encrypted servers at FGH offices. De-identified data were extracted from these secure databases and sent via secure file transfer to relevant key FGH and VUMC personnel (i.e., the biostatisticians) for analysis.

8. *Stakeholder engagement*

FGH technical teams have ongoing collaborations with key stakeholders working in the health facilities and communities with which they are engaged. The concept note and evaluation plan for this secondary data analysis evaluation was elaborated with support from the provincial- and district-level authorities, and approved by sponsoring institution CDC-Mozambique.

9. *Deviations from Scope of Work (SOW)/protocol*

There was no significant deviation from the proposed concept note. However, as detailed in the *Limitations* section above, there was one outcome that we were unable to evaluate in these analyses.

10. *Data quality assurance*

Programmatic data used in this evaluation were subject to routine data verification processes conducted by trained members of FGH's Monitoring and Evaluation (M&E) team. All data were stored securely on password-protected databases at district- and provincial level FGH offices. The performance of the program indicators was monitored by HF staff. All subsequent indicators were collected and internally reported monthly by the Health Information Systems (HIS) team, following the regular reporting period for program data.

Upon receipt of the requested extracted dataset for this evaluation/analysis, data were cleaned and reviewed to ensure they were consistent and appropriate with the evaluation inclusion criteria.

4. Findings

4.1.   Demographics

A total of 13,803 patients enrolled in HIV-care were included in the analysis. **Table 1** describes the main demographics. Four percent of the identified patients were children under 5 years of age (n=500), 6% (n=365) were between 5 and 14 years of age. The remaining 90% (n=12,938) of patients were considered adults per programmatic reporting (i.e., 15 years of age and older).

Overall, 38% (n=5,267) of patients were diagnosed within PITC services; 29% (n=4,055) in VCT services, and 19% (n=2,612) in MCH services.

Table 1. Characteristics of the patients (n=13,803)

	<5 N=500	5-14 N=365	15+ N=12938	[ALL] N=13803
Sex				
Female	257 (51.4%)	222 (60.8%)	7907 (61.1%)	8386 (60.8%)
Male	243 (48.6%)	143 (39.2%)	5031 (38.9%)	5417 (39.2%)
Entry Point into Care				
MCH	202 (40.4%)	4 (1.10%)	2406 (18.6%)	2612 (18.9%)
No info	35 (7.00%)	66 (18.1%)	985 (7.61%)	1086 (7.87%)
Other	22 (4.40%)	29 (7.95%)	732 (5.66%)	783 (5.67%)
PITC	177 (35.4%)	178 (48.8%)	4912 (38.0%)	5267 (38.2%)
VCT	64 (12.8%)	88 (24.1%)	3903 (30.2%)	4055 (29.4%)
Health Facility				
17 de Setembro	45 (9.00%)	48 (13.2%)	1677 (13.0%)	1770 (12.8%)

24 de Julho	41 (8.20%)	37 (10.1%)	1138 (8.80%)	1216 (8.81%)
4 de Dezembro	24 (4.80%)	30 (8.22%)	1092 (8.44%)	1146 (8.30%)
Chabeco	26 (5.20%)	37 (10.1%)	839 (6.48%)	902 (6.53%)
Coalane	55 (11.0%)	39 (10.7%)	1245 (9.62%)	1339 (9.70%)
Incidua	44 (8.80%)	21 (5.75%)	968 (7.48%)	1033 (7.48%)
Madal	34 (6.80%)	26 (7.12%)	1034 (7.99%)	1094 (7.93%)
Malanha	20 (4.00%)	11 (3.01%)	389 (3.01%)	420 (3.04%)
Maquival Rio	9 (1.80%)	5 (1.37%)	227 (1.75%)	241 (1.75%)
Maquival Sede	48 (9.60%)	16 (4.38%)	889 (6.87%)	953 (6.90%)
Micajuine	34 (6.80%)	22 (6.03%)	851 (6.58%)	907 (6.57%)
Namuinho	52 (10.4%)	24 (6.58%)	866 (6.69%)	942 (6.82%)
Sangarivera	36 (7.20%)	29 (7.95%)	709 (5.48%)	774 (5.61%)
Varela	19 (3.80%)	7 (1.92%)	429 (3.32%)	455 (3.30%)
Zalala	13 (2.60%)	13 (3.56%)	585 (4.52%)	611 (4.43%)
Marital status*				
Living alone			3851 (38.3%)	
Living together			6195 (61.7%)	
Level of education attained*				
Primary or less			7640 (65.4%)	
Secondary or higher			4040 (34.6%)	

* **NOTE**: These demographic variables were reported for adult-aged patients only.

## 4.2. Uptake of HIV-positive patients into HIV services

Over this 12-month period, in PITC setting, there was an increase seen in the last quarter of the evaluation period. The proportion of newly identified as HIV-positive being diagnosed through PITC increased from 37% in October 2017 to 45% in September 2018,. There was no significant increase in the number of registered HIV-diagnosed patients overall (i.e., across all HTC sectors combined) (**Figures 1a-c**).
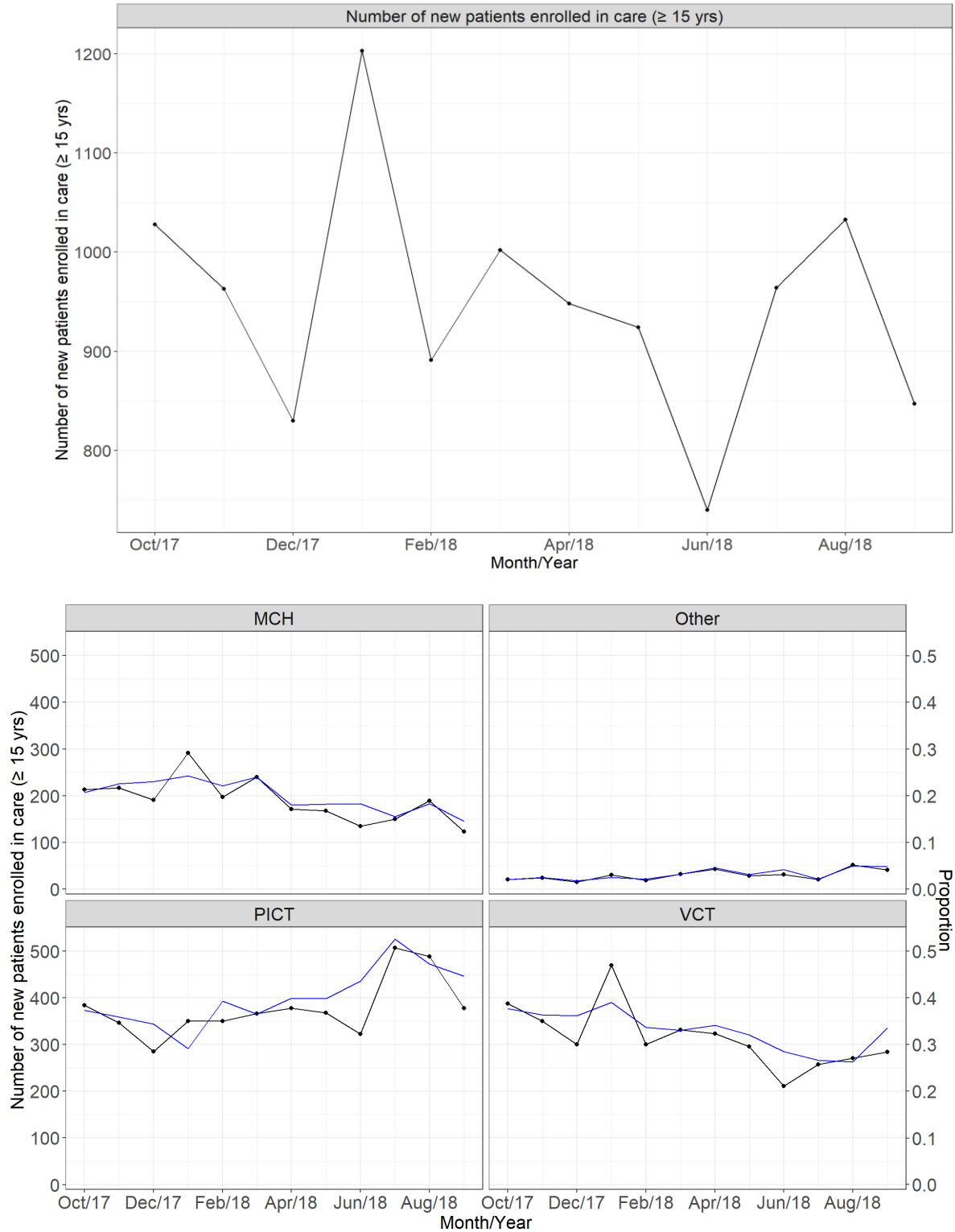
Figure 1a. Top figure: Total number of HIV-positive patients, registered at HIV services. Bottom figure: the black line corresponds to the number of HIV-positive patients registered at HIV services per sector (October 2017 - September 2018) and the blue are the respective proportion of patients registered (Adults ≥15 years of age).
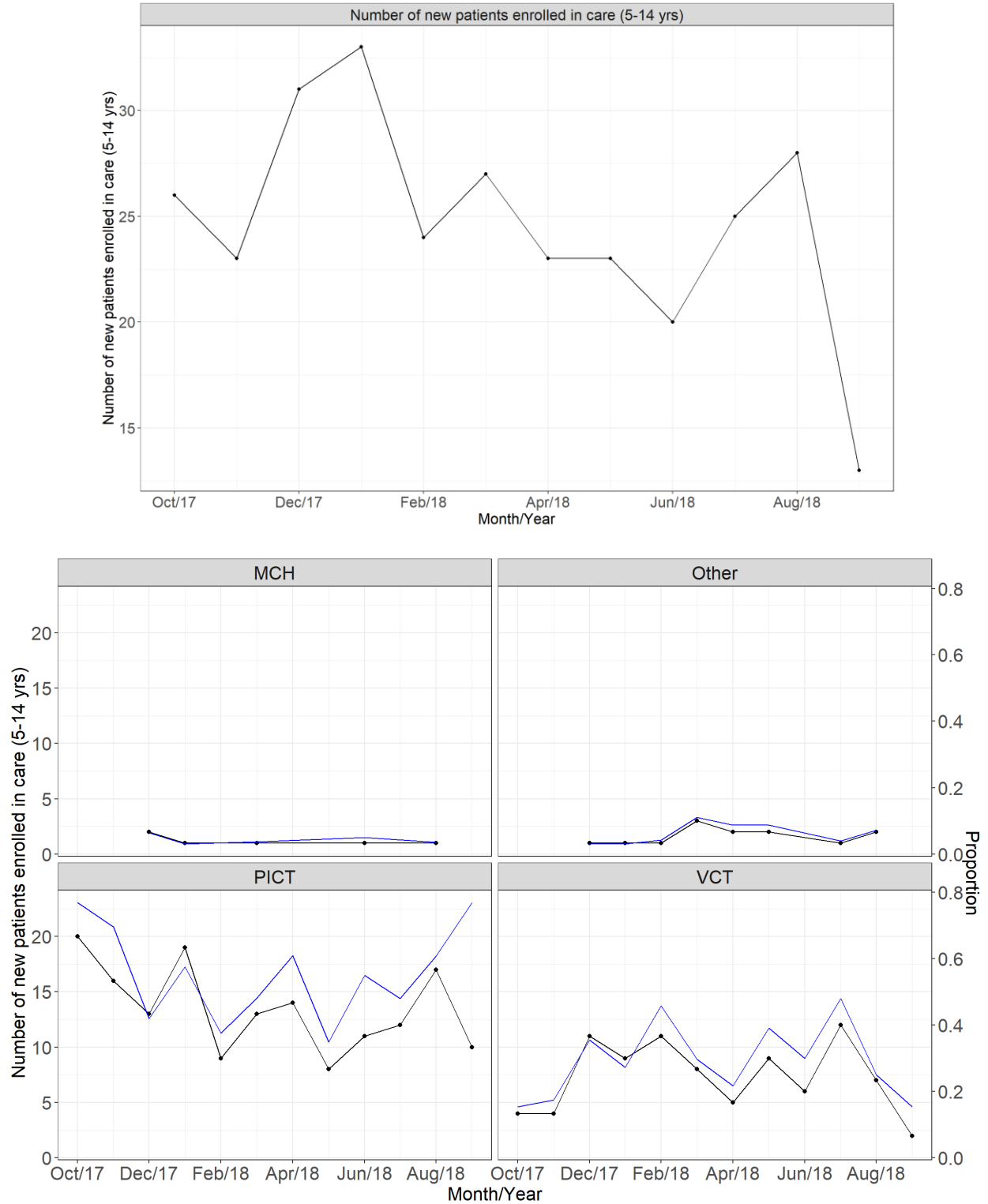
Figure 1b. Top figure: Total number of HIV-positive patients, registered at HIV services. Bottom figure: the black line corresponds to the number of HIV-positive patients registered at HIV services per sector (October 2017 - September 2018) and the blue are the respective proportion of patients registered (Children 5-14 years of age).
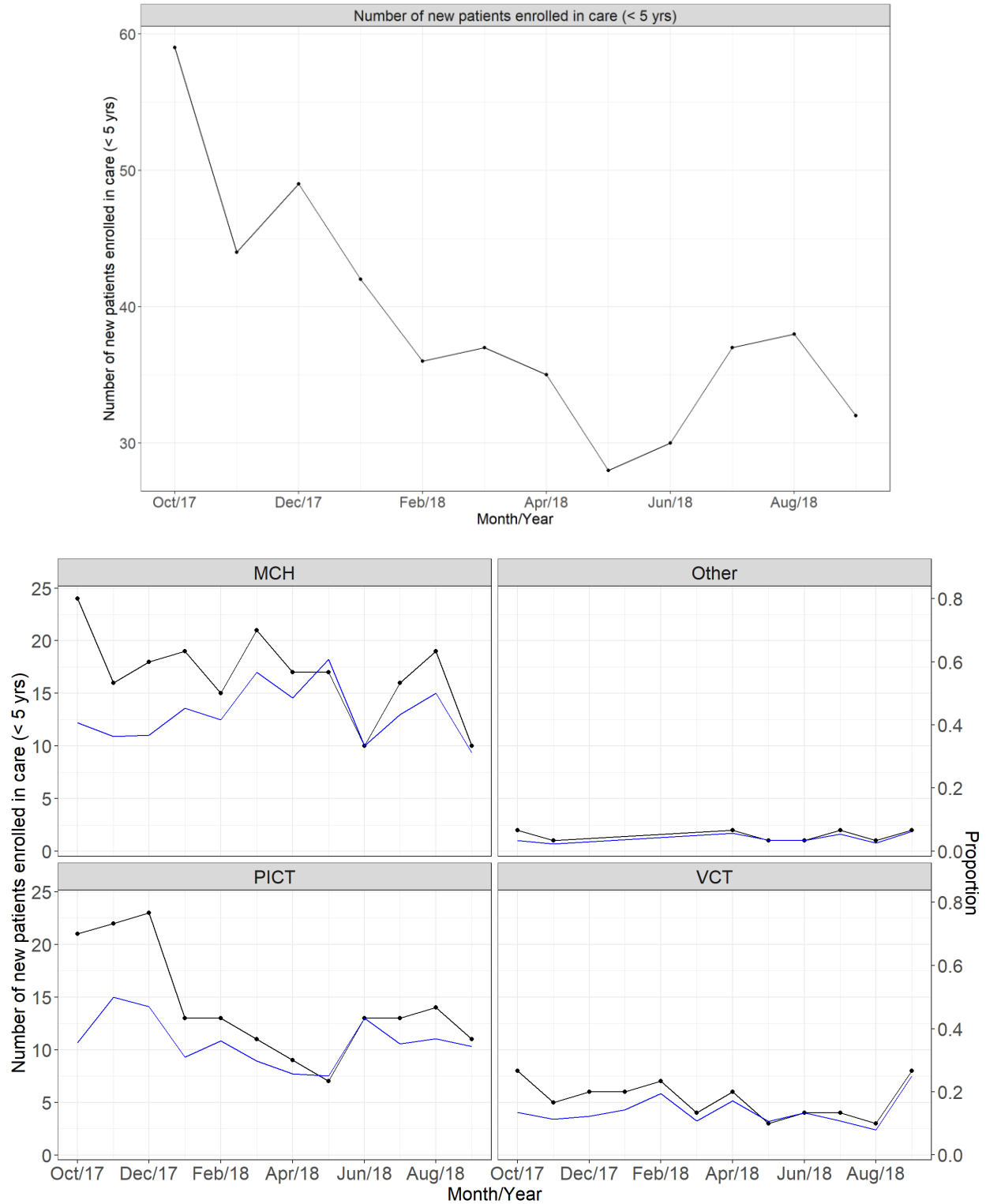
Figure 1c. Top figure: Total number of HIV-positive patients, registered at HIV services. Bottom figure: the black line corresponds to the number of HIV-positive patients registered at HIV services per sector (October 2017 - September 2018) and the blue are the respective proportion of patients registered (Children <5 years of age).

4.3. Trends in clinical, immunologic, and virologic status of new HIV positive persons at their time of presentation into care by whether they underwent HTC in a VCT versus PITC setting

1. **Clinical staging** at entry into care: this trend analysis was not performed, as all the patients included in the evaluation were classified as being in WHO clinical stage 1.

2. **Immunologic status** at entry, per age group.

Patient group: Adults ≥15 years of age

The median number of days from enrollment into care to first CD4 cell count was 11 days (IQR 7-16).

The median CD4 cell count among patients 15 years of age and older was 346 (IQR 187-549) cells/mm^3. By entry point, the median CD4 cell count at entry into care was lower among patients diagnosed via PITC (**Table 2**).

Table 2. Immunologic status at entry, per sector

	N	Median (IQR)
PITC (N=4912)	1616 (35%)	305 (158 ; 502)
MCH (N=2406)	1711 (42%)	394 (259 ; 560)
VCT (N=3903)	1772 (45%)	330 (176 ; 533)
OTHER* (N=732)	113 (16%)	375 (159 ; 616)
NA (N=985)**	123 (14%)	437 (232 ; 632)

* *Other* category includes any entry point that is not PITC, MCH or VCT (including services/sectors for Tuberculosis [TB], gender-based violence [GBV], community testing, referred from another HF, adolescent, and young adult friendly services [SAAJ], private clinics, etc.).

** *NA*, or *not available*, refers to data for which the entry point is not indicated/ unknown.

Overall, median CD4 cell count changed from 357 cells/mm^3 (IQR 201-550) (October 2017) to 310 cells/mm^3 (IQR 179-538) (June 2018) (**Figure 2**). Within the PITC sector, the values changed from 333 cells/mm^3 (IQR 173-510) to 282 cells/mm^3 (IQR 167-428).
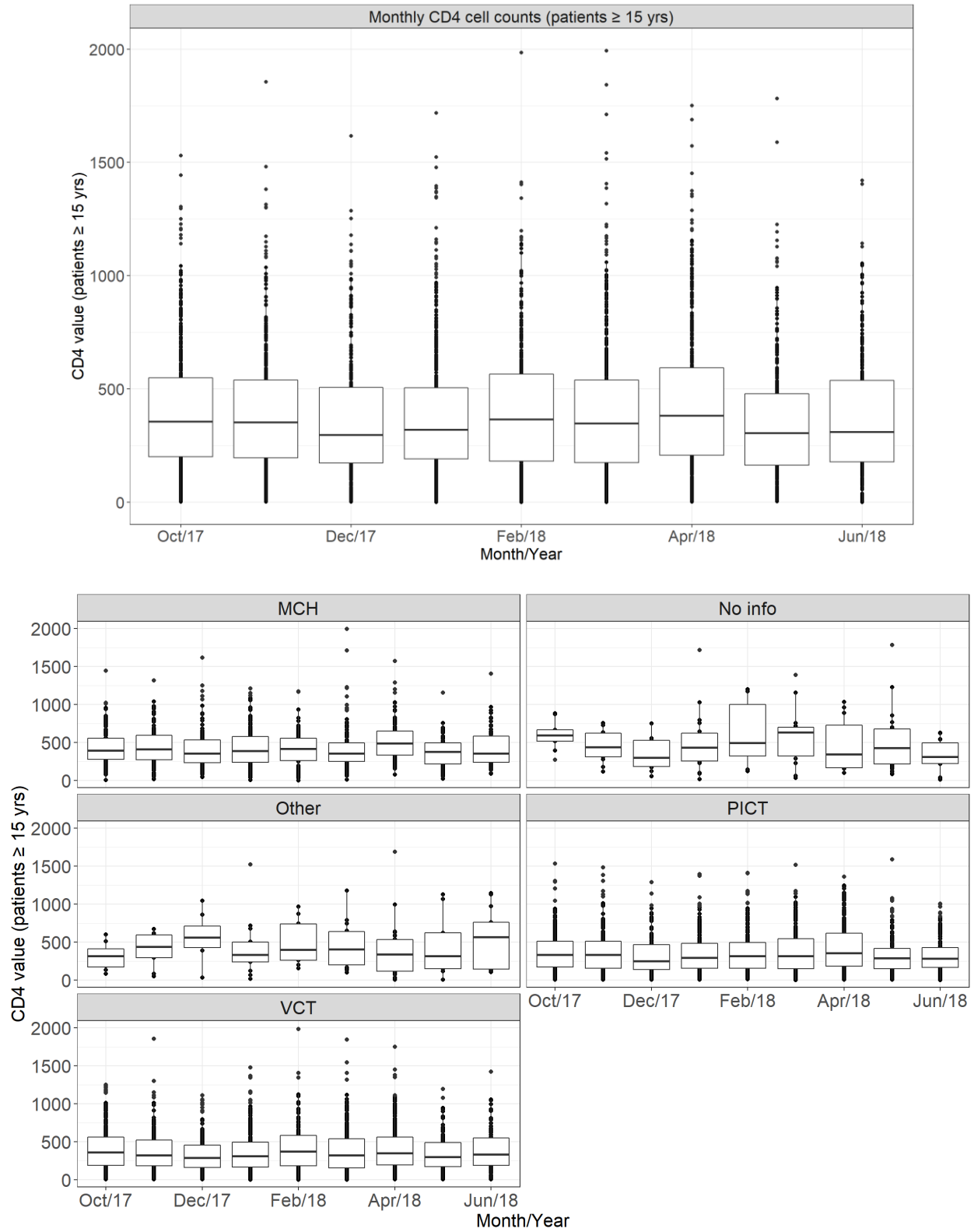
Figure 2. Monthly CD4 cell counts, per entry point (Adults ≥15 years of age).

Patient group: Children 5-14 years of age

The median number of days from enrollment into care to first CD4 cell count was 10 days (IQR 7-15). The median CD4 cell count among patients 5-14 years of age was 389 cells/mm^3 (IQR 231-731), values by service delivery domain are shown in **Table 3**.

Table 3. Immunologic status at entry, per sector

	N	**Median (IQR)**
PITC (N=145)	52 (36%)	384 (193 ; 677)
MCH (N=5)	3 (60%)	341 (180 ; 511)
VCT (N=88)	39 (44%)	546 (240 ; 826)
OTHER* (N=23)	4 (13%)	497 (258 ; 695)
NA (N=65)**	8 (12%)	468 (277 ; 960)

* *Other* category includes any entry point that is not PITC, MCH or VCT (including services/sectors for Tuberculosis [TB], gender-based violence [GBV], community testing, referred from another HF, adolescent, and young adult friendly services [SAAJ], private clinics, etc.).

** *NA*, or *not available*, refers to data for which the entry point is not indicated/ unknown.

Overall, median CD4 cell count changed from 382 cells/mm^3 (IQR 245-716) (October 2017) to 260 cells/mm^3 (IQR 224-550) (June 2018) (**Figure 3**). For PITC, the values varied from 476 cells/mm^3 (IQR 269-679) to 314 cells/mm^3 (IQR187-640) in the same period.
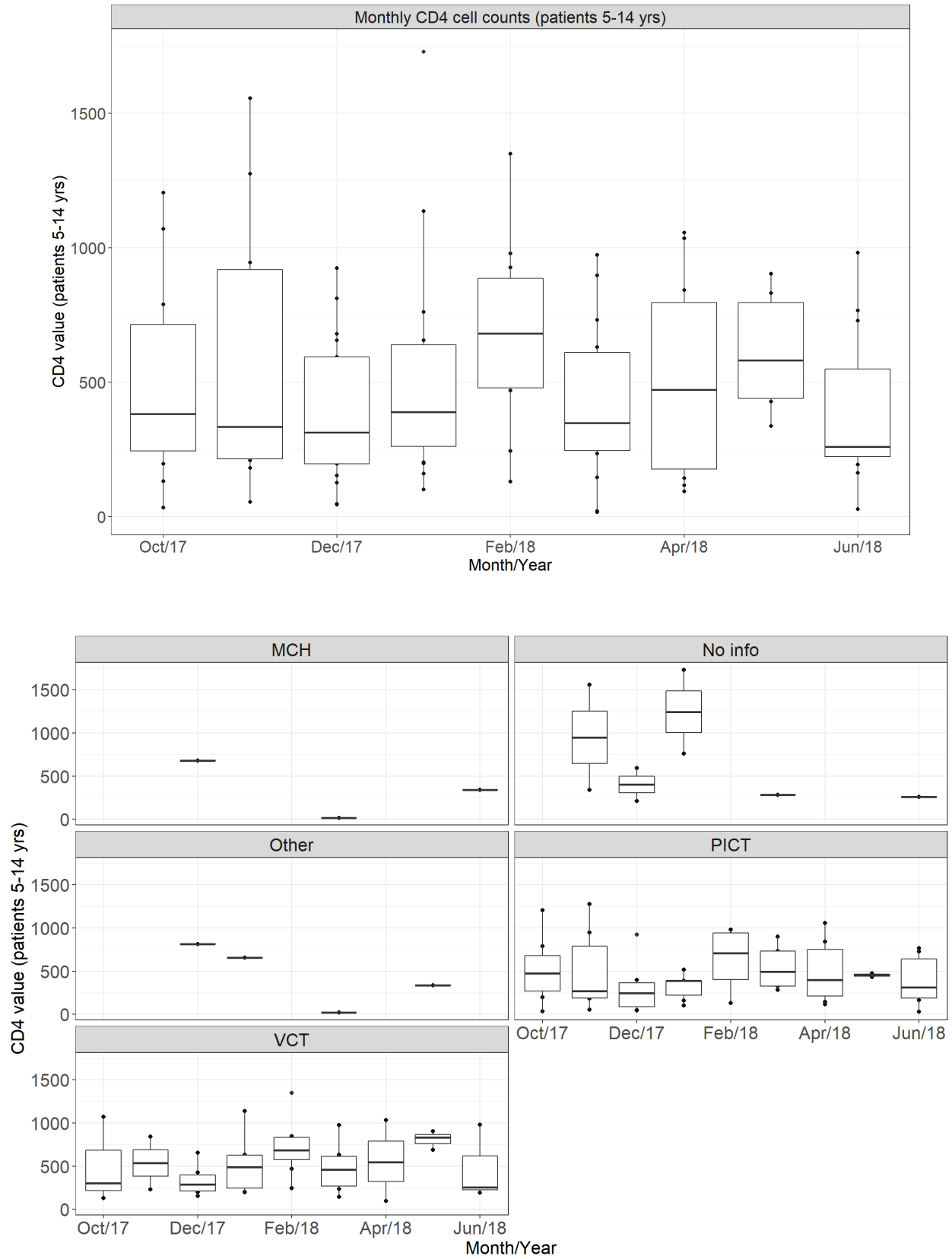
Figure 3. Monthly CD4 cell counts, per entry point (Children 5-14 years of age).

Patient group: Children below 5 years of age

Among children below 5 years of age, CD4 cell count percentages were used. Data were available for 80 children (16%). The table below (**Table 4**) shows the mean and median for CD4 cell count percentage, per sector.

Table 4. Immunologic status among children 0-4 years, by entry point

	N	**Median (IQR)**
PITC (N = 135)	31 (23%)	20.0 (14.5 ; 25.6)
MCH (N = 157)	26 (17%)	21.9 (9.6 ; 27.1)
VCT (N = 49)	20 (41%)	19.7 (14.5 ; 27.8)
NA (N = 30)	3 (10%)	37.6 (27.3 ; 40.3)

The median CD4 cell count percentage changed from 18% (IQR 14-29) in October 2017 to 14% (IQR 2-29) in June 2018 (**Figure 4**). For PITC, in the same period, the percentage changed from 17% (IQR 15-20) to 21% (IQR 13-23).
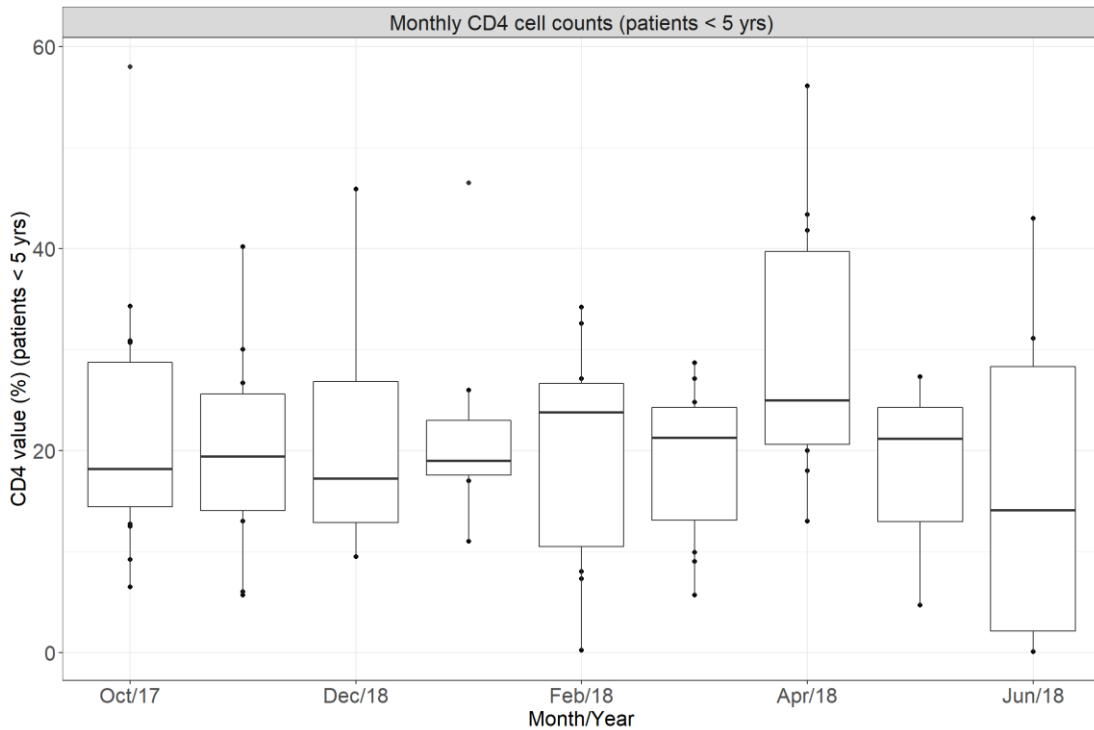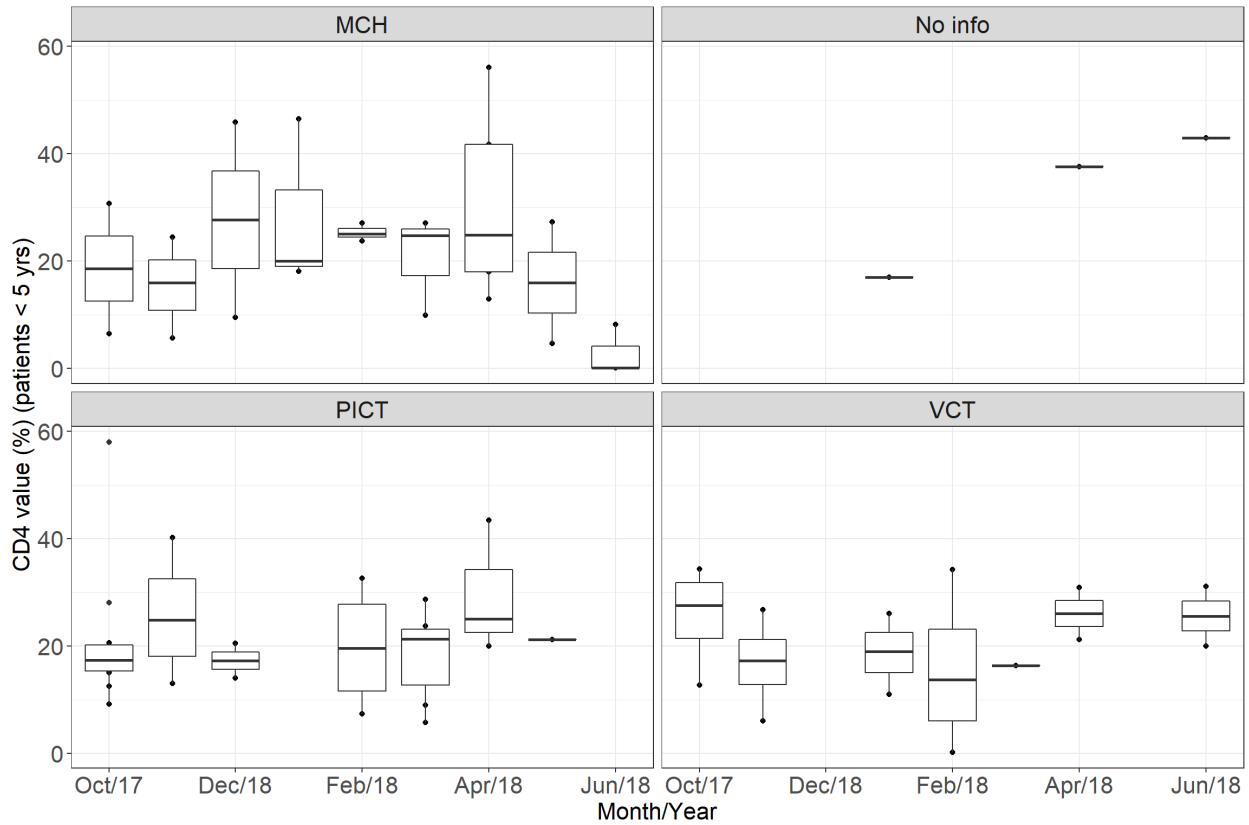
Figure 4. Monthly CD4 cell count percentages (Children 0-4 years of age).

Virologic suppression

A total of 935 (7%) of the 13,803 ART-treated patients included in this analysis had a VL measured between 6 and 12 months after ART initiation, with breakdown being as follows: 69 (7%) of the 935 initial documented VL were from children (0-14 years of age) and the remaining 866 (93%) initial documented VL were from adults (≥15 years of age).

Eighty-two percent (764) of the 935 patients who were enrolled into care in October 2017 had an undetectable viral load, while in March 2018, a reduction to 76% was seen. Viral suppression rates per age group are shown in **Figure 5**.
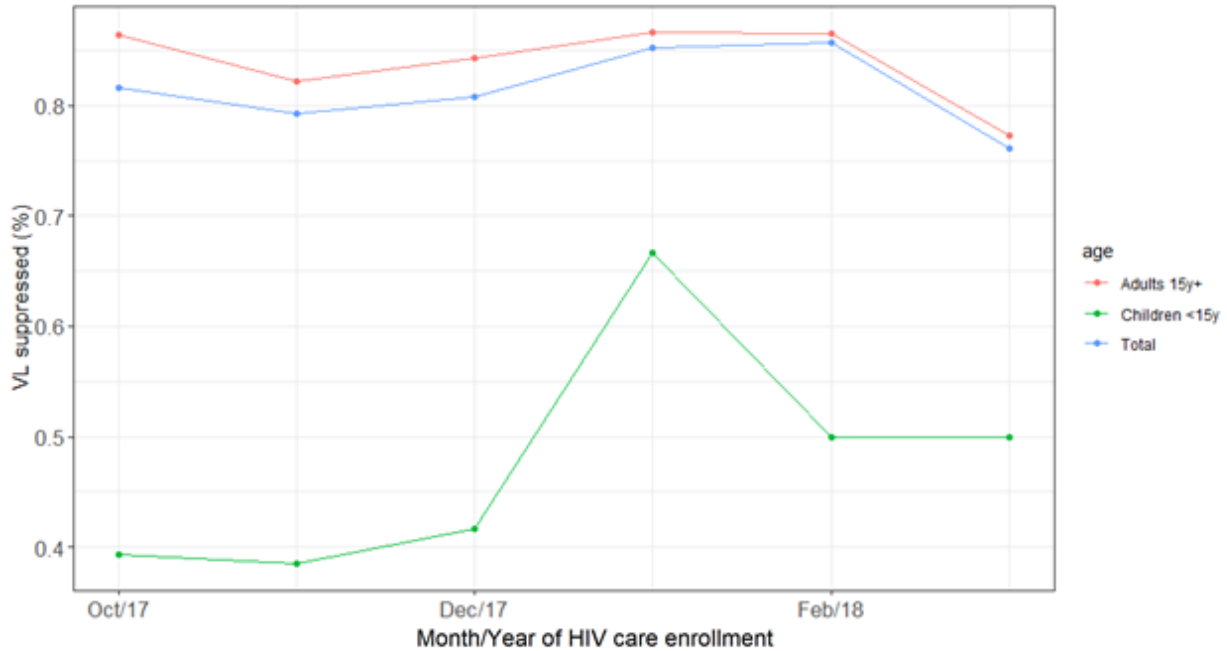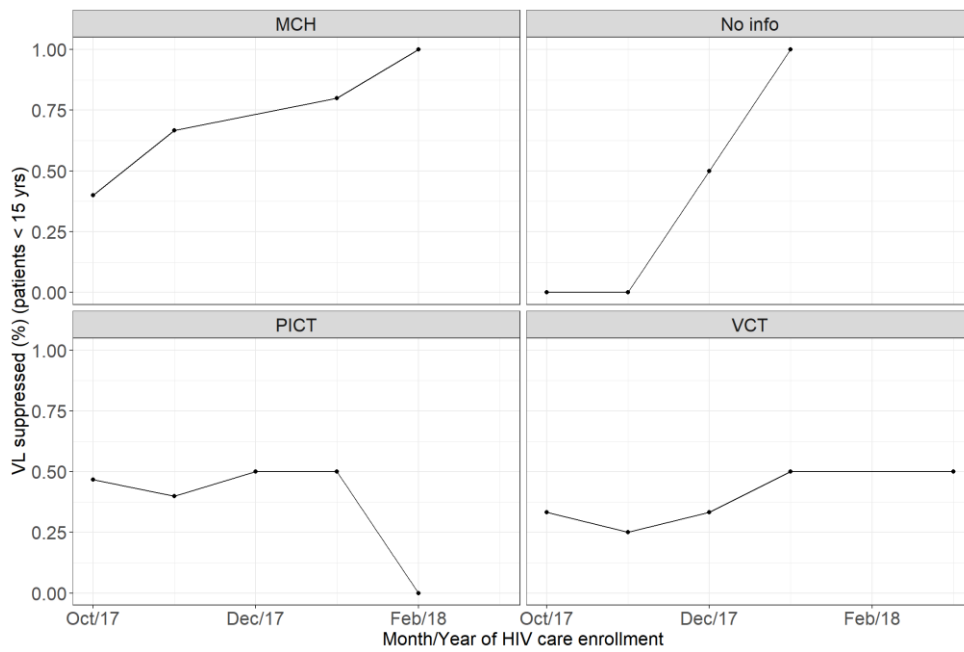
Figure 5. Trends in viral suppression rates, per month/year of enrollment for adults (15 years or older); children (5-14 years) and children (<5 years) *(Note: for this analysis, data are presented for children together, with consolidation of age groups 0-4 and 5-14 years, as there were few data available in the age group 0-4 years).*

Per entry point, viral suppression rates varied (**Figures 6a-b**), however, only a small absolute number (69) of VL tests done among children was noted, which proved a limitation in interpretation of these rate results.

a)
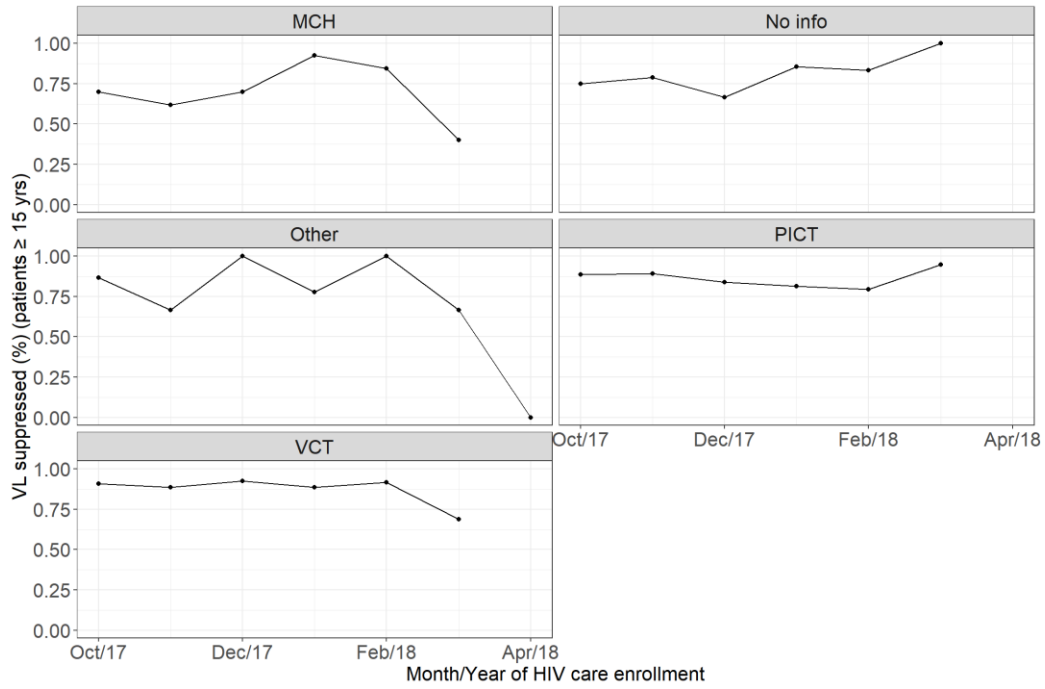
b)

Figure 6. Trends in viral suppression rate, per entry point and per month of enrollment for **a)**: Adults ≥15 years of age, and **b)** Children <15 years of age).

4.4. Association of the level of immunodeficiency at time of presentation into care with the timeliness of ART initiation

Among the 13,803 patients enrolled in HIV services during the evaluation period, 96% initiated ART within the 15 days. The analysis as per proposed specific objective was therefore not performed.

4.5. Association of the level of immunosuppression at time of presentation into care with early retention in care rates among persons initiated on ART

Early retention in care

Early (3-month) retention was calculated as having at least three ART pick-ups within 99 days from ART initiation date. The average monthly proportion of patients retained in care across all sites were computed and are highlighted in **Figure 8** (red dots). The average 3-month retention rate varied from 58% in October 2017 to 61% in June 2018, for those patients with a PITC entry point into care.

The probability of being retained was calculated by regressing retention on calendar time (months since evaluation start) via a generalized linear mixed effect model, with evaluation site set as clusters. Calendar time was treated as continuous variable and entered the model via restricted cubic splines to allow for non-linear relationships. These probabilities are also shown in **Figures 7** and **8**; the grey areas correspond to the associated 95% confidence intervals.

T

Per entry point, the 3-month retention rates vary across the different entry points. Variation was also seen within each of the entry points over the course of the evaluation period (**Figure 8**). Among children less than 5 years of age, no variation in 3-month retention was observed.
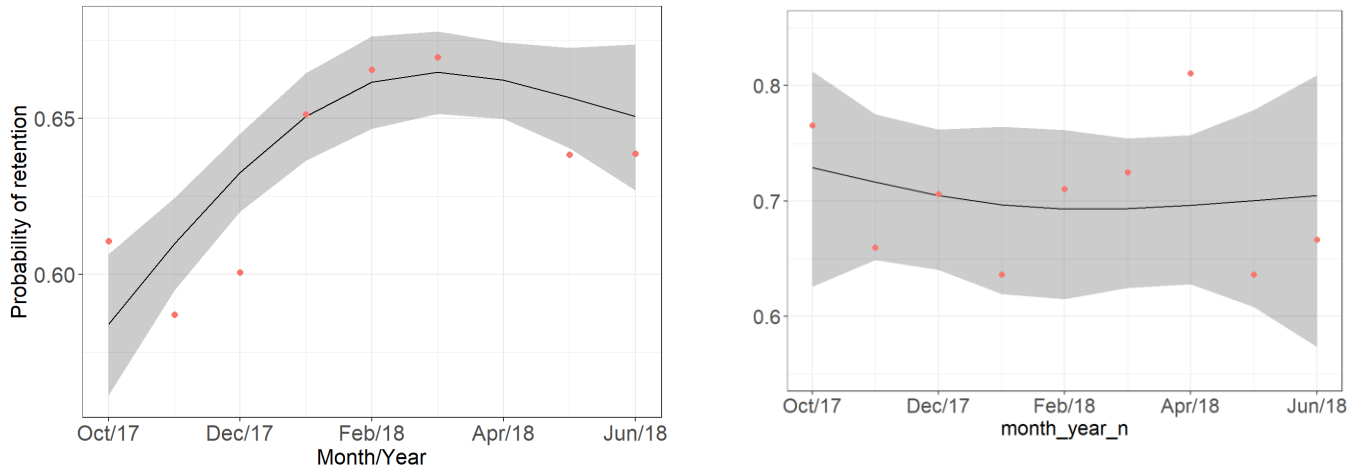
Figure 7. Trends in retention, per month, with associated 95% confidence interval, by age group (left: ≥5 years; right: <5 years). Red dots correspond to the average monthly retention across all sites.
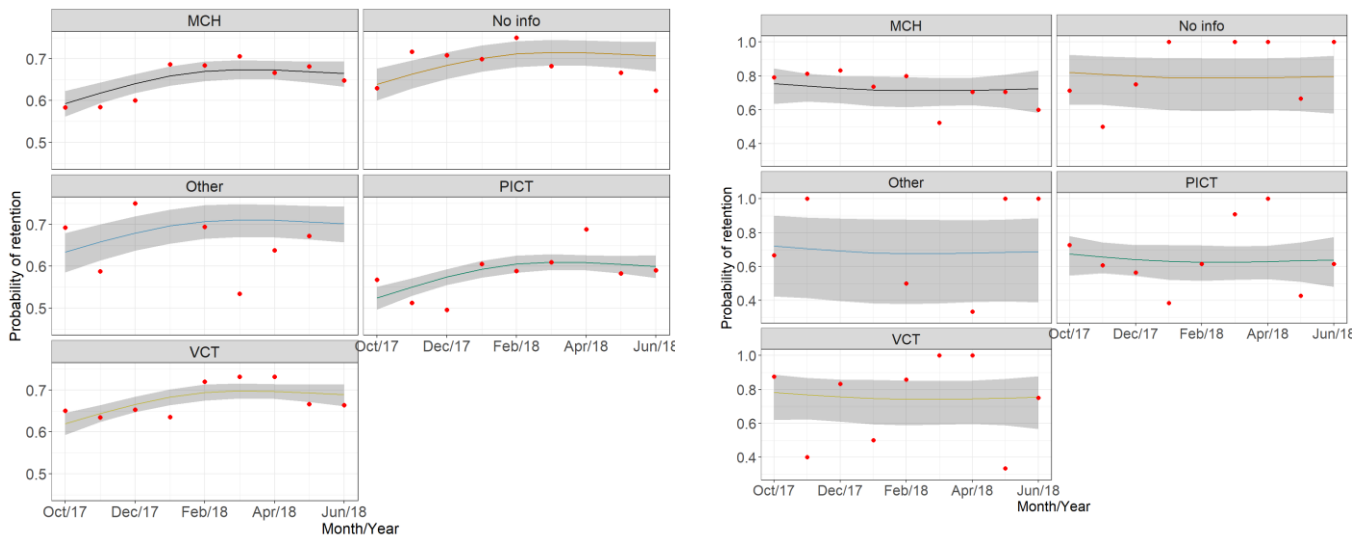
Figure 8. Trends in retention, per month, with associated 95% confidence interval, per HIV entry point, (left: ≥5 years of age; right: <5 years of age). Red dots correspond to the average monthly retention across all sites.

*Association of immune deficiency at enrollment with early retention in care*

For the association of immunodeficiency and 3-month retention status, we defined the CD4 cell count as the CD4 cell count result obtained within the first month after enrollment in HIV care, as a CD4 cell count analysis/ available result more than one month after enrollment already provides some implication that a patient is retained in care.

A total of 10,460 observations were included in the analysis.

Patient group: Adults ≥15 years of age

We estimated the probability of being retained in terms of CD4 counts to evaluate the association between immune deficiency at enrollment and early retention status. The outcome (retention) was regressed on CD4 count using generalized linear mixed effects models, with evaluation sites as clusters. CD4 count was modelled via restricted cubic splines. The fitted curves are presented in **Figures 9a** and **9b**, for all entry points combined and stratified by entry point, respectively.

The probability of being retained at 3 months slightly increases with levels of CD4 cell count until reaching about 500 cells/mm^3, but stabilizes, or even wanes slightly, as CD4 cell count at enrollment increases beyond this threshold. This was seen for the total number of adults enrolled at all entry points, and per HTC entry point (**Figures 9a-b**).
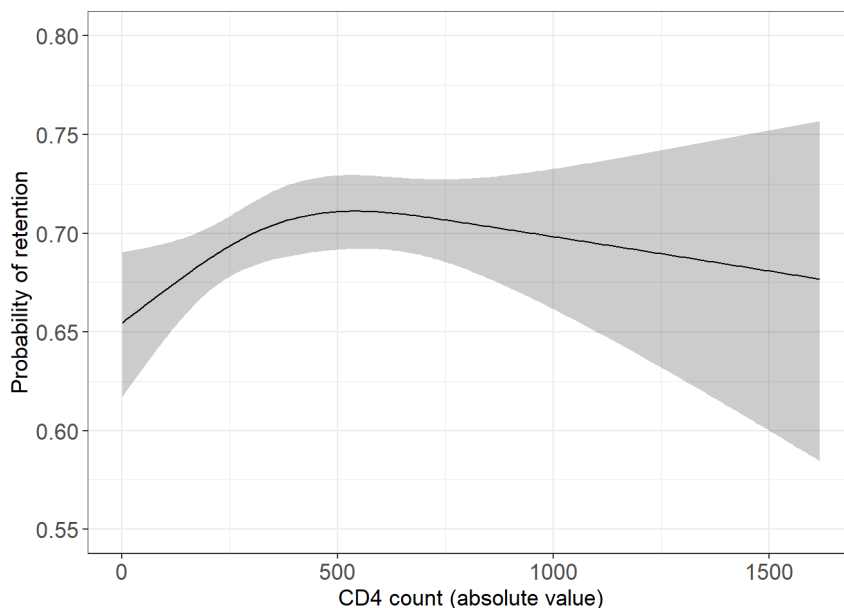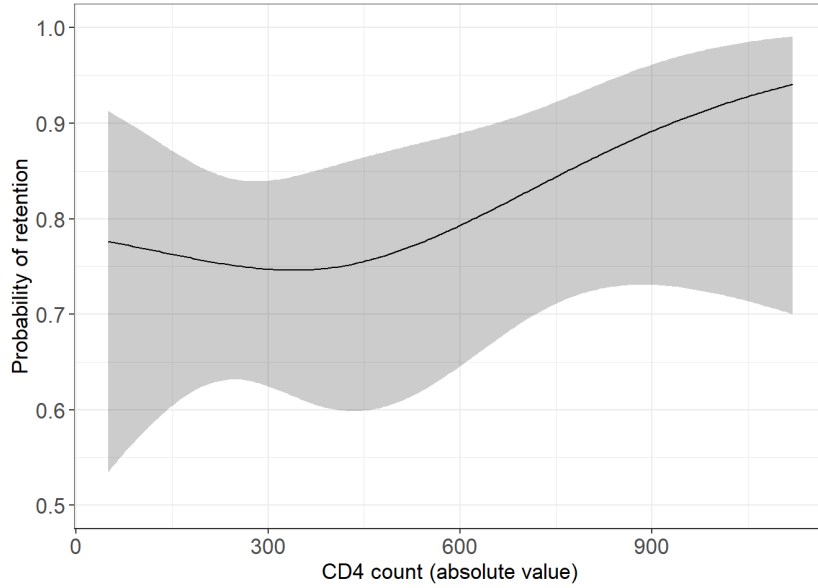

Figure 9a. Probability of being retained at 3 months, per immune deficiency level, with associated 95% confidence interval (Adults ≥15 years of age).
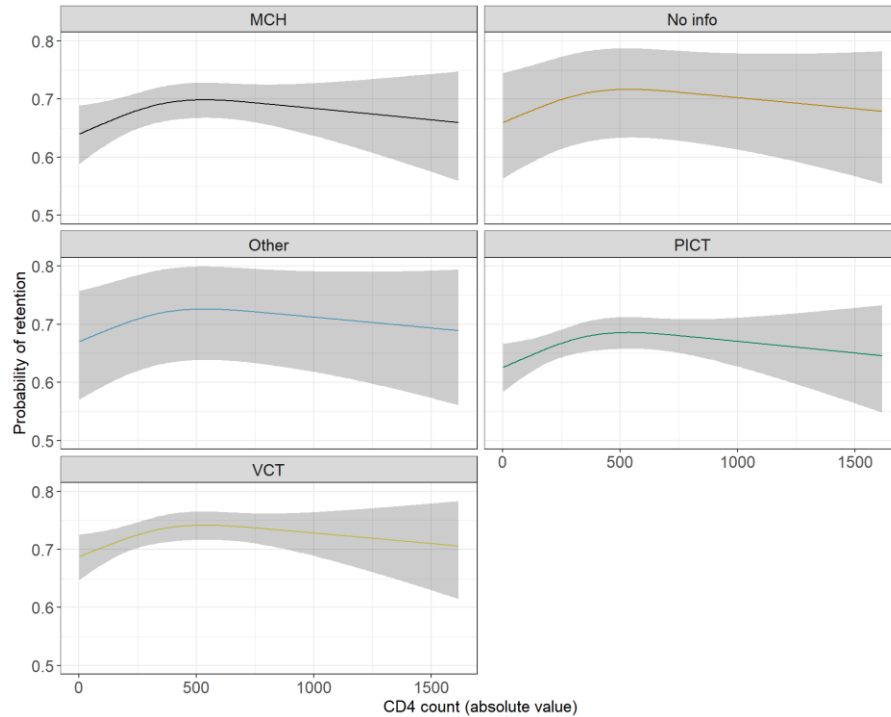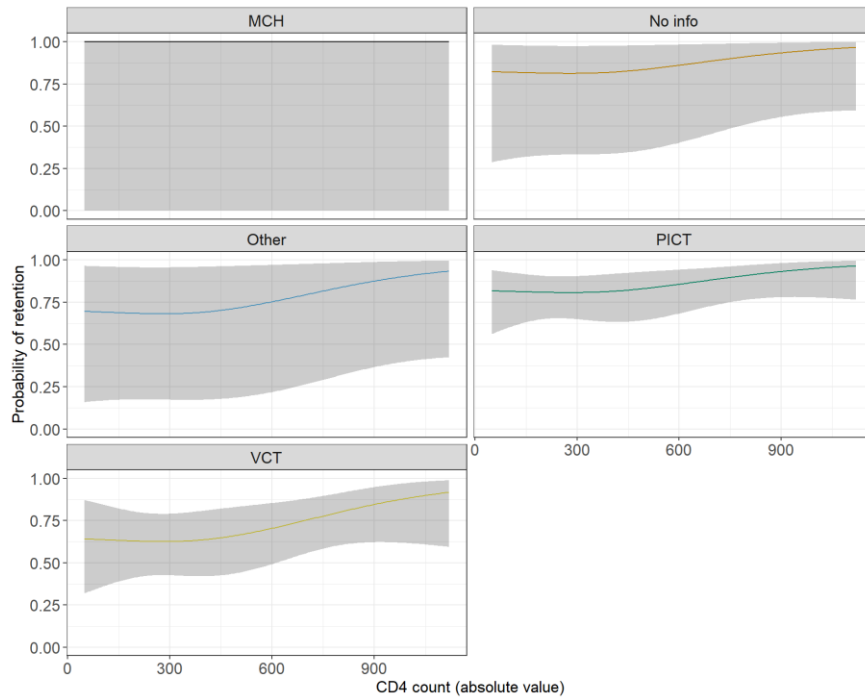
Figure 9b. Probability of being retained at 3 months, per immune deficiency level, with associated 95% confidence interval, per entry point (Adults ≥15 years of age).

Patient group: Children 5-14 years of age

Among children between 5-14 years of age, 214 observations were included. Probability of early retention in care was estimated similarly to the adult group, i.e., by modelling CD4 via restricted cubic splines and using a mixed effect models with eval sites as clusters. In general, the probability of being retained increased with higher CD4 cell counts, as shown in **Figures 10a-b**. However, this increase was not statistically significant at the 5% level; varying CD4 levels from the 1st to 3rd quartile, for example, led to an odds ratio of 1.69, with a 95% confidence interval equal to [0.68; 4.19], and a p-value equal to 0.257.
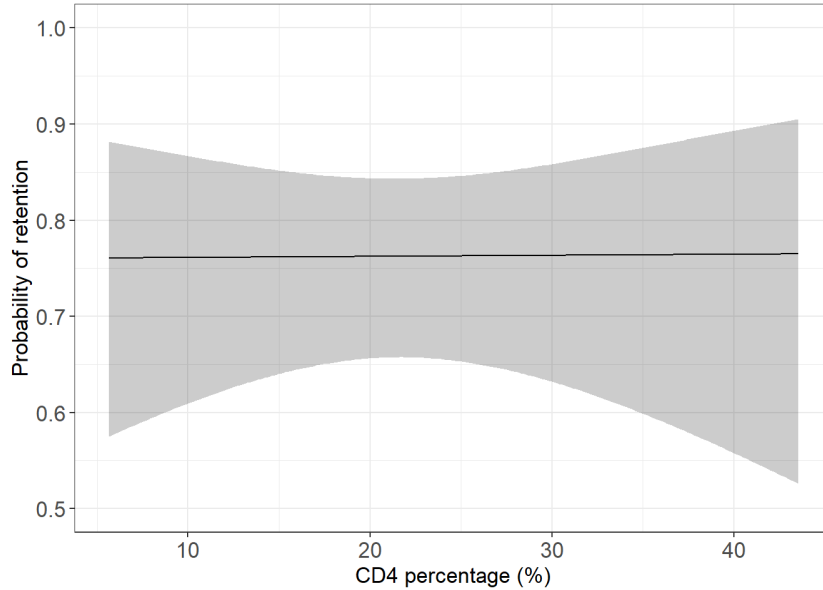
Figure 10a. Probability of being retained at 3 months, per immune deficiency level, with associated 95% confidence interval (5-14 years of age).

Figure 10b. Probability of being retained at 3 months, per immune deficiency level, with associated 95% confidence interval, per entry point (5-14 years of age).

Patient group: Children <5 years

Among children less than 5 years of age, only 78 observations were included. No significant association was seen between CD4 cell count percentage and probability of retention (slope was not significant at 5% level, p-value=0.98, obtained from varying CD4 % from the 1st to 3rd quantile) (**Figures 11a-b**).

Figure 11a. Probability of being retained at 3 months, per immune deficiency level, with associated 95% confidence interval (<5 years of age).
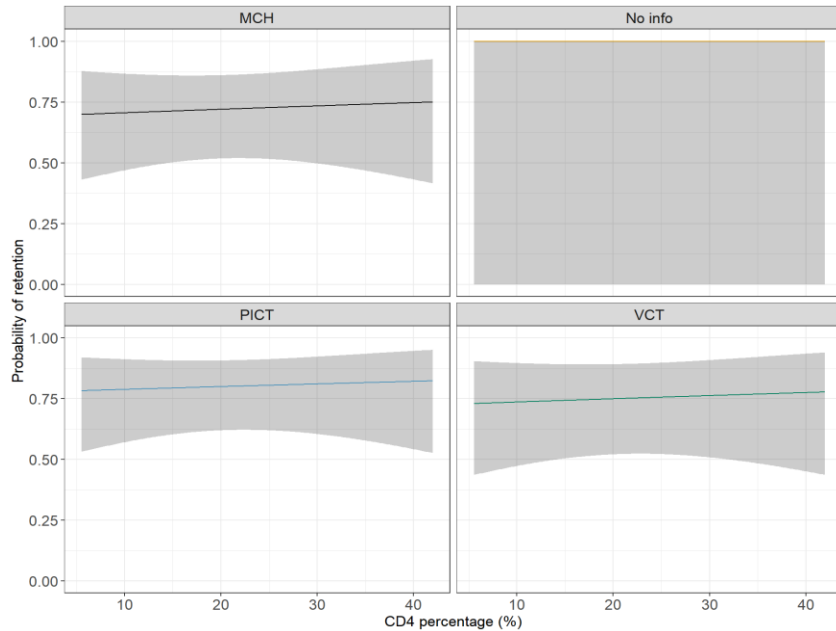

Figure 11b. Probability of being retained at 3 months, per immune deficiency level, with associated 95% confidence interval, per entry point (<5 years of age).

5. Discussion and Conclusions

During the evaluation period (October 2017 to September 2018), more than a third (38%) of all patients registered in HIV care had been identified through PITC services. However, evaluation results found that across the period of PITC intensification, a variation across months was seen in the number of newly diagnosed patients in the PITC setting, specifically with an increase in the last quarter of the evaluation period.

A key inquiry in this programmatic evaluation was to assess whether immunologic status, or more specifically, the level of immunosuppression, at enrollment into HIV care changed among patients identified as HIV-positive through PITC services (compared to those identified in VCT services) when intensification of the PITC services was systematically supported. Results indicated that the immunologic status did not significantly change overall for this patient cohort during the evaluation period, regardless of sector for HTC. The overall median CD4 cell count was lower for patients diagnosed with HIV at PITC and VCT services, compared to MCH services. This was an anticipated finding, as pregnant and lactating women are HIV tested through an opt-out strategy in MCH sectors as per MOH recommendations/guidelines, and as such are likely receiving testing at an earlier stage of disease progression; while patients attending services in other HF sectors might not be offered/counseled to do HIV testing unless they are feeling sick or the patient and/or provider suspects HIV infection. Overall, within the findings of this evaluation, it was not possible to confirm our hypothesis that patients newly identified as HIV-positive during a period of optimized/intensified PITC services have less advanced immunosuppression at the time of HTC when compared to persons newly diagnosed with HIV within free-standing VCT services.

There was an unexpected 15 percentage point decrease in the percent of patients with an undetectable first VL after ART initiation over the evaluation period, however, the absolute number of available VL results trended downward toward the end of the one-year period. We hypothesized that this was related to the shorter amount of follow-up time for patients enrolling in care later in the evaluation period, as data extraction was performed in December 2018 and patients may not have had routine VL testing and/or results returned to HF yet by that point in time. No significant differences were found in first VL results between settings for initial HTC.

Overall, for patients 5 years of age and older, the three-month retention in care rate was relatively high and increased slightly over the evaluation period. Among children less than 5 years of age, there was no variation in early retention in care rates seen over time.

CD4 cell count coverage in general was low among children and adults. This is a trend seen in Mozambique, as the CD4 analysis is no longer compulsory for decision-making regarding ART initiation.

Among patients 15 years of age and older, the probability of being retained in care at three months slightly increases with lower levels of CD4 cell count at enrollment in care but stabilizes and

possibly decreases slightly as CD4 cell count at enrollment increases. Among children between 5 and 14 years of age, the probability of being retained generally increases with increasing CD4 cell counts. No differences in probability of retention were seen among children less than 5 years of age over the evaluation period. The probability for early retention in care for all children (patients <15 years of age) was slightly higher than for adult patients, which may be due to greater motivation on the part of parents/caregivers to keep their children engaged in treatment that improves their health and chances for survival [7]. A positive trend was seen in the proportion of patients remaining in care at three months post-enrollment, measured as retained (i.e., active) in care at the end of the follow-up period.

Notably, there were two intended objectives for which analyses were subsequently not performed due to the homogeneity of the data. As all patients within the evaluation cohort were documented as having WHO clinical stage 1 disease progression, it was not possible to assess for any trend in clinical status comparing by HTC sector (i.e., one of the components of the first objective). Similarly, as nearly all (96%) patients within the cohort began ART within 15 days of presentation into HIV care, it was determined that an analysis looking at the level of immunosuppression at the time of presentation into care and ART initiation timeliness would not be informative for any possible association (i.e., second objective).

We noted above the limitations in the design of this evaluation, however an additional limitation was related to the fact that we did not collect data on the number of patients HIV tested at each of the sectors, as this was not within the scope of this evaluation; as such we were not able to assess for any trends in HIV positivity rates across the sectors providing HTC services.

We wish to acknowledge that we are precluded from making many programmatic recommendations based on these findings, not only for the reasons noted in the *Limitations* section, but also as this PITC optimization approach has been superseded by other PITC improvement strategies being led by the MOH and implemented in partnership by FGH and DPS-Z.

While these findings shed light on the critical inquiries regarding this PITC optimization strategy's effect on programmatic performance at the time of implementation, a key takeaway for these evaluative efforts was underscoring the importance of piloting, expanding and evaluating such evolving programmatic strategies for success in optimizing PITC yield.

6. Dissemination Plan

The report will be translated into Portuguese and shared/disseminated with stakeholders/partners at local/district level, where results will be discussed as needed to reflect on improvement strategies aiming at increasing the number of patients identified as HIV-positive in PITC and other services, as well as patient retention in care.

7. Appendices

Approved protocol/ SOW

The secondary data analysis is covered under the protocol "*Quality Improvement for HIV Care and Treatment in Zambézia province of the Republic of Mozambique under the President´s Emergency Plan for AIDS Relief (PEPFAR)*", approved by Mozambique IRB (CIBS-Z) and US VUMC IRB. The approved concept note is submitted along with this final report for reference.

Informed consent

Informed consent was not required for use of data in this evaluation, as it was a secondary analysis of routinely collected, de-identified, programmatic data. A waiver of consent was approved, as the evaluation involved no more than minimal risk, would not have been possible without the waiver, and the waiver did not adversely affect the rights nor welfare of the patients whose data were included in the evaluation.

*Bio-sketches*

Not applicable.

Conflict of interest statement

The collaborators in this evaluation have no conflicts of interest to declare.

Evaluation costs

Evaluation costs were limited to the personnel time required for extraction and analysis of routine secondary data, results review and discussion, and report preparation.

Evaluation logical framework
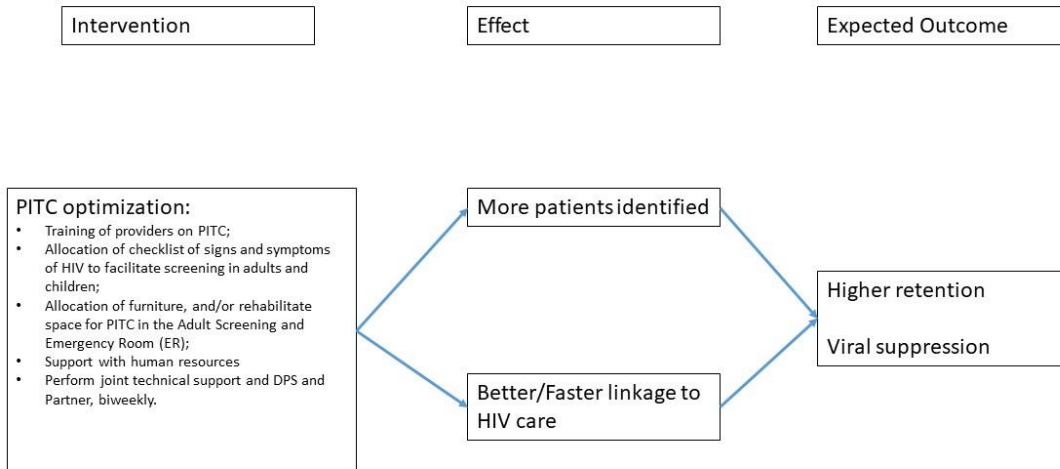
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