Report

Documentation of

Pediatric AIDS Care in Cambodia

2018-2020

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I. Introduction

Some newly identified people living with HIV (PLHIV) fail to link to or enroll in care and initiate treatment, and those on antiretroviral treatment (ART) often miss appointments and fail to return to care/treatment. Addressing poor linkage and retention is critical for achieving HIV/AIDS epidemic control. Identifying those who missed the appointment/lost to follow-up will allow targeted interventions to help return those patients back to treatment and help the national program to reach the third 90 target of the global HIV indicator.

Loss to follow-up remains a major problem in Cambodia. Although most LTF among PLHIV on ART can be explained by undocumented deaths and transfers out, may be most of them stopped treatment or are taking ART irregularly. A common reason for lost to follow-up in Cambodia is migration to Thailand, for example, in Sampov Loun 12/13 patients who lost to follow-up in 2017 reported to move to Thailand, while most of other patients the reason for lost was unknown in Battambang, and Banteay Meachey provinces.

About 79% of PLHIV on ART have viral load testing and about 75% of PLHIV on ART have viral load suppressed. There are some concerns regarding why patients do not have viral load tested - because they missed the appointment, or they are lost to follow-up?

Tuberculosis is the commonest cause of morbidity and mortality among HIV-infected persons globally. Since 2008 WHO issued its guidance to recommend IPT as a public health priority for people living with HIV, especially in high-burden settings. Despite a huge evidence for the efficacy of IPT/TPT (1), global recommendations for its routine use (2), and the national programs recommendations, the uptake of IPT/TPT has been moving up slowly or even low.

II. Rationale

Early infant diagnosis is critical and if ART is administered as early as possible in the course of infection, it can help children living with HIV live longer and healthier. If strictly follow clinicians advise on three “Rights” of adherence – right drug, right dose, and right (regular) visit can extremely reduce the HIV viral load in the bloodstream and increase levels of CD4 cells, then slowing the progression of the disease.

In Cambodia pediatric AIDS care has many gaps need improving such as lost to follow-up and reengagement, partners of adolescents, availability of the right drugs, capacity of healthcare workers including motivation counseling, TB screening, related health education, etc.

Data of quarter three 2020 show 2,378 children (1,154 female) aged 0-14 years old were on ART and number of lost to follow-up in the quarter was 41 (28 female).

The lost to follow-up >90 days after the appointment date among children living with HIV on ART were high. The data from Camblitz in 2018, 2019 and 2020, the lost to follow-up rate at five pediatric ART clinics were 44.7%, 10.0%, 15.4%, 43.6%, and 17.2% respectively.

The percentage of routine viral load test among children (0-14) on ART was as low as the average of 59% for a year in 2019. While percentage of patients with viral load suppressed at average was 82%.

The lost follow-up patients cause some consequences such as increased risk of HIV drugs resistance since they do not take drug rightly and regularly; they affect the whole cascade of the 95:95:95; and consume of national resources to fight against HIV.

Identifying the line listing of patients who did not receive viral load tests as national algorithm would help ART clinics to take appropriate interventions to resolve the problems; the national program and all partners can make it clear whether the proportion of viral load testing that was missing was among those who lost to follow-up or else.

Results from this secondary analysis would highlight priority areas that need intervening of HIV care and treatment among children.

III. Literature review

3.1 Lost to follow-up

In a prospective cohort analysis of the data from January 1, 1999 to December 31, 2014 conducted by Suttipong Kawilapat, Nicolas Salvadori et al. in Thailand found that the lost to follow-up rate was 2.9% a year, 7.3% at 05 years and 22.2% at 10 years. The lost to follow-up in this analysis was defined 09 months after the last contact date (4).

In an institution-based retrospective data analysis of 361 children with HIV who had been on ART from January 1st 2006 to December 30, 2017 conducted by Selam Fishiha Kassa et al. in Gondar, Ethiopia found the overall rate of lost to follow-up was 6.2 events per 100 child-year. The predictor of lost to follow-up for children with HIV were children who got care from their biological parents, WHO clinical stage III/IV, history of regimen substitutions, poor/fair medication adherence and history of TB treatment (5).

Julius Kiwanka, Jacinta Mukulu Waila et al. found in a retrospective analysis of the data extracted from routine program in Masaka, Uganda that the overall incidence rate of LTFU was 7.5 per 100 person-years. Cumulative incidence of LTFU increased with duration of follow up from 8.9% at 6 months to 20.2% t 48 months. Predictors of raised risk of LTFU were: starting ART within 7 days following HIV diagnosis, lack of a telephone set, CD4 cell count of 200-250µ/ml and baseline WHO clinical stage 3 or 4 (6).

Mpinganjira, Tchereni, Gunda and Mwapasa conducted a nested qualitative study in HIV care in Salima and Mangochi districts, Malawi from July to December 2016. The study found reasons that contributing to LTFU as follow: lack of support from husbands or family member; long distance to health facilities; poverty; community-level stigma; ART side effects; perceived good health after taking ART and adoption of other alternative HIV treatment options (7).

In a review of 245,257 patients who were ever enrolled from the period of 2004-2017 conducted by Ahmad Aliyu, Babatunde Adelekan et al. in Nigeria found 30.6% had a loss to follow-up event, and 2.8% died. Males, non-pregnant female, patients on ≥ 3-monthly ARV refills, patients with un-

suppressed viral loads on ART, patients on adult 2nd line regimen or pediatric on 1st line regimen were significantly more likely to be lost to follow-up (8).

3.2 Viral load status

In a cross-sectional study conducted by Kolab Chhim et al. in August 2016 among 328 PLHIV aged 15-17 years old indicated that 76.8% of patients had virally suppressed. Patients who were aged 17 years old, patients who have been on ART for more than nine years, patients who had a relative as the main caregiver had viral non-suppression rate significantly lower than their comparison groups (9).

Adolescents living with HIV confront with many challenges to viral load suppression. A cross-sectional study which enrolled 841 participants conducted by Victoria Simms, Sara Bernays et al., 2019 in Zimbabwe found 35.1% of participants were virological non-suppression. The non-suppression rate were significantly higher among male sex, participants with not knowing one's HIV status, or knowing one's status but not disclosing it to anybody (10).

HIV-positive children (under 15 years) enrolled on antiviral therapy (ART) has increased in recent years, but up to 60% of children started on ART do not have viral load suppression. Sarah Nabukeera Joseph Kagaayi et al., 2020 conducted a retrospective cohort study in which enrolled 300 HIV-positive children (0-14 years) in Kampala, Uganda. The study found that among the 23% of viral load non-suppression patients, the lead factors were WHO clinical stage 4 at ART initiation, and ART-induced side effects (11).

Viral load determination is the most important indicator of ART response in Nigeria for the National implementation plan for the scale up of viral load testing. In an analysis of viral load samples collected from 663 children living with HIV aged 0-18 years between December 2017 – December 2019 from four states within Nigeria showed that viral load was ≥1000 copies/ml in 51.3% of children while viral load >1000 copies/ml among female was 47.2% and among male was 59.9%. Viral load >1000 copies/ml varied among age-groups: 0 – 9 years (50.3%) and 10-18 years (52.1%) (12).

In another cross-sectional study that recruited 250 pediatric HIV positive patients form October 2017 to July 2018 conducted by Adwoa Afrane et al., in Ghana found 38.4% of participants had viral load >1000 copies/ml. Sex female more likely to have non-suppressed viral load than male (54.2% vs 32.2%). CD4 level at study recruitment was significantly associated with virological non-suppression. Participants with history of TB treatment were likely to have virological non-suppression. Participants with NVP based regimen was 7.9 times more likely to have virological non-suppression (13).

About 28% of 1,567 children aged 1-14 years enrolled in a cross-sectional study that was conducted by Melashu et al. from July 01, 2017 to June 2018 had virological non-suppression. Of these non-suppression viral load children, 24% were aged below 5 years. Children on nevirapine-based regimen had about two times more non-suppressed viral load compared to those who were on efavirenz-based regimen (14).

In a report titled "Understanding and Improving Viral Load Suppression in Children with HIV in Eastern and Southern Africa" by UNICEF indicated one out of every three children who had a viral load test did not have virological suppression, and the viral load suppression among children living with HIV remained low from 69% to 65% across three years from 2016 to 2018. Children aged 1-4 years had the lowest rates of viral load suppression, with 62%, 58%, and 54% respectively in 2016, 2017 and 2018. The report also indicated the association between viral load suppression and being on ART for a longer duration and adhering to ART appointment (15).

3.3 TB prophylaxis therapy

WHO recommends TB/HIV services offered to PLHIV including regular TB screening and TPT if TB disease is ruled out, should be done regularly at least once a quarter. TPT may be started during pre-ART assessment or before starting MMD (16).

In a correspondence titled "Challenges in expanding TB preventive therapy in high-burden stings: beyond logistics is evidence and ethics" by Saurav Basu highlighted concerns found in Masini et al.'s article regarding the issues of logistic and operation (17).

Expanded TPT options now include child-friendly dispersible fixed dose combination tablets of daily rifampicin and isoniazid for 3 (3RH), 12 weekly doses of rifampentine and isoniazid (3HP) or a daily dose for 1 month (1HP; recently also available as a fixed dose combination tablet), a daily dose of rifampicin for 4 months (4R) and traditional daily isoniazid for 6-9 months (6-9 H). However, the scale-up and implementation of TPT will only be achieved if it is perceived as a priority by TB program and major donors, with clear goal, a practical implementation plan, reliable drug supply and effective monitoring and evaluation systems (18).

In a descriptive observational study using secondary data of the provision of TPT in children in Surabaya conducted by Rizka Aprilidyawati et al., 2020 found that the implementation of TPT with INH for children is still low at 5.3%, 28.8%, and 16.6% in 2016, 2017, and 2018 respectively (19).

As children living with HIV are at particular risk for rapid progression to TB disease. INH is safe for use and generally has lower toxicity in children than in adults. WHO strongly recommends six months of INH for all children living with HIV 12 months or older who live in a setting with a high prevalence of TB, and those less than 12 months with a known TB exposure, in whom TB disease has been excluded (20).

A report by Michael Melgar, Catherine Nichols, J. Sean Cavanaugh, et al., in MMWR March 2020 Vol. 69 No.12 summarized data on TB symptom screening and TPT initiation and completion among ART patients in 16 countries supported by the U.S. President's Emergency Plan for AIDS Relief during April 1, 2017 – March 31, 2019. During April 1, 2017–September 30, 2018, TB symptom screening increased from 54% to 84%. Overall, nearly 2 million ART patients initiated TPT, and 60% completed treatment during October 1, 2017–March 31, 2019. Although TPT initiations increased substantially, completion among those who initiated TPT increased only from 55% to 66% (21).

3.4 Dead

In the study of Suttipong Kawilapat, Nicolas Salvadori et al. 73 children of 873 children died in the follow-up period from 1999 to 2014 that accounted for 8.3% (4).

In a meta-analysis of 12 pooled studies with 12,112 children of HIV-infected women found crude mortality rate per 1,000 child-years of follow-up were 39.3 and 381.6 for HIV-uninfected and HIV-infected children, respectively. When the mother died during follow-up, children were more than twice likely to die than when mothers survived. Children born to mothers with CD4<350 cells/ml or to women with unknown CD4 were at significantly increased risk of dying. Children who had never been breastfed were at more than twice the risk of dying than ever breasted children. Regarding HIV infection status, children with the infection were likely to die more than uninfected children: aHRs were 12.45 (10.15-15.27) for perinatally infected children, 3.08 (2.29-4.14) for children infected through breastfeeding and 7.21 (5.53-9.39) for children with unknown timing of infection (22).

Heena Brahmbhatt, Godfrey Kigozi, Fred Wabwire-Mangen et al. conducted a prospective study in rural Rakai Distict, Uganda. The two-year child mortality rates were 128 of 1000 children born to HIV negative mothers, 165.5 of 1000 uninfected children born to HIV positive mothers, and 540.1 of 1000 HIV-infected children (23).

IV. Objectives of secondary analyzes

4.1 General objective

To review HIV care and treatment among pediatric patients from 2018 through 2020.

4.2 Specific objectives:

- Identify patient status and patient's visit status,
- Identify percentage of viral load coverage and viral load suppression,
- Identify percentage of TPT coverage,
- Identify the MMD implementation
- Dolutegravir-based regimens among pediatric patients (additional analysis using data from pediatric database)
- Identify sites where the interventions are most needed.

V. Methodology

Secondary analysis of the data from blitz when the data from 01 January 2018 through December 31, 2020 were collected at 11 ART clinics in PNH, KCM, PSH, BMC, BTB, and KPS. In addition, 1,109 pediatric patients in national pediatric database were analyzed to explore the coverage of dolutegravir-based regimen among these patients.

VI. Results:

6.1 Demographic data

Majority of patients are in age-groups 0-4 and 5-9 years for both female and male. Of 911 females 47.5% and 35.7% were in age 0-4 and 5-9 years respectively. Among 1,060 males 46.5% and 36.1% were in age 0-4 and 5-9 respectively.

Table 1: Distribution of patients by sex and age

Sex		Age group			Total
		0-4	5-9	10-14	
Female	n	433	325	153	911
	%	47.5	35.7	16.8	100
Male	n	493	383	184	1,060
	%	46.5	36.1	17.4	100
Total	n	926	708	337	1,971
	%	47.0	35.9	17.1	100

6.2 Patient status

Four categories of patient status have been designed and used in the ART database: active, dead, lost to follow-up and transferred out. In Phnom Penh, 80.3% of 1,040 reviewed patients were still active, 1.3% were dead, 3.8% were lost to follow-up, and 14.7% were transferred out. In provinces, 71.3% of 931 patients reviewed were active, 1.0% were dead, 3.4% were lost to follow-up, and 24.3% were transferred out.

Table 2: Patient status in Phnom Penh and Provinces

Patient Status	Phnom Penh		Provinces	
	n	%	n	%
Active	835	80.3	664	71.3
Dead	13	1.3	9	1.0
Lost to follow-up	39	3.8	32	3.4
Transferred Out	153	14.7	226	24.3
Total	1,040	100	931	100

When reviewing patient status by ART site, all categories of patient status varied hugely by site. The mean of active status was 73% with ±16% standard deviation. The median was 80%. Sites with high percentage (>80%) of active status P0206, P0102, P0103 and P0202. While sites with low percentage of active status (<60%) were P0101, P0201, P0301, and P1801.
Mean of LTF status was 2.5% with ±2.5% standard deviation. The range of LTF was from 0% to 8.8% that was seen at P1801. Mean of transfer out was 23% with ±15% standard deviation. The median was 18.7%. ART sites where there was high transfer-out percentage were P0201, P0301, P1801, and P0101 with 47.4%, 42.3%, 38.0%, and 37.3% respectively.

Table 3: Patient status by site

Patient Status		Site ID											
		1204	P0101	P0102	P0103	P0201	P0202	P0203	P0206	P0301	P0501	P1801	Total
Active	n	835	30	24	23	17	181	21	50	82	189	47	1,499
	%	80.3	58.8	88.9	85.2	44.7	81.9	80.8	98.0	55.0	72.1	59.5	76.1
Dead	n	13	2	0	0	2	2	0	0	2	1	0	22
	%	1.3	3.9	0.0	0.0	5.3	0.9	0.0	0.0	1.3	0.4	0.0	1.1
Lost to follow-up	n	39	0	1	1	1	2	0	0	2	23	2	71
	%	3.8	0.0	3.7	3.7	2.6	0.9	0.0	0.0	1.3	8.8	2.5	3.6
Transferred Out	n	153	19	2	3	18	36	5	1	63	49	30	379
	%	14.7	37.3	7.4	11.1	47.4	16.3	19.2	2.0	42.3	18.7	38.0	19.2
Total	n	1,040	51	27	27	38	221	26	51	149	262	79	1,971
	%	100	100	100	100	100	100	100	100	100	100	100	100

6.3 Patients' visit status

Patient visit status refers to how regular the patients come for their follow-up visit the ART clinic. Of the 1,971 charts reviewed: 59 (3%) patients missed their clinical visit 1-30 days. About 2% missed appointment for 31-90 days, and 398 (20.2%) lost to follow-up for more than 90 days.

Table 4: Appointment status

Appointment Status	Number	Percent
Active	1,472	74.7
1-30days	59	3.0
31-90days	42	2.1
>90days	398	20.2
Total	1,971	100

When reviewing patient visit status separately between Phnom Penh and provinces, for the whole cohort of PLHIV registered in the ART services until the date when blitz was conducted, 71.3% of patients in the provinces were active, while almost 78% of patients in Phnom Penh were active. The lost to follow-up in the provinces was 23.7% and in Phnom Penh was 17.0%.

Table 5: Appointment status in Phnom and Provinces

	Provinces		Phnom Penh	
Appointment Status	Number	Percent	Number	Percent
Active	664	71.3	808	77.7
1-30days	25	2.7	34	3.3
31-90days	21	2.3	21	2.0
>90days	221	23.7	177	17.0
Total	931	100	1,040	100

When comparing patient visit status and patient status of the database, among 1,499 patients labelled as active in the database, blitz found 1,443 (96.3%) were active, 3%, 0.6% and 0.5% were missing clinical appointment for 1-30 days, missing clinical appointment for 31-90 days and greater than 90 days respectively. However, during the period of 2018-2020 the definition of lost to follow-up was any patients who did not show up for greater than 90 days after the appointment date. Following this definition, there were only 08 – 06 in the provinces and 02 in Phnom Penh of PLHIV who lost to follow-up were still labelled as "active" in the database (Table 6, 7).

Table 6: Comparison between appointment status from blitz and Patient status from database

Appointment Status		Patient Status of database				
		Active	Dead	Lost to follow-up	Transf. out	Total
Active	n	1,443	1	0	28	1,472
	%	96.3	4.6	0.0	7.4	74.7
1-30days	n	39	1	1	18	59
	%	3.0	5.0	1.0	5.0	3.0
31-90days	n	9	4	0	29	42
	%	0.6	18.2	0.0	7.7	2.1
>90days	n	8	16	70	304	398
	%	0.5	72.7	98.6	80.2	20.2
Total	n	1,499	22	71	379	1,971
	%	100.0	100.0	100.0	100.0	100.0

Table 7: Comparison between appointment status from blitz and Patient status from database, Phnom Penh and Provinces

Appointment Status		Patient Status of database							
		Provinces				Phnom Penh			
		Active	Dead	LTF	Trans.out	Active	Dead	LTF	Trans.out
Active	n	644	0	0	20	799	1	0	8
	%	97.0	0.0	0.0	8.9	95.7	7.7	0.0	5.2
1-30days	n	13	0	0	12	26	1	1	6
	%	2.0	0.0	0.0	5.3	3.1	7.7	2.6	3.9
31-90days	n	1	1	0	19	8	3	0	10
	%	0.2	11.1	0.0	8.4	1.0	23.1	0.0	6.5
>90days	n	6	8	32	175	2	8	38	129
	%	0.9	88.9	100.0	77.4	0.2	61.5	97.4	84.3
Total	n	664	9	32	226	835	13	39	153
	%	100	100	100	100	100	100	100	100

Table 8 and 9 show appointment status of HIV-infected children of the whole cohort from the date they registered at the ART clinics until the date when blitz was conducted. The overall active status in age-group of 0-4 years was 82.0%, 69.5% and 65.6% in age-group 5-9 years and 10-14 years respectively. Active status in provinces as well as in Phnom Penh were higher in age group of 0-4 years old 76% and 87% respectively.

Table 8: Appointment Status by Age-group

Appointment Status		Age group			Total
		0-4	5-9	10-14	
Active	n	759	492	221	1,472
	%	82.0	69.5	65.6	74.7
1-30days	n	27	24	8	59
	%	2.9	3.4	2.4	3.0
31-90days	n	15	15	12	42
	%	1.6	2.1	3.6	2.1
>90days	n	125	177	96	398
	%	14.0	25.0	28.0	20.0
Total	n	926	708	337	1,971
	%	100.0	100.0	100.0	100.0

Table 9: Appointment Status by Age-group Provinces versus in Phnom Penh

Appointment Status		Age-group					
		Provinces			Phnom Penh		
		0-4	5-9	10-14	0-4	5-9	10-14
Active	n	344	210	110	415	282	111
	%	76.4	67.5	64.7	87.2	71.0	66.5
1-30days	n	11	9	5	16	15	3
	%	2.4	2.9	2.9	3.4	3.8	1.8
31-90days	n	9	8	4	6	7	8
	%	2.0	2.6	2.4	1.3	1.8	4.8
>90days	n	86	84	51	39	93	45
	%	19.1	27.0	30.0	8.2	23.4	27.0
Total	n	450	311	170	476	397	167
	%	100	100	100	100	100	100

Further analysis was conducted to see the appointment status among "active" patients in the ART database at site only. Among 835 patients and 664 patients who were labelled "Active" in the database in Phnom Penh and in provinces as shown in Table 2, there were only 02 (0.2%) and 06 (0.9%) patients who were lost to follow-up for more than 90 days after their appointment date in Phnom Penh and provinces respectively. Almost 96% and 97% of pediatric patients came for the visit as scheduled in Phnom Penh and in the province respectively.

Table 10: Appointment Status of Patients who are Labelled "Active" in the Database at ART Clinics in Phnom Penh versus Provinces

	Phnom Penh		Provinces	
Appointment Status	Number	Percent	Number	Percent
Active	799	95.7	644	97.0
1-30days	26	3.1	13	2.0
31-90days	8	1.0	1	0.2
>90days	2	0.2	6	0.9
Total	835	100	664	100

6.4 Viral load status

The eligibility of viral load test is followed the national viral load algorithm. When reviewing the viral load test performance, the percentage of viral load test not performed among eligible patients was 31%. But when reviewing the viral load performance only among "Active" patients, the percentage of "eligible but not performed" was only about 19%, and if seeing separately between provinces and Phnom Penh, they were 12.6% in the provinces and in Phnom Penh respectively (Table 13).

Viral load test performance varied greatly by ART site with mean of 61.4% and standard deviation of 25.8%. ART sites where more than 80% of pediatric patients had received at least a viral load test were Phnom Penh (86.2%), Battambang provincial referral hospital (89.0%), Roka referral hospital (94.0%) and Kampong Speu provincial referral hospital (80.4%). On the other hand, site P1801, P0101, P0102 and site P0203 had 17%, 30%, 41.7% and 42.9% of pediatric HIV patients had received at least a viral load (Fig.1).

Table 11: Viral load test performance among all PLHIV

VL performance	Number	%
No VL information	11	0.5
Have been performed	1,319	66.9
Eligible but not performed	617	31.3
Result pending	24	1.2
Total	1,971	100

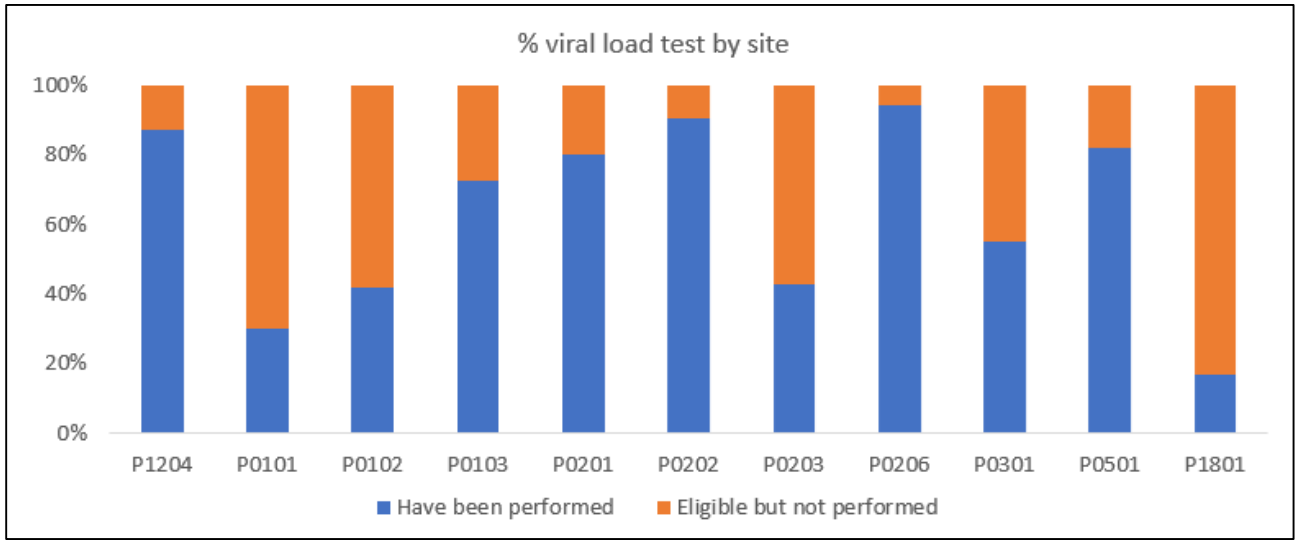
Table 12: Viral load test performance among "Active" patients

VL performance	Number	%
Have been performed	1,185	79.3
Eligible but not performed	290	19.4
Result pending	20	1.3
Total	1,495	100

Table 13: Viral load test performance among "Active" patients in Provinces and in Phnom Penh

Viral Load performance	Provinces		Phnom Penh	
	Number	%	Number	%
Have been performed	468	70.6	717	86.2
Eligible but not performed	185	27.9	105	12.6
Result pending	10	1.5	10	1.2
Total	663	100	832	100

Figure 1: Percentage of viral load test among "Active" patients by site



The goal of antiretroviral therapy is to keep suppression of the viral load, restore immunologic function, improve quality of life and reduce HIV-related morbidity and mortality. According to the national viral load algorithm a patient has an undetectable viral load when the value of the viral load test is <40 copies/ml, while viral load suppression defined as having viral load <1000 copies/ml.

Among actual active patients, around 87%, and 83% were virally suppression in Phnom Penh and in the provinces respectively.

Table 14: Percentage of "Active" patients with viral load suppressed

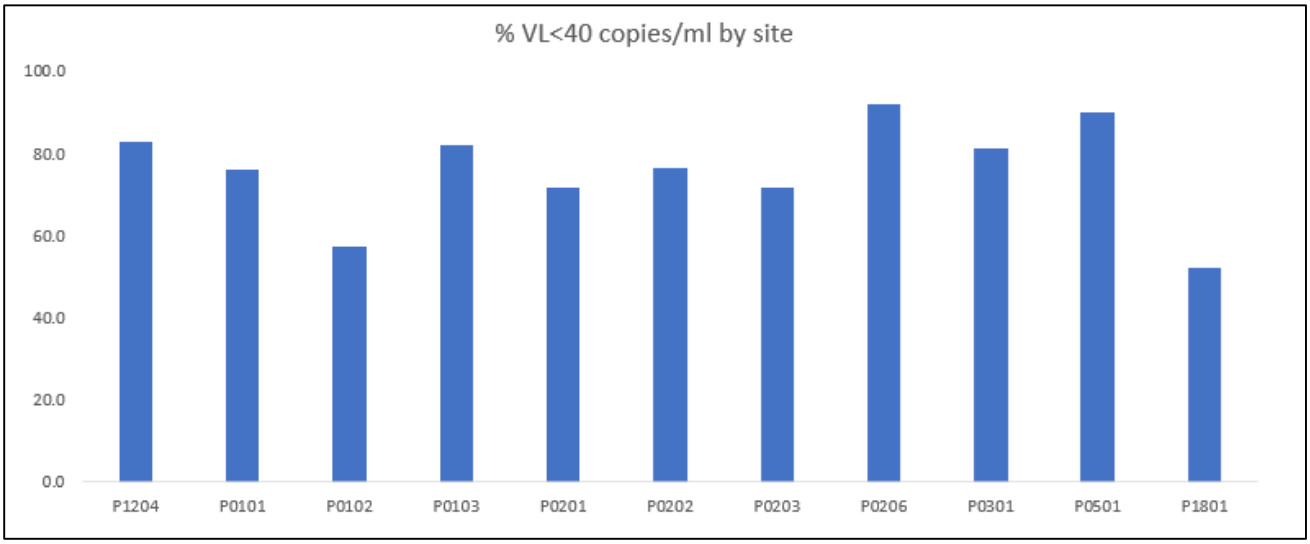
Viral load value	Provinces		Phnom Penh	
	Number	Percent	Number	Percent
<1000 copies/ml	551	83.0	724	86.7
1000+ copies/ml	90	13.6	92	11.0
No viral load result documented	23	3.5	19	2.3
Total	664	100	835	100

Table 15: Percentage of "Active" patients with viral load undetectable

Viral load	Provinces		Phnom Penh	
	Number	Percent	Number	Percent
<40	511	77.0	676	81.0
40-999	40	6.0	48	5.8
1000+	90	13.6	92	11.0
No VL value documented	23	3.5	19	2.3
Total	664	100	835	100

The percent of PLHIV achieved viral load <40 copies/ml varied by site. In average, 75.7% of patients had undetectable viral load with standard deviation of ±12.2, and range of 52.3% to 92.0%. Site with highest percent (92%) of patients had undetectable viral load was Roka referral hospital and site with the lowest percent (52%) of patients had undetectable viral load was P1801 and second lowest was site P0102. The median of patients had undetectable viral load 76.6%.

Figure 2: Percent PLHIV with viral load <40 copies/ml by ART site



When reviewing viral load suppression, in average, 83.9% of patients had virally suppressed with standard deviation of ±10.5%, and range of 61.4% to 95.5%. Site with highest percent (95.5%) of patients had suppressed viral load was Poi Pet referral hospital and site with the lowest percent (61.4%) of patients had suppressed viral load was P1801.

6.5 TB prophylaxis therapy

Table 16-18 showed the performance of TPT among active HIV-infected children on ART in the reviewed provinces. Most of children were not currently on TPT and almost all of those who were not on TPT were eligible for TPT or had no information of TPT at both locations, Phnom Penh and provinces.

Table 16: TPT performance among active pediatric patients

Is currently on TPT?	Number	%
No	1,379	92.0
Yes, completed	93	6.2
Yes, ongoing	27	1.8
Total	1,499	100

More than 94% of pediatric patients in Phnom Penh were not currently on TPT, while 89% of pediatric patients in the provinces were not currently on TPT. Among those who are not on TPT, almost 10% and 47% are eligible for TPT in Phnom Penh and in the provinces respectively (Tables 17 and 18).

Table 17: TPT performance among active pediatric patients in the province vs in Phnom Penh

Is currently on TPT?	Provinces		Phnom Penh	
	Number	%	Number	%
No	591	89.0	788	94.4
Yes, completed	63	9.5	30	3.6
Yes, ongoing	10	1.5	17	2.0
Total	664	100	835	100

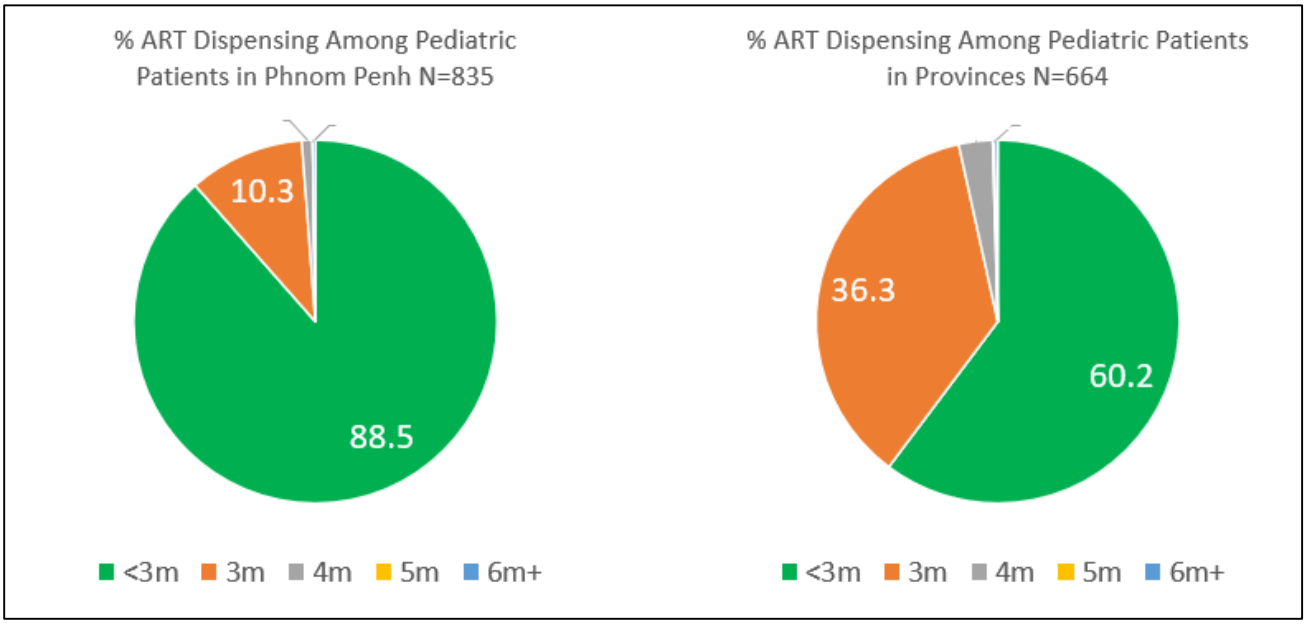
Table 18: Eligible for TPT among Active pediatric patients in provinces versus in Phnom Penh

Eligible for TPT	Provinces		Phnom Penh	
	Number	%	Number	%
No information	308	52.1	678	86.0
No, not eligible	5	0.9	32	4.1
Yes, eligible	278	47.0	78	9.9
Total	591	100	788	100

6.6 Multi-month dispensing

Most of children in Phnom Penh have been receiving less than 3 months ARV drugs dispensing, while in the provinces 60.2% of patients have been receiving ARV dispensing less than 3 months and 36.3% have been receiving ARV dispensing for 3 months.

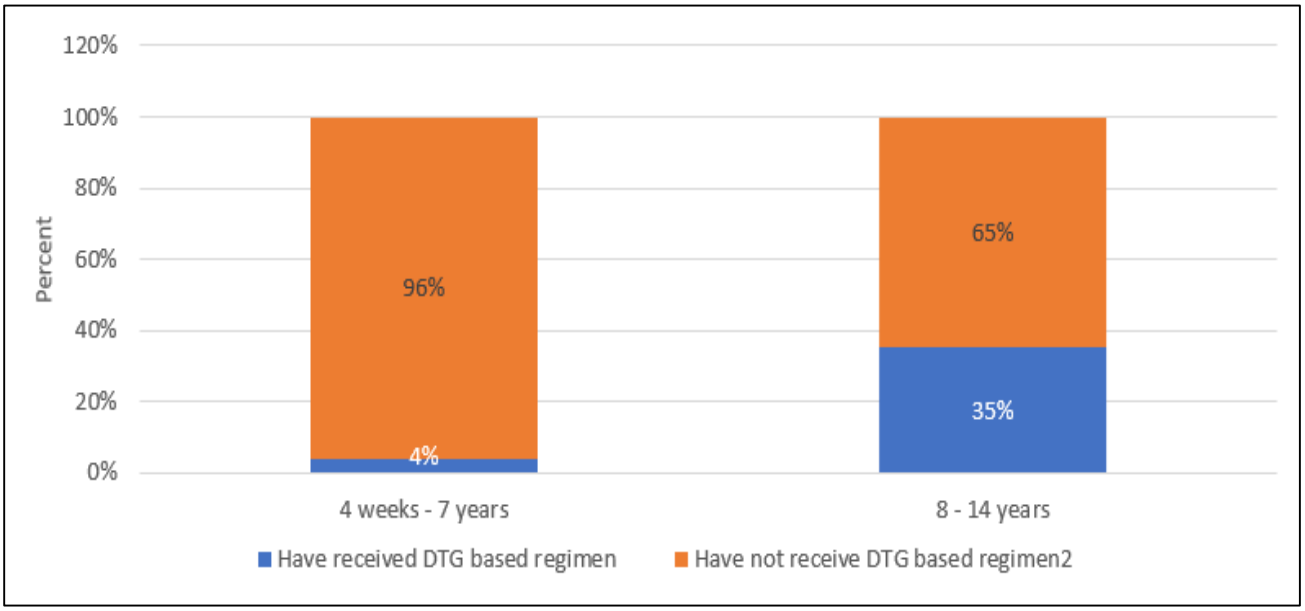
Figure 3: Percentage of ART dispensing among pediatric patients in Phnom Penh and in the Provinces



6.7 DTG Implementation Status

To see the coverage of DTG-based regimen among pediatric patients, additional analysis was done on 1,109 patients taken form NCHADS's database, 473 patients were in PNH, and 636 patients were in the provinces. Figure 4 showed the distributions of DTG-based regimen by age-group with 35% and 4% in age 8-14 years and 4-7 weeks groups respectively.

Figure 4: Percentage of pediatric patients on DTG-based regimen by age-group



6.8 Deaths

There were total 22 deaths for the period of three years. In Phnom Penh there were 9 deaths in a year, while in the provinces 13 deaths in two years.

Table 19: Number of deaths by sex

Sex	Number	Percent
Female	9	40.9
Male	13	59.1
Total	22	100

Table 20: Number of deaths by sex in Provinces and in Phnom Penh

Sex		Site		Total
		Provinces	Phnom Penh	
Female	n	6	3	9
	%	66.7	33.3	100
Male	n	7	6	13
	%	53.9	46.2	100
Total	n	13	9	22
	%	59.1	40.9	100

Among the 22 deaths, 31.8% had viral load greater than 1000 copies/ml. since 31.8% of deaths had no viral load information documented, this percentage may not reflect the real situation.

Table 21: Viral status of dead patients

Viral load	Number	Percent
<1,000 copies/ml	8	36.4
1,000+ copies/ml	7	31.8
No viral load	7	31.8
Total	22	100

When reviewing the number of years on ART before dying, it showed 50-50 of less than 5 years and 5 years or greater.

Table 22: Number of years on ART to die

Number of Year on ART Before Death	Number	Percent
<5 years	10	45
5+ years	10	45
Missing ART start date	02	10
Total	22	100

VII. Discussion

Overall, 3.8% and 3.4% of pediatric patients in Phnom Penh and in provinces were lost the follow-up. The rate seemed low and in good shape compared with national cut-off point stated in the CQI SOP (the percentage of lost to follow-up should not exceed 9%). The lost to follow-up in the review period was defined as any patients come for a visit late more than 90 after appointment date. The patient status categorized in ART database in four categories: Active, Dead, Lost to follow-up, and Transferred out, while blitz categorized appointment status in four categories: Active, missed clinical appointment for 1-30 days, missed clinical appointment for 31-90 days, and missed clinical appointment greater than 90 days (LTF). When analysis focused on the actual active patients in the ART database, blitz found more than 96% of patients had regular visit and only 0.6% of patients missed clinical appointment within 31-90 days. On the other hand, data entry clerks and data management at ART sites were very good in keeping quality and consistent data because only 8 patients (0.5%) who missed clinical appointment for greater than 90 days found by blitz were still labelled “active” in the ART database at site.

The lost to follow-up rate in a year of HIV-infected children in Cambodia was 1% higher compared with the rate in Thailand in the study by Suttipong Kawilapat et al. but it was almost twice times lower than in Ethiopia, and in Uganda where the lost to follow-up were 6.2 and 7.5 per 100 persons per year respectively. However, the lost to follow-up in Thailand was defined 09 months after the last contact date (4). The predictor of lost to follow-up for children with HIV in Ethipia were children who got care from their biological parents, WHO clinical stage 3/4, history of regimen substitutions, poor adherence, and history of TB treatment, whereas the predictors in Uganda were starting ART within 7 days following HIV diagnosis, lack of a telephone set, CD4 cell count of 200-250 µ/ml and baseline WHO clinical stage 3/4. In Malawi, reasons that contribute to lost to follow-up were lack of support from family, long distance to health facilities, poverty, community-level stigma, ART side effects, perceived good health after taking ART and adoption of other alternative HIV treatment options.

Although several factors/reasons in African countries were the same as in Cambodia, others seemed differ from the factors/reasons found in Cambodia where they were the issue of transportation cost, the caregiver-related issues that make them unable to accompany or bring the sick child to ART clinic, caregiver/parents were working far away and brings sick children with them, and changes of caregivers.

There was up to 19% of eligible but not performed viral load test among active patients. This could be associated with the reasons that the child was not brought to the clinic mentioned above, and most often the caregiver come to pick-up ARV without bringing the sick child to have blood drawn for viral load test. The viral load suppression rate was 83.9% among HIV-infected children on ART that had viral load test, and viral load non-suppression was 16.1%. The suppression rate was high comparing the viral load suppression rate found in a cross-sectional study by Kolab Chhim et al. in 2018 (76.8%). However, in our analyses included all HIV-infected children at 11 large pediatric ART sites composed of 1,971 patients and different years of study. The suppression rate in Cambodia was also higher than in Eastern and Southern Africa where the viral load suppression rates was 65% in 2018. Regarding viral load non-suppression rate of 16.1% was lower than in Zimbabwe, Uganda, Nigeria, Ghana, and in Ethiopia where the viral load non-suppression rates were 35.1%, 23%, 51.3%, 38.4%, and 28% respectively.

Factors associated with viral load non-suppression in those African countries were sex, longer duration and adhering to ART, efavirenz-based and nevirapine-based regimens, age smaller than 5 years, history of TB treatment, WHO clinical stage at ART initiation and ART-induced side effects. While in Cambodia, the viral load non-suppression may associate with challenges that PAC is facing at the moment such as HIV drugs availability in term of right size, right form, and right dose. Taking drugs for children is challenging due to kids themselves, caregivers, number of drugs, size and form of drugs. The ARV forecasting, procurement and supply chain also need improving.

TB preventive treatment is treatment offered to individuals who are considered to be at risk of developing TB disease, in order to reduce that risk. Blitz found that TPT among HIV-infected children in Cambodia was very low. Only 6.2% of pediatric patients completed TPT, and 1.8% were ongoing TPT while 71.5% had no information of TPT documented in the chart. Although TPT options now were expanded to child-friendly, the scale-up and implementation of TPT among children are still challenging globally. The key challenges include but not limit to clear goal, practical implementation plan, reliable logistic and operation and drug supply chain, and effective monitoring and evaluation system.

VIII. Limitations:

The individual factors associated with lost to follow-up, and individual factors of not have viral test performed were not collected, only the collective factors and reasons were collected. The cause of death was not specified. The individual factors associated with viral load suppression were not analyzed for the purposes of the documentation. The quality of TPT documentation in patient's chart was very poor so the results of TPT performance may be under reported.

IX. Conclusion and Recommendations

Pediatric AIDS care is important, but challenging. Because children's immune systems are not fully developed, children living with HIV get sick more severely than adults particularly tuberculosis, diarrhea, and respiratory illness that common in HIV-positive children. With the low rate of viral load test done (79%) and viral load suppression (85%) among active pediatric patients have contributed to increased susceptible to opportunistic infections. Tuberculosis is the leading cause of death for people living with HIV. TB preventive therapy (TPT) is recommended by the World Health Organization for people living with HIV infection without active TB disease (children with a negative clinical screen for cough, fever, contact with a person with TB, or poor weight gain). Percentage of children living with HIV receiving TPT is very low (8%) that make children living with HIV at higher risk contacting TB.

If ART team members, National Center for HIV/AIDS, Dermatology and STD, National Center Anti-tuberculosis, cannot make the performance of viral load tests and TPT improved, the life of children living with HIV are in danger and probably have short survival time.

To improve the pediatric AIDS care performance some recommendations are suggested as follow:

9.1 At ART Clinic

- Clear charts of the patients who were no longer active at ART clinics (ref. slides 15, 18):
- Pediatric sites review line list of patients who did not receive viral load testing for the last 12 months, then take actions reasonably.
- Refresher training on planning, forecasting, and requesting ARV and TPT. DTG and MMD must be included and should be implemented widely according to the findings from TLD documentation of the NCHADS.
- Have clinicians trained/retrained on TPT:
    - What is TPT?
    - How does TPT work?
    - Who should take TPT?
    - Why should I take treatment when I do not feel ill?
    - What TPT options are available? Can I take whichever one suits me?
    - What should I do if I develop adverse drug reactions?
    - Should I also get vitamin B6 with TPT?
    - Is it necessary to test for liver function before starting TPT?
    - Do I need to take TPT if I am living with HIV and receiving antiretroviral treatment (ART), and have a high CD4 cell count?
    - Should PLHIV on ART receive rifapentine?
    - How can we rule-out active TB in PLHIV prior to TPT? Should pregnant women living with HIV take TPT?
    - Should pregnant women living with HIV take TPT?
    - Should TPT be given if someone in the household has multidrug-resistant TB?

- Can TPT worsen the TB drug-resistance problem in the world?
- How do I know if I have TB disease?
- How can you test for TB infection?
- How is TST done?
- How are IGRAs done?
- Should TPT be provided under direct observation (DOT)?
- What can be done to encourage treatment adherence and support completion of TPT?
- Should a course of TPT be repeated?

9.2 At National Level

- Strengthens collaboration between the two national programs – NCHADS and CENAT to assure appropriate availability and access to TPT regimens.
- Develops and disseminates pDTG transition plan.
- Retrains clinicians at pediatric sites on TPT, and viral load literacy.
- Organizes P-D-C-A regional workshop to review the pediatric AIDS care performance, to develop improvement plan and implement it regularly.
- Organizes national planning workshop on pDTG, 3+MMD, and drug forecast.
- Trains PAC providers on planning, and M&E of the successes of the PAC services in Cambodia

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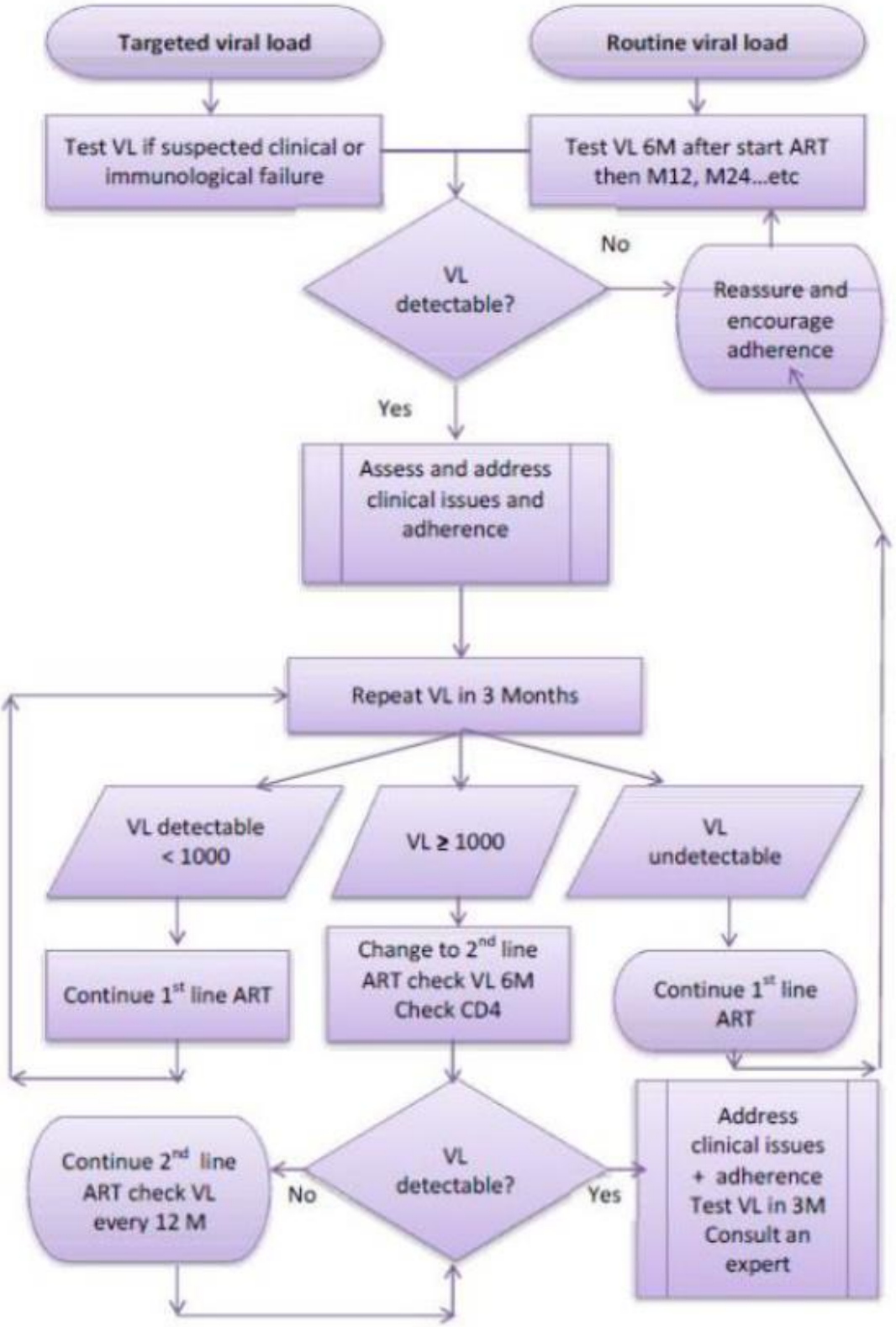
XI. Appendixes

Appendix 1: National Viral Load Algorithm



Appendix 2: Algorithm for TB screening in children living with HIV aged ≥12 months

Figure 7: Algorithm for TB screening in children living with HIV aged ≥ 12 months