

Viral load suppression in Myanmar: Implications for fast track monitoring and for key population programming

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Abstract

An overview of viral suppression within a cohort of patients treated by NGOs in Myanmar was studied to get an insight into treatment adherence among Key Populations (KP). Secondary data from eight NGO-supported sites across nine states and regions were analysed. Patients on antiretroviral therapy (ART) for at least 6 months and who had not received a viral load (VL) tests during the period 6 months before March 2016 were eligible for inclusion in the study. Data validity checks resulted in the inclusion of 9,988 of 10,500 patients reviewed. Variables studied included gender, age, key populations (KP), duration of HIV infection, ARV (antiretroviral) regimen, duration of treatment, last CD4 count, and service providers and clinic location.

Viral suppression (VL determination < 1,000 copies/ml) was measured in 95.1% of the study population. Out of a total sample of 9,988 cases, 56.0% were males and 44.0% were females and 72.5% were 20-44 years old. Among the population studied, 76.4% of them represent the general population (GP) and 23.6% are KP. KP includes men having sex with men (MSM) 11.4%, People Who Inject Drugs (PWID) 6.5%, and female sex workers (FSW) 5.7%. Mean value of the last CD4 count was 497.8 (SD 256.5), mean duration HIV infection was 59.0 months (SD 36.2), and mean duration of antiretroviral therapy (ART) was 42.5 months (SD 26.5).

Treatment outcome was associated with the clinic's geographic region ($p < 0.001$), ART regimen ($p < 0.001$), gender ($p = 0.023$), age ($p < 0.01$), and duration of ART ($p = 0.006$). Significant difference was also found among the KP types ($p = 0.02$) with FSW (96.1%) exhibiting the highest rate followed by MSM (95.8%), GP (95.1%), and PWID (92.8%). In multivariate analysis, geographic location ($p = 0.000$), age > 20 years ($p < 0.001$), CD4 count > 200 ($p < 0.001$), and KP ($p = 0.004$) were associated with viral suppression. Although the study was not designed to explore treatment adherence among KPs and in addition it was not nationally representative, the results nevertheless showed that UNAIDS fast track targets can be achieved as well as adherence can be high among the populations who are often considered difficult to retain in HIV treatment cascade.

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Introduction

Myanmar aims to achieve 90-90-90-90-90 targets, based on UNAIDS's fast track strategy, by 2020 in its recent National Strategic Plan (NSP) on HIV/AIDS (2016-2020). This means 90% of targeted population will have access to prevention services; 90% of People Living with HIV (PLHIV) know their status; 90% of PLHIV who know their status receive treatment; 90% of PLHIV on treatment have suppressed viral loads; 90% of PLHIV at risk of and affected by HIV report no discrimination. Hence, management information about the current status of the country in each step is crucial in moving towards the targets in NSP. In Myanmar, National AIDS Programme and all partners who are providing ART are only able to do targeted viral load (VL) testing (i.e. VL testing for suspected treatment failure cases only) to confirm treatment failure. It showed 87% (8,400 out of 9,700 who received viral load test) viral suppression during the year 2015¹. The National policy aims to scale up viral load testing by moving from targeted to routine monitoring, and to test and gradually replace the current CD4 monitoring. This is to be done provided that the VL PCR machines are well functioning and quality assurance system is in place. Given this strategic direction, baseline viral load monitoring data for ART eligible patients being treated by NGOs service providers in the nine States and Regions becomes important.

Monitoring of individuals on ART is important to ensure treatment efficacy and improved health comes. WHO guidelines recommend viral load testing as part of routine therapeutic monitoring for all People Living with HIV (PLHIV) so as to assess treatment response and detect treatment failure². In particular, monitoring Viral Load suppression rates is used to measure the treatment success in a cohort of antiretroviral therapy (ART) patients. However, there are very limited information in Myanmar regarding baseline viral load suppression rate that is based on a large cohort, reference for routine viral load monitoring measures, and the associated factors for viral suppression.

The present study aims to provide information on ART treatment outcomes and its associated factors from among NGO service providers in the country (nationwide) so as to obtain reference data for future improvement of the HIV treatment and care programme in Myanmar.

Methods

Secondary data analysis was done on approximately 11,000 ARV patients who have started treatment for at least six months and patients who have not received any viral load testing in the past six months. These eligible patients are receiving ARV from 8 NGO partners and 23 general practitioners in 29 townships in 9 States and Regions (Yangon, Mandalay, Bago, Ayeyarwaddy, Shan, Sagaing, Mon, Kayin and Kachin). The following variables were studied.

Dependent variables:

- *VL detectability* can be classified as detectable and undetectable according to the detection threshold of Bio centric technique of the VL machines
- *Viral load suppression* is defined as the plasma viral load less than 1,000 copies/ml

Independent variables:

- Demographic data such as age, gender, types of key populations, service providers and locations of service provided
- Treatment data such as duration of HIV, duration of ART, duration of 2nd line ART and current ARV regimen and CD4 count

Excel sheet from each organization was checked for completeness before they were combined into one data set. For validity, 10% of cases from each organization's data was randomly chosen and checked with primary data source for consistency and to exclude errors in data entry. If there was inconsistency and incompleteness, they were validated with the responsible persons from the organization providing the data. About 200 samples were omitted due to incompleteness and inconsistencies. All the data were then combined into one data set and transposed to SPSS software for analysis.

For descriptive analysis, continuous variables such as age, CD4, duration of ART were analyzed into mean and SD, range or median depending on their distributions. Proportions of the sample with viral load suppression (plasma viral load less than 1,000 copies/ml) were calculated. Bivariate analysis between treatment outcome variables and independent variables was carried out to find out associations between ARV treatment outcomes. Multivariate analysis was further carried out to find out the independent associations between viral suppression and independent variables.

Ethical consideration

Ethical approval for this study was obtained from the Ethics Review Committee, Department of Medical Research. Patients' identifiable data were not collected and original data from treatment partners was used with their permission for this research purpose only.

Findings

Table 1 shows the demographic and key population background of the subjects in the study.

The study involved a total of 9,988 patients from eight non-profit organizations. Most of the study participants were seeking health care from the NGO clinics in Yangon Region (54.00%) and Mon State (19.71%). Other significant portions of the patients are from Kachin, Shan and Bago with 8.40%, 6.54% and 4.67% respectively. The proportion of male and female in the study was 56.2 % and 43.98% respectively. It was found that the majority 72.51% (7,242 cases) of the patients are in their active and productive ages (20-44 years). About 3% of the patients were found to be paediatric ART cohorts.

Table 1. Demographic and key population background of participants in the study

	Number of Participants	Percent
Age (in years)		
<15	312	3.12 %
15-19	149	1.49%
20-44	7,242	72.51%
40-59	2,092	20.95%
60+	193	1.93%
Gender		
Male	5,595	56.02%
Female	4,393	43.98%
Key Population (KP)		
FSW	569	5.70%
MSM	1,135	11.36%
PWID	651	6.52%
General Population	7,633	76.42%
Organization		
AFXB	860	8.61%
ALLIANCE	2,259	22.62%
Consortium	1,119	11.20%
IOM	1,461	14.63%
MDM	1,847	18.49%
Malteser	693	6.94%
PSI	825	8.26%
PU-AMI	924	9.25%
State/Region		
Ayarwaddy	18	0.18%
Bago	466	4.67%
Kachin	839	8.40%
Kayin	188	1.88%
Mandalay	126	1.26%
Mon	1,969	19.71%
Sagaing	288	2.88%
Shan E	646	6.47%
Shan-South	7	0.07%
Wa Special Region II	47	0.47%
Yangon	5,394	54.00%

Regarding the various types of key populations, majority (over 76%) were recorded as general population although some of them might belong to one of the hidden key population groups. Among known key population groups, MSM was the highest with a number of 1,135 participants (11.36%). MSM and FSW were mostly concentrated in Yangon, Mandalay, Mon and Bago Regions. For PWID, it was almost confined to Kachin State.

Disease characteristics

As shown in Table 2, over 90% of the participants had CD4 results of over 200 cells/mm³. Mean CD4 count was nearly 500 (497.78 ± 256.45).

Mean duration of HIV infection among the study population was nearly 5 years (59 months) with a maximum duration of about 20 years. Subsequently, the most frequent HIV infection duration (38.49%) was between 2 and 4 years closely followed by HIV duration of 5-9 years (38.25%). HIV infection with duration of less than 2 years was also not uncommon with 1,759 patients (17.61%).

Mean and median CD4 counts were 497 (SD 256) and 466 (IQR 325-628) respectively. Immunological suppression was found out to be about 92% (CD4 > 200 cells/mm³).

Table 2. Disease characteristics of the HIV positive people on ART (N = 9,988)

	Mean	S.D	Frequency	Percent
Last CD4 result (cells/mm³)				
<200	497.78	256.45	820	8.21
200+			9,168	91.79
Duration since HIV diagnosis	59.00 (months)	36.19 (months)		
<2 years			1,759	17.61
2-4 years			3,844	38.49
5-9 years			3,820	38.25
10-14 years			530	5.31
15-20 years			35	0.35
Duration of ART	42.52 (months)	26.53 (months)		
<2 years			2,662	26.65
2-4 years			4,953	49.59
5-9 years			2,325	23.28
10-14 years			48	0.48

Duration of ART treatment among people living with HIV infection in the study ranged from 6 months up to nearly 14 years. Duration of ART in inclusion criteria for the study was at least 6 months so as to have enough duration to reflect the effects of ART treatment. Median duration on ART in the study was 3 years (36 months). The majority (over 75%) of the study population had been taking ART for 2 to 9 years.

Type of ART

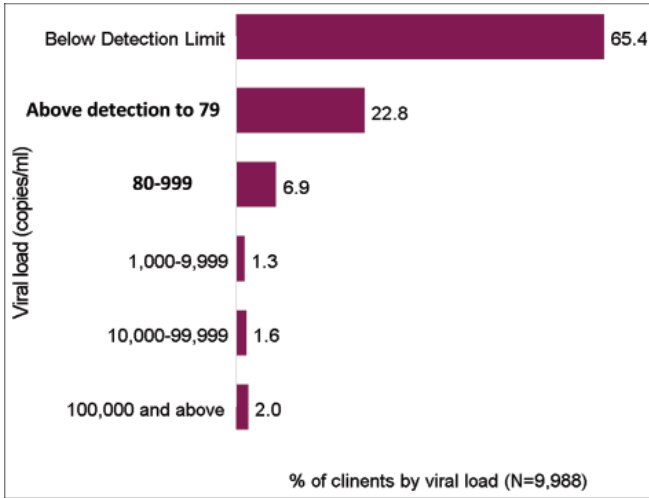
Almost all of the participants (97.28%) were currently on First line antiretroviral therapy whereas only 2.72% were on second line. When looking at specific ART regimens, about half of patients were on TDF + 3TC + EFV regimen (57.1%) followed by AZT + 3TC + NVP regimen (26.6%) and AZT + 3TC + EFV (10.2%) and ABC + 3TC + EFV (0.9%) respectively.

Table 3. Distribution of ART regimen among study population (N = 9,988)

Current ART Regime		
	Freq.	%
AZT + 3TC + EFV	1,021	10.22%
AZT + 3TC + NVP	2,656	26.59%
TDF + 3TC + EFV	5,700	57.07%
Other combinations	611	6.12%
Total	9,988	100.00%

Viral load

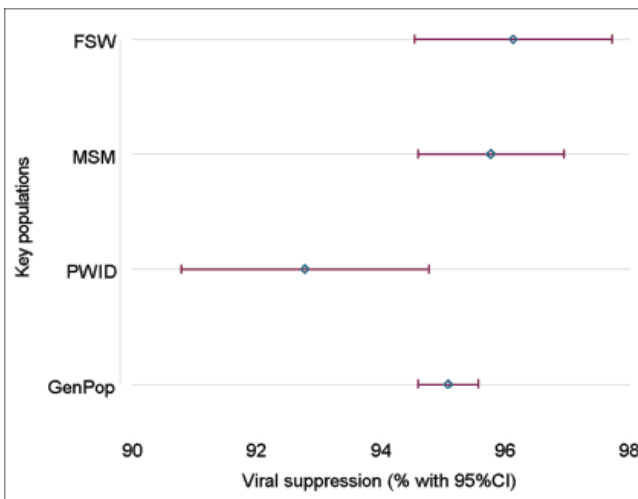
Figure 1. Distribution of viral load among the study participants (N = 9,988)



The viral load results are shown in Figure 1. Treatment outcomes among participants living with HIV infection seem to be good because 65% had undetectable viral loads and over 95% of the patients had VL suppression. However, 492 out of 9,988 patients (4.93%) had viral load counts of 1,000 copies/ml and above. For these 492 patients defined as having virological failure, 61% were males and 39% were females. Among them, 22 patients were on second line ART and 470 were on first line ART regimen.

Viral load suppression was found to be statistically associated with the location from where the participants were seeking/obtaining treatment. Treatment success was relatively lower in remote areas like Shan East and Wa Special Region II when compared to other regions.

Figure 2. Proportions of three KP having viral suppression



Treatment success in PWID was comparatively lower ($p = 0.02$) than general population and other key populations.

Table 4 shows that patients taking the first line ART tend to have higher chance of success in their treatments (95% vs 91%, $p < 0.02$). When looking at current ART regimen, a great majority were on TDF + 3TC + EFV regimen followed by AZT + 3TC + NVP regimen. Bivariate analysis showed more promising result for the AZT + 3TC + NVP regimen than other regimens, with 96.5% getting viral suppression ($p < 0.001$). It needs to be highlighted that information on the changes/modifications in regimen among these patients throughout their ART life was not available.

Table 4. Association between viral suppression and type of ART

Type of ART	viral suppression (copies/ml)		Total
	VL \geq 1000	VL $<$ 1000	
Second line	22	250	272
	8.09	91.91	100.00
First line	470	9,246	9,716
	4.84	95.16	100.00
Total	492	9,496	9,988
	4.93	95.07	100.00

Statistically significant association was also found between gender and viral load suppression rate (95.63% vs 94.64%, $p = 0.023$). (Figure 3) For those with viral load suppression, mean duration in months was 42.73 while those with non-suppression were 38.48 months. The difference in mean duration was statistically different. (Figure 4)

Figure 3. Gender differential in viral load suppression in the study population taking ART

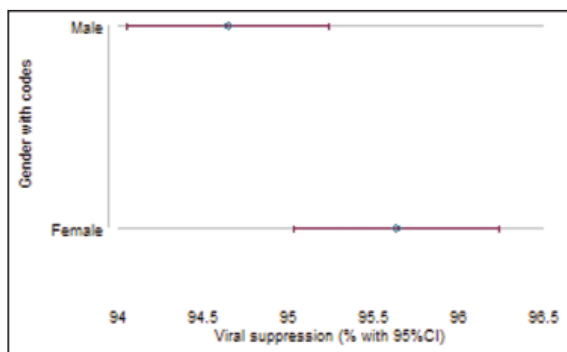


Figure 4. Association between mean duration of ART with viral load suppression

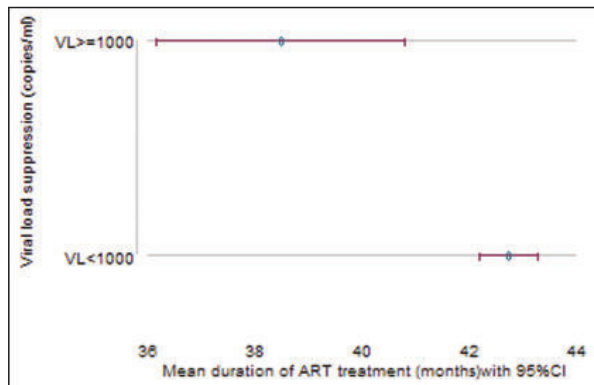


Table 5. Multiple logistic regression showing association between viral suppression and related factors

	Odds Ratio	Std. Err.	z	P> z	[95% Conf. Interval]
Gender					
Male	1	(base)			
Female	1.057875	.1177201	0.51	0.613	.8505758 1.315698
agegrp					
<15	1	(base)			
15-19	1.142667	.3328723	0.46	0.647	.6455868 2.022482
20-44	4.1096	.7018406	8.28	0.000	2.940565 5.743392
45-59	6.776309	1.401818	9.25	0.000	4.517568 10.1644
60+	5.791861	2.370722	4.29	0.000	2.596598 12.91908
KeyPop					
FSW	.9005242	.2211493	-0.43	0.670	.5564916 1.457244
MSM	.9343307	.16789	-0.38	0.705	.6569739 1.32878
PWID	.2232656	.1156437	-2.89	0.004	.0808964 .6161894
GenPop	1	(base)			
Duration of Hiv					
<2years	1	(base)			
2-4 years	1.005424	.1753546	0.03	0.975	.7143195 1.415162
5-9 years	.8573932	.1646755	-0.80	0.423	.5884285 1.249299
10-14 years	1.145002	.3455284	0.45	0.654	.63378 2.068589
15-20 years	1.244406	1.298697	0.21	0.834	.1609254 9.622764
CD4 count					
<200	1	(base)			
200+	7.265401	.8416904	17.12	0.000	5.789601 9.11739
Duration of ART					
<2years	1	(base)			
2-4 years	.9824875	.1551903	-0.11	0.911	.7208987 1.338998
5-9 years	.9962804	.2022584	-0.02	0.985	.6692312 1.483157
10-14 years	.8608708	.6709992	-0.19	0.848	.1868424 3.966437
First/second line ART					
Second line	1	(base)			
First line	1.023688	.1981429	0.12	0.904	.7005047 1.495976
States and regions					
Ayarwaddy	1	(empty)			
Bago	8.058465	4.731026	3.55	0.000	2.549895 25.46727
Kachin	2.570406	1.293526	1.88	0.061	.9586166 6.892212
Kayin	.9126766	.2758907	-0.30	0.762	.5046721 1.650534
Mandalay	1.057048	.4417009	0.13	0.894	.4660249 2.397618
Mon	.8712715	.1124973	-1.07	0.286	.6764685 1.122172
Sagaing	1.771345	.6279523	1.61	0.107	.884193 3.548617
Shan E	.4083323	.0653075	-5.60	0.000	.2984524 .5586663
Shan-South	1	(empty)			
Wa Special Reg..	.2186696	.0902054	-3.69	0.000	.0974207 .4908237
Yangon	1	(base)			
ART regime					
AZT+3TC+EFV	1.028346	.1792473	0.16	0.873	.7307509 1.447135
AZT+3TC+NVP	1.246352	.1806191	1.52	0.129	.9381799 1.655752
TDF+3TC+EFV	1	(base)			
Other	1.018234	.1967337	0.09	0.925	.6972469 1.486993

In multiple logistic regressions, those in higher age group have a higher chance of viral load suppression than the younger age group. Patients with CD4 > 200 have seven times higher chance of viral suppression than those with low CD4 count. Among KP, PWID population has the least chance of getting viral suppression than general population.

Regarding gender, female had higher viral load suppression than male in bivariate analysis, however, the association is not strong in multivariate analysis. Association with duration of ART, duration of HIV and first/second line treatment, and ART regimen were no longer significant.

Discussion

In this cross sectional study, it was found that 95% of people living with HIV (PLHIV) in routine ART programme of NGO clinics had virological suppression. According to National AIDS Programme (NAP), among those who had a viral load test in 2015, 86.6% had achieved viral suppression and it accounted for about 9% of people on treatment¹. This ART cohort constituted about 10% of total PLHIV on ART in Myanmar with a wide geographical coverage. This reflects the success of the ART programme in its attempt to achieve a 90% suppression for those on ART (90-90-90 UNAIDS target).

About one fourth of study population were reported to be KP. Geographical distribution of KP was consistent with the HIV prevalence among KP as reported in the Integrated biological and behavioural survey (IBBS) and HIV Sentinel Surveillance (HSS) reports. In Yangon, among MSM the HIV prevalence was highest at 26.6% and 24.6% for FSW⁵. Distribution of positive MSM and FSW is concentrated in Yangon.

This study reported much lower proportions of treatment failure than in the previous study. A 2017 study reported a high rate of virological failure, with one third of 7,888 patients taking treatment at the Union Integrated Health Care (IHC) model care centers in public hospitals considered to have failed⁶. However, the study was not directly comparable with our study in the sense that VL measurements were done at different points of care and according to clinical requirements. Adults or older age group, being KP, CD4 count are found to be factors associated with virological failure in this study. Gender showed no strong association with virological failure.

It is a fact that ART non-adherence is among one of the important factors associated with treatment failure. The study could not deliberate the factors for ART adherence, which is reported to be an important factor^{3, 4}, since this study was based on the analysis of secondary data. Future studies on systematic assessment of determinants of virological failure in children and adults are needed, taking into consideration a wide range of factors including age at ART initiation, ART adherence, plasma drug levels, disease staging, etc.

This study reports the first evidence on the prevalence of virological failure among the large ART cohort taking treatment from the NGO sector in Myanmar. Treatment outcome for MSM and FSW population is observed to be relatively good. PWIDs constitute the lowest proportion among the three KP in this ART cohort. Although viral suppression rate is high compared to other studies,^{7, 8, 9} viral load suppression in PWID population is the least satisfactory. Given that the HIV prevalence among PWID is significantly high, interventions to improve treatment outcome among PWID are strongly encouraged taking into account the factors that specifically effect this population. A more detailed look into factors such as current drug use, use of Methadone Maintenance Therapy (MMT) and ART adherence regarding PWID who are taking ART are needed in future studies. Recent study in China revealed virological suppression varied among active drug user group (41.1%), drug abstinence group (68.7%) and MMT group (51.9%)¹⁰. Our study findings

showed consistency with the recent study among large ART cohort which stated that being adolescent is one factor associated with virological failure⁶.

The same study also reported that only 74% of those with treatment failure were switched to a second line ART while the rest were lost to follow up or died. First line ART failure by virological parameter is (4.84%). Viral load confirmation was done for 400 PLHIV who had viral load > 1,000, and among those confirmed 62.50% still had > 1,000/ml. It was quite alarming to find that a large proportion still had failure after adherence to counseling and these patients need urgent consideration to change to second line regimens as necessary.

Regional variation was found to be interesting. The underlying causes of low viral suppression in Shan East and Wa Special Regions need to be studied more. These areas are the relatively conflict prone regions and ART adherence is expected to be low but nevertheless the influencing factors need to be better understood.

The present study found that the association of last CD4 was strong as in other studies⁷. Duration of taking ART did not show a strong association with viral load suppression. A great majority of patients were on TDF + 3TC + EFV regimen followed by AZT + 3TC + NVP regimen. The study proved those currently on AZT + 3TC + NVP regimen had a higher chance of virological suppression than other regimens. The study did not have information on the history of change in treatment regimen among the study population. However, 2017 study reported that those whose first ART regimen was not TDF + 3TC + EFV had a higher risk of switching to the second line treatment. Information on drug resistance for this highly recommended WHO regimen is urgently needed in order to provide concrete recommendations. In the 2015 Togo study, it revealed that drug resistance was as high as 97% of virological failure patients on first line ART¹¹.

With the enhancement of tests and treat strategies for KP as well as general population, systematic treatment monitoring should be in place and move towards routine viral load testing. Strategic Direction 2 of National Strategic Plan (NSP) III is improving health outcomes for all people living with HIV for which the indicator is set for 90% of PLHIV on ART to get tested for viral load. Proportion of PLHIV on ART who have achieved viral suppression among those tested for viral load in the last 12 months was reported to be 87% in 2015 (NSP).

The study population comes from patients undergoing treatment in NGO clinics and represents predominantly private sector. Assessment of a wider ART group including the public sector patients is needed for a more candid assessment of treatment outcomes of ART programmes in Myanmar. It is encouraging that NAP acknowledged the need to scaling up viral load testing capacity (with quality control systems) as a part of routine monitoring of ART patients.

Strengths and limitations of the study

Strength of the study includes a large sample size and quality control for validity of results by using the same laboratory chain for all samples tested. The study covered a wide geographical area and as such the results are fairly representative of the patients undergoing treatment in NGO clinics. However, only limited information was available from the NGO clinics and some important variables such as initial ART regimen, change in regimen during treatment, information on other co-infections and adherence factors, etc could not be analyzed.

Weak association between treatment outcomes and different ART regimens should be interpreted with caution since there can be other programme factors which can affect this association. The study could not take into account those who passed away or were lost to follow up at the time of viral load testing. The study looked into those who were on ART cross sectionally.

Conclusions

Virological treatment outcome was associated with CD4 count, the clinic's geographic region, gender, age and duration of ART. Significant difference was also found among the KP types with FSW (96.1%) exhibiting the highest rate followed by MSM (95.8%), GP (95.1%) and PWID (92.8%). The results showed that UNAIDS fast track targets can be achieved with more efforts targeting on care and treatment sector for general populations as well as KP.

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