AN ASSESSMENT OF HAI-CÔTE D'IVOIRE'S PERFORMANCE IN MEETING THE 3RD 90-UNAIDS TREATMENT GOAL OF 90% VIRAL LOAD SUPPRESSION AMONG THOSE RECEIVING ART

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Abstract

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UNAIDS updated treatment goal recommendations are now 95-95-95 by the year 2030. Prior to 2020, UNAIDS' 2014 90-90-90 treatment goal indicated that 90% of all people living with HIV are aware of their HIV status, 90% of all people diagnosed with HIV will receive ART and 90% of people receiving ART will have viral suppression. Many countries were still not on track to achieving these targets. This present study was undertaken during the former 90-90-90 goals and focuses on the 3rd 90 goal of viral suppression; a WHO recommended vital indicator of ART success and detection of treatment failure. There is a strong body of evidence that viral suppression and undetectable VL levels are instrumental in the prevention of new infections via sexual transmission.

Health Alliance International (HAI) is an international NGO in Côte d'Ivoire that has partnered with CDC/PEPFAR and has been in the forefront in fighting HIV/AIDS, collaborating with MSHP, Côte d'Ivoire's Health Ministry. HAI supports more than 300 health facilities across 6

regions, in provision of HIV care and treatment services. With improved laboratory information systems, efforts continue to scale up VL monitoring in Côte d'Ivoire. Therefore, our primary aim for this study was to assess how effective HAI-led activities were, at supporting its clinical services sites in meeting the UNAIDS 3rd 90 target of VL suppression in specific regions of Côte d'Ivoire from 2015-2018. Our study showed an overall VL suppression rate of 76.4% among our study participants, higher than the 2019 estimated national rate of 50%, but lower than the initial UNAIDS recommended 90% target.

Our specific Aim 1 of the evaluation was to determine the predictors of VL suppression among those taking ART, during the study period. There was varying geographic variations with rates of 75.4% in Bounkani-Gontougou, 79.7% in Gbeke, 73.0% in Hambol and 73.2% in Poro-Tchologo-Bagoue. Majority (94.1%) of the participants were adults (≥15 years) and they had a higher VL suppression than children (78.1% vs 48.5%). Majority of the patients were female (73.3%), and they had a higher VL suppression than male patients (77.4% vs 73.6%). Also, in our study, the majority of the patients (98.9%) had HIV subtype-1 (HIV-1) but patients with HIV subtype-2 (HIV-2) had a higher VL suppression rate (81.7% vs 76.3%). Patients whose blood specimens were collected and tested between 2017-2018 were significantly more likely to be virally suppressed compared to those whose samples were collected and tested earlier between 2015-2016 (76.6% vs. 75.1% respectively).

Our specific Aim 2 of the evaluation was to determine the predictors of undetectable VL among those with VL suppression. In our study, the overall undetectable VL was at 69.1% among the subsample of those who were virally suppressed leaving 30.9% with detectable but suppressed

VL. Adults ≥15 years of age who made up the majority of the VL suppressed subsample (96.2%) had a higher prevalence of undetectable VL (69.6% vs 55.2%). Also, virally suppressed female participants had a higher undetectable VL prevalence than their male counterparts (70.7% vs 64.4%). Undetected VL in the 4 health districts among those virally suppressed was higher in Gbeke (75.5%) than in Hambol (72.1%), Bounkani-Gontougou (70.3%) and Poro-Tchologo-Bagoue (56.5%).

Our study findings suggest increased efforts are needed to help patients on ART achieve viral suppression. It is vital for strategies to be implemented that are aimed at sustaining adherence counselling of patients, close monitoring and follow-up of patients and increased access to VL testing. This could potentially lead to optimizing VL suppression rates at country level and contribute towards attaining the UNAIDS treatment goals.

1. Introduction

HIV Global burden

HIV is one of the leading causes of global mortality and sub-Saharan Africa has experienced the greatest morbidity and mortality, where 71% of people living with HIV (PLHIV) resided, 65% of new infections and 75% of HIV-related deaths occurred in 2017. More recently in 2019, of the 38 million PLHIV, 67.4% were living in sub-Saharan Africa.[1] [2] [3]

Since its discovery in the early 1980's, the HIV epidemic has substantially evolved globally.[4] The phases of disease progression have seen radical changes in terms of diagnosis, prevention, treatment and surveillance. Over the past 20 years, the compelling diversification of antiretroviral therapy (ART) in both access and formulations has made huge strides towards the global fight against HIV/AIDS. UNAIDS estimates that ART access reached 46% of PLHIV by 2015, leading to a 26% reduction in annual HIV-linked mortality since 2010. Also, the costs associated with ART drugs have markedly decreased and the pharmacological formulations have become simpler and safer.[5] Other strategic efforts have been adopted with significant impact globally, towards ending the epidemic. These include large-scale HIV testing, prevention via reduction of new infections and AIDS-related deaths, viral load (VL) suppression, care linkage and retention.

Despite the upsurge of HIV care and services that have contributed to an overall decline in the epidemic, especially in identified geographical hotspots, many countries are still not on track to meet the Sustainable Developmental Goal (SDG) target that aims to end the epidemic by

2030.[1] [2] [6] In spite of the rapid increase in use of ART globally, 28% of PLHIV in east and southern Africa and 41% of PLHIV in west and central Africa were not receiving any treatment as of 2019.[3] The prevalence of HIV is higher among women and girls and gaps continue to exist in the care continuum – a significant barrier towards ending the epidemic.[7] The HIV care continuum model can be understood using Figure 1.[8]

Figure 1: HIV Care continuum model

Source: HIV.gov (US Department of Health and Human Services)
https://www.hiv.gov/federal-response/policies-issues/hiv-aids-care-continuum

90-90-90

In October 2014, UNAIDS, launched '*90-90-90'* - An ambitious treatment target to help end the AIDS epidemic. The treatment goal constitutes a 3-component provision in an effort to eradicate HIV/AIDS by 2020 as follows:[9]

(1) 90% of all people living with HIV are aware of their HIV status

(2) 90% of all people diagnosed with HIV will receive ART

(3) 90% of people receiving ART's will have viral suppression.

Countries and organizations that adopted the 90-90-90 treatment targets utilized this approach for systematic evaluation of existing programs to estimate impact, monitor progress and reconfigure further implementation efforts.[10] Following its launch, many countries started reporting data to UNAIDS to measure country and region-specific progress towards achieving the treatment target.

Côte d'Ivoire & West Africa trends

Côte d'Ivoire boasted the 12th largest economy in Africa in 2019 but is also recovering from recent civil and ethnic unrest which disrupted the nation's health system.[11] The number of PLHIV in Côte d'Ivoire is estimated at 430,000, the second highest HIV burden in West Africa. This includes 290,000 individuals aged 15–49 years and 32,000 children aged <15 years. The HIV prevalence among those aged 15–49 years was 2.4% in 2019. Although progress is being made toward meeting the UNAIDS targets, only 73% of Ivorians know their status, 63% PLHIV are on ART, and only 50% are virally suppressed.[12] [13] There were geographical variations in prevalence, ranging from 1.7% in the Gôh-Djiboua region to 3.4% in Abidjan, the capital city.[14] Women ≥15 years were disproportionately affected as 260,000 (60.5%) of the 430,000 PLHIV were women. There was an estimated 12,000 individuals newly infected with HIV and 13,000 AIDS-related deaths in 2019.[12] In 2015, Côte d'Ivoire adopted the 90-90-90 approach to combat HIV.

In 2016, data showed that many west and central African countries had adopted the UNAIDS target approach but nonetheless, these regions were trailing behind on achieving these goals. Subsequently, UNAIDS and key regional and international partners urgently called for expedient

catch up to attain these goals by 2020 in an effort to end the AIDS epidemic by 2030 [Fast-Track targets]. Besides the 90-90-90 target by 2020, fast-track approach calls for the updated 95-95-95 strategy, which implores nations to shift trajectory by further strengthening commitments and accelerating efforts to end the epidemic by 2030.[15]

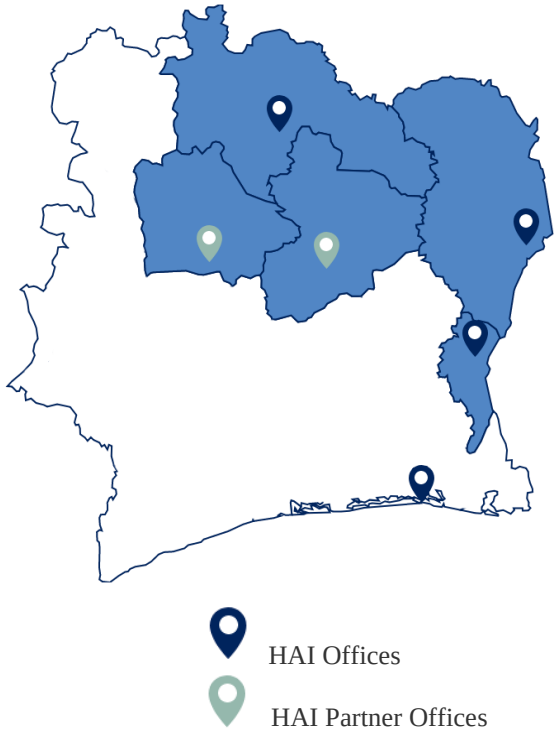
Despite the challenges in high prevalence resource-deficient settings, achieving the 90-90-90 goal in sub-Saharan Africa is not impossible as demonstrated by Botswana's success. A study conducted between 2013-2015 across Botswana showed that 83.3% of the study population knew their HIV status, 87.4% were on ART and 96.5% had viral suppression; estimates higher than some high-income countries (in Europe and north America).[16]

Health Alliance International

Several non-governmental organizations (NGO's) and international donors such as the US and its US President's Emergency Plan for AIDS Relief Program (PEPFAR) have been in the forefront in fighting HIV/AIDS, collaborating with local, regional and national governments. Health Alliance International (HAI), a US based non-profit NGO and affiliate of the University of Washington's Department of Global Health, started working in Côte d'Ivoire in 1992, partnering with the Ministry of Health - Ministère de la Santé et de l'Hygiène Publique (MSHP) and other NGO's towards building sustainable capacity in strengthening the overall health system. In 2015, HAI became an implementing partner of the US Centers for Disease Control and Prevention (CDC) under PEPFAR funding, to bolster HIV/AIDS programs in the northern regions of the country. HAI collaborates with the MSHP and supports the provision of HIV care and treatment services to more than 300 health facilities across 6 regions. HAI also collaborates

with other community-based organizations via advocacy, program implementation, research and evaluation.[17] [18] The overall objective of these partnerships is to strengthen national health delivery systems, while facilitating the achievement of UNAIDS 90-90-90 targets. Figure 2. shows a map of HAI- Côte d'Ivoire catchment areas.[11]

Figure 2. Map of HAI-Côte d'Ivoire catchment areas



Source: HAI
https://www.healthallianceinternational.org/ci/

HIV Viral Load

An essential prerequisite to achieving UNAIDS 3rd-90 treatment goal of viral suppression includes increasing access to VL testing. In 2013, the World Health Organization (WHO) recommended routine VL testing as the desired method of monitoring ART effectiveness and

confirming treatment failure.[19] An HIV VL test is a nucleic acid amplification test which measures the amount of HIV RNA present in the patient's blood. The results are described as the number of copies of RNA in a milliliter of blood. Upon HIV diagnosis, immediate ART initiation and adherence to an effective ART regimen may reduce the amount of virus in the blood resulting in VL suppression.

For our study, HIV viral suppression is defined as having a quantitative VL value of less than 1,000 copies of the HIV virus in a milliliter of blood (1,000 copies/ml). At very low levels, the amount of virus in the blood cannot be detected with testing and this is known as "undetectable viral load".[20] In the present study, an undetectable VL status was defined as having quantitative VL values of less than 20 copies (<20 copies/ml). Patients with VL values greater or equal to 1,000 copies (≥1,000 copies/ml) were considered to be virally unsuppressed. Viral suppression demonstrates the effectiveness of treatment and is key to reducing HIV-related illnesses and deaths. Evidence strongly shows that adherence to ART results in suppressed VL and undetectable VL levels, which substantially prevents the risk of sexual HIV transmission.[21] Treatment as prevention has also been widely adopted to prevent transmission of new infections, especially among high-risk populations.[20]

Diagnostics and Laboratory system

Côte d'Ivoire has a tiered laboratory system composed of 9 reference laboratories, 77 laboratories at regional and general hospitals, and over 100 laboratories among the district health centers. These laboratories provide critical HIV diagnostic and related testing services for the Ivorian population. Scale-up and promotion of HIV VL and early infant diagnosis (EID) testing

within this network is essential for routine patient monitoring and to moving Côte d'Ivoire closer to achieving UNAIDS targets. Scale up of VL/EID testing in Côte d'Ivoire has presented challenges including sustainability costs, capable infrastructure, stable laboratory commodities, prolonged result turn-around times, staff training and data management.[19] [22]

PEPFAR has invested significant resources to expand access to VL/EID testing and in 2016 funded a 5-year project solely dedicated to improving access to quality assured diagnostic testing. The UW International Training and Education Center for Health (UW-I-TECH) has implemented the LABQUASI project since 2016 and helped MSHP implement several foundational activities in every region to help improve the HIV diagnostic network and laboratory system. From 2016-2021, the number of labs capable of performing VL testing increased from 5 to 17, and through the national HIV rapid testing quality improvement initiative, quality assured HIV testing services are more available to more Ivorians than ever before. The open-source electronic lab information system OpenELIS (OE) was developed by UW-I-TECH and adapted for Côte d'Ivoire. MSHP's Direction de l'Informatique et de l'Information (DIIS) adopted OE as its preferred laboratory information system (LIS) in 2015, and UW-I-TECH was the lead partner for the DIIS in the scale-up and deployment of the system. Critical data captured in OE is now populating the VL and EID dashboards[23] [24] that the CDC, MSHP, PNLS, and partners such as HAI use for decision making.

Study Aim

The primary objective of this program evaluation study was to assess how effective HAI-led activities were, at supporting its clinical services sites in meeting the UNAIDS 3rd 90 target of

VL suppression in specific regions of Côte d'Ivoire from 2015-2018. The specific objective of the evaluation was to determine the predictors of VL suppression and undetectable VL during the study period.

This study is based on the results of an HAI 5-year CDC/PEPFAR funded project LINKS (Leadership, Impact, National engagement, Knowledge and Sustainability), which commenced in 2015. The primary purpose of project LINKS is to progressively shift care to local leadership and MSHP led management while supporting and advancing Côte d'Ivoire's public health system.

2. Methods

Study design

This evaluation was a retrospective study with analysis of secondary data (routinely collected demographic and laboratory data of HIV-infected patients receiving ART at selected health care facilities in Côte d'Ivoire). The study was approved by MSHP and University of Washington Institutional Review Boards (IRB). Any identifying patient information was excluded during data collection for this study.

Study setting

Data for this evaluation was collected from patients receiving ART in 354 health facilities located across 17 health districts in the Gbeke, Hambol, Bounkani-Gontougou and Poro-Tchologo-Bagoue health regions of Côte d'Ivoire. These health facilities are located in the central, north-central and northern regions of the country. The estimated HIV prevalence for

each region is 2.7% (Gbeke-Hambol), 3.0% (Bounkani-Gontougou), and 2.0% (Poro-Tchologo-Bagoue).[14] The majority of the health facilities in these regions are public health facilities, with a few private and faith-based sites. In Côte d'Ivoire, public health facilities are classified into three categories: primary level facilities (urban and rural health centers); secondary level facilities (general hospitals, regional hospitals and certain specialized hospitals) and tertiary level facilities (teaching hospitals, referral hospitals and specialized health institutes).

Data sources and data collection

Data utilized in this evaluation were extracted from OpenELIS, an open-source electronic LIS developed by UW-I-TECH as described earlier. OE collects laboratory data on all HIV VL and EID tests from blood specimens collected from patients receiving ART at HAI-supported sites. The OE database contains basic ART patient level demographic, clinical and immunological data. The database was constituted as part of routine VL monitoring of ART patients based on national treatment guidelines in Côte d'Ivoire. For this evaluation study, we extracted data for blood samples that were collected from patients from 2015-2018.

Blood specimens for VL testing were collected at HAI-supported health facilities and a VL laboratory requisition form was completed for each specimen collected. The form includes patient identifiers, demographic information, the type of specimen collected, and whether the requisition is for a routine test (where VL testing is used to routinely monitor patients on ART) or targeted test (where VL testing is used to confirm suspected treatment failure based on clinical and/or immunological criteria). Blood specimens are transported to laboratories located either at

CHU Bouake, CHR Korhogo, or CHR Abengourou as these are the three health facilities with a molecular laboratory with the capacity to conduct VL testing.

Data from the requisition form were entered into the LIS and the specimen was placed in a testing queue. These laboratories use the Roche COBAS Ampliprep/COBAS TaqMan viral load assays to determine VL. The VL results were then validated and recorded as absolute values for detectable levels, or as "<LL" (less than lowest limit) for undetectable levels. Data from the LIS at the three VL testing laboratories were routinely synced with a central server via dedicated internet connections. After testing, VL results were entered automatically into the LIS via linking the patient identification numbers and a report is printed for delivery back to the referring health facility and the patient is notified of his/her results.

Variables of interest in the dataset

Outcome variables

There were two outcome variables in this study. The first was the VL suppression rate. Only the last/most recent VL result obtained from serial testing was considered for this study. Patients with a VL result of <1000 copies/ml in the parent sample were considered to be virally suppressed while patients with a VL result of ≥1000 copies/ml were considered to have unsuppressed VL. The second outcome variable was undetectable VL, i.e., when VL in a patient's body is so low that standard blood tests cannot detect it. This was estimated from the subsample of patients with VL suppression in the parent sample. Patients with their VL result with <20 copies/ml were considered to have undetectable VL while those with absolute values between 20-999 copies/ml were considered as detectable, but virally suppressed.

Explanatory variables

The explanatory variables extracted from the database included age which was classified as children (0–14 years), adults (15 years and above) - a classification widely used in PEPFAR funded projects; gender (male/female), patient's HIV subtype (HIV-1 and HIV-2), the period of collection of the blood specimen (2015-2016/2017-2018), the region where patients were receiving ART treatment, and the location of the molecular laboratory (CHU Bouake/ CHR Korhogo/CHR Abengourou).

Data analysis

Data extracted were cleaned, and imported into STATA 15.0 (Stata Corp, College Station, Texas, USA) for analysis. Continuous variables were summarized by median and inter-quartile range (IQR) while categorical variables were summarized using frequencies and percentages. Pearson Chi-squared ($\chi 2$) test for categorical variables was used to assess any bivariate association. Logistic regression analysis was used to determine the association between the outcome variables and the predictor variables. All variables that were significant with a $p<0.2$ in bivariate analysis were considered candidate variables for multivariate analysis. Prior to the regression analysis, multicollinearity was examined among the predictor variables. The variable, "location of molecular laboratory" was dropped from the multivariate models due to multicollinearity (i.e. a situation when independent variables in a regression model are correlated). Model 1 examined the independent predictors of VL suppression. All patients in the dataset with VL suppression were coded as "1" while patients with unsuppressed VL were coded as "0". The model was adjusted for the following variables: age, gender, patient's HIV subtype,

period of blood specimen collection and region where the patient was receiving ART treatment. Model 2 examined the predictors of undetectable VL among the subsample of patients with VL suppression. The model was adjusted for the following: age, gender, period of blood specimen collection and region where the patient receives ART treatment. The variable "patient's HIV subtype" was not included in Model 2 because it was not significant in bivariate analysis. Adjusted odds ratio (AOR) with 95% confidence levels was used to quantify the strength of the association between predictors and outcome variables. All statistical tests were two-tailed and were considered statistically significant at P-value<0.05.

3. Results

Patients demographic and relevant characteristics

A total of 50,131 unique patient records were analyzed for this study (Table 1). The median age of patients was 40 years (IQR:33-49). The majority (73.3%) of the patients were female, and most were receiving ART in the Gbeke region (40.4%) followed by the Poro-Tchologo-Bagoue region (26.9%). Nearly all the patients (98.9%) had HIV-subtype-1 virus (HIV-1) and 48.5% of the VL test were conducted at the molecular laboratory located at CHU Bouake.

Table 1. Patients demographic and other relevant characteristics

Characteristics	Number	Proportion
Total sample	**50,131**	**100%**
Age group (years)		
<15	2,958	5.9%
≥15	47,173	94.1%
Gender		
Male	13,418	26.7%
Female	36,713	73.3%
Patient's HIV subtype		
HIV-1	49,573	98.9%
HIV-2	558	1.1%

Period of blood specimen collection and testing		
2015-2016	7,500	14.9%
2017-2018	42,631	85.1%
Region where patient receives ART treatment		
Bounkani-Gontougou	12,341	24.6%
Gbeke	20,236	40.4%
Hambol	4,080	8.1%
Poro-Tchologo-Bagoue	13,474	26.9%
Location of molecular laboratory[1]		
CHR Abengourou	12,341	24.6%
CHU Bouake	24,316	48.5%
CHR Korhogo	13,474	26.9%

[1]CHR=Centre Hospitalier Regional, CHU=Centre Hospitalier Universitaire

Bivariate association between relevant characteristics and VL suppression

Of the 50,131 patient records analyzed for this study, 76.4% (38,280) had VL suppression (Table 2). In a bivariate analysis, adults were significantly more likely to have had VL suppression compared to children (78.1% vs 48.5%, $p<0.001$). Compared to males, females were significantly more likely to have had VL suppression (77.4% vs 73.6%, $p<0.001$). Patients with HIV subtype-2 were more likely to have had VL suppression compared to those with HIV subtype-1 (81.7% vs 76.3%, $p<0.003$). Patients whose blood specimens were collected and tested between 2017-2018 were significantly more likely to have had VL suppression than those whose specimens were collected between 2015-2016 (76.6% vs 75.1%, $p<0.001$). Additionally, patients receiving ART treatment in the Gbeke health region were more likely to have had VL suppression compared to those in the other three regions. Patients whose VL specimens were processed and tested at CHU Bouake were more likely to have had VL suppression compared to those whose samples were tested at CHR Abengourou and CHR Korhogo.

Table 2. Patients demographic and other relevant characteristics by VL suppression

Characteristics	VL suppression		P-value[1]
	Yes (<1000 copies/ml)	No (≥1000copies/ml)	
Total sample	**38,280(76.4%)**	**11,851(23.6%)**	
Age group			<0.001
<15	1,434(48.5%)	1,524(51.5%)	
≥15	36,846(78.1%)	10,327(21.9%)	
Gender			<0.001
Male	9,870(73.6%)	3,548(26.4%)	
Female	28,410(77.4%)	8,303(22.6%)	
Patient's HIV subtype			0.003
HIV-1	37,824(76.3%)	11,749(23.7%)	
HIV-2	456(81.7%)	102(18.3%)	
Period of blood specimen collection and testing			0.006
2015-2016	5,633(75.1%)	1,867(24.9%)	
2017-2018	32,647(76.6%)	9,984(23.4%)	
Region where patient receives ART treatment			<0.001
Bounkani-gontougou	9,309(75.4%)	3,032(24.6%)	
Gbeke	16,127(79.7%)	4,109(20.3%)	
Hambol	2,978(73.0%)	1,102(27.0%)	
Poro-Tchologo-Bagoue	9,866(73.2%)	3,608(26.8%)	
Location of molecular laboratory[2]			p<0.001
CHR Abengourou	9,309(75.4%)	3,032(24.6%)	
CHU Bouake	19,105(78.6%)	5,211(21.4%)	
CHR Korhogo	9,866(73.2%)	3,608(26.8%)	

[1]P-value from Pearson's Chi-squared test
[2]CHR=Centre Hospitalier Regional, CHU=Centre Hospitalier Universitaire

Predictors of VL suppression

Adult patients were significantly more likely to have viral suppression than children (AOR= 3.77:95%CI, 3.49-4.07) (Table 3). Compared to males, females were significantly more likely to have VL suppression (AOR=1.01:95%CI, 1.05-1.15). Patients receiving ART treatment from the Gbeke health region were significantly more likely to have viral suppression compared to those in the Bounkani-Gontougou region (AOR= 1.33:95%CI, 1.26-1.40). Patients receiving treatment in the Hambol health region (AOR=0.91:95%CI, 0.83-0.98) and in Poro-Tchologo-

Bagoue regions (AOR=0.90:95%CI, 0.85-0.95) were significantly less likely to have had viral suppression compared to those in the Bounkani-Gontougou region. Patients with HIV subtype-2 virus were significantly more likely to be virally suppressed compared to those with HIV subtype-1 (AOR=1.30:95%CI, 1.04-1.62).

Table 3. Multivariate regression analysis of predictors of VL suppression

Variable	Multivariate Adjusted model AOR (95%CI)	P-value[1]
Age group (years)		
<15	1.0	
≥15	3.77(3.49-4.07)	p<0.001
Gender		
Male	1.0	
Female	1.10(1.05-1.15)	p<0.001
Patient's HIV subtype		
HIV-1	1.0	
HIV-2	1.30(1.04-1.62)	0.017
Period of blood specimen collection and testing		
2015-2016	1.0	
2017-2018	1.13(1.07-1.20)	p<0.001
Region where patient receives ART treatment		
Bounkani-Gontougou	1.0	
Gbeke	1.33(1.26-1.40)	p<0.001
Hambol	0.91(0.83-0.98)	0.018
Poro-Tchologo-Bagoue	0.90(0.85-0.95)	p<0.001

[1] If STATA output for p-value was 0.000, it was considered as p<0.001
AOR=Adjusted Odds Ratio; CI=Confidence Interval

Bivariate associations between relevant characteristics and undetectable VL

Among the 38,280 patients with VL suppression (i.e., <1000 copies/ml) in the parent sample, 69.1% (26,445) had an undetectable VL level (i.e. <20 copies/ml) (Table 4). There were more adults in the subsample than children; and adults (aged 15 years and above) were significantly more likely to have had an undetectable VL compared to children (69.6% vs 55.2%, p<0.001).

74.2% of patients in the subsample were females; and females were significantly more likely to have an undetectable VL compared to men (70.7% vs 64.4%, p<0.001). 85.3% of the blood specimens for VL testing in the subsample were collected and tested between 2017-2018. Patients whose blood specimens were collected and tested between 2015-2016 were significantly more likely (78.2% vs 67.5%, p<0.001) to have had undetectable VL compared to those whose samples were collected between 2017-2018. An estimated 42.1% of patients with VL suppression were receiving ART in the Gbeke region. Patients with undetectable VL were more likely to be receiving treatment in the Gbeke region compared to the other regions (p<0.001). There was no significant difference in undetectable VL among patients with HIV subtype-1 and HIV subtype-2. VL tests that were conducted at CHU Bouake were more likely to have had undetectable VL load compared to tests conducted in the other three regions.

Table 4. Bivariate associations between relevant characteristics by undetectable VL

Characteristics	Subsample N(%)	Viral Load suppression (<1000copies/ml)		P-value[1]
		Undetectable (<20 copies/ml)	Detectable, but suppressed (20-999 copies/ml)	
Subsample	**38,280(100%)**	**26,445(69.1%)**	**11,835(30.9%)**	
Age group (years)				p<0.001
<15	1,434(3.8%)	791(55.2%)	643(44.8%)	
≥15	36,846(96.2%)	25,654(69.6%)	11,192(30.4%)	
Gender				p<0.001
Male	9,870(25.8%)	6,353(64.4%)	3,517(35.6%)	
Female	28,410(74.2%)	20,092(70.7%)	8,318(29.3%)	
Patient's HIV subtype				0.261
HIV-1	37,824(98.8%)	26,141(69.1%)	11,683(30.9%)	
HIV-2	456(1.2%)	304(66.7%)	152(33.3%)	
Period of blood specimen collection and testing				p<0.001
2015-2016	5,633(14.7%)	4,407(78.2%)	1,226(21.8%)	
2017-2018	32,647(85.3%)	22,038(67.5%)	10,609(32.5%)	

Region where patient receives ART treatment				p<0.001
Bounkani-Gontougou	9,309(24.3%)	6,541(70.3%)	2,768(29.7%)	
Gbeke	16,127(42.1%)	12,179(75.5%)	3,948(24.5%)	
Hambol	2,978(7.8%)	2,147(72.1%)	831(27.9%)	
Poro-Tcholo-Bagoue	9,866(25.8%)	5,578(56.5%)	4,288(43.4%)	
Location of molecular laboratory[2]				p<0.001
CHR Abengourou	9,309(24.3%)	6,541(70.3%)	2,768(29.7%)	
CHU Bouake	19,105(49.9%)	14,326(75.0%)	4,779(25.0%)	
CHR Korhogo	9,866(25.8%)	5,578(56.5%)	4,288(43.5%)	

[1]P-value from Pearson Chi-squared test, If STATA output for p-value was 0.000, it was considered as p<0.001
[2]CHR=Centre Hospitalier Regional, CHU=Centre Hospitalier Universitaire

Predictors of undetectable VL among patients with VL suppression

Adults patients (≥15 years) were almost twice as likely (AOR=1.81:95%CI, 1.63-2.02) to have had an undetectable VL compared to children (Table 5). Female patients were more likely (AOR=1.30:95%CI, 1.24-1.37) to have had an undetectable VL compared to males. Patients whose blood specimens were collected, and tests performed between 2017-2018 were significantly less likely (AOR=0.62:95%CI, 0.58-0.67) to have had an undetectable VL compared to those whose blood specimens were collected and tests performed between 2015-2016. Patients receiving ART in health facilities located in the Gbeke health region were significantly more likely (AOR=1.29:95%CI, 1.22-1.36) to have had an undetectable VL compared to those receiving treatment in the Bounkani-Gontougou region.

Table 5. Multivariate analysis of undetectable VL (<200 copies/ml) among patients with VL suppression

Characteristics	Multivariate Adjusted model[1] Odds Ratio (95%CI)	P-value[2]
Age group (years)		
<15	1.0	
≥15	1.81(1.63-2.02)	p<0.001
Gender		

Male	1.0	
Female	1.30(1.24-1.37)	p<0.001
Year of blood specimen collection and testing		
2015-2016	1.0	
2017-2018	0.63(0.58-0.67)	p<0.001
Region where patient receives ART treatment		
Bounkani-gontougou	1.0	
Gbeke	1.29(1.22-1.37)	p<0.001
Hambol	1.06(0.97-1.16)	0.200
Poro-Tchologo-Bagoue	0.56(0.53-0.59)	p<0.001

[1]Only for variables significant in bivariate associations
[2]If STATA output for p-value was 0.000, it was considered as p<0.001

4. Discussion

VL suppression

HIV VL suppression is the most important indicator of successful ART. The purpose of this study was to estimate VL suppression among patients receiving ART at HAI-supported health facilities in Côte d'Ivoire and to determine the proportion of patients with VL suppression who had undetectable VL. The overall viral suppression rate in the study sample was 76.4%, with respectively regional rates of 75.4% in Bounkani-Gontougou, 79.7% in Gbeke, 73.0% in Hambol and 73.2% in Poro-Tchologo-Bagoue. The overall viral suppression rate in the study was much higher than the 2019 estimated national rate of 50% among those on treatment [12] but lower than the then UNAIDS recommended 90%. The results of the present study therefore provide a glimpse of HAI's contribution towards national efforts aimed at achieving the 90–90–90 UNAIDS target. Previous studies have reported a VL suppression rate of 80.1% in Cameroon [25] and 90.6% in Kenya.[26] As noted above, there was a slight disparity in VL suppression across HAI-supported regions. The disparity could be attributed to differences in HIV case management, adherence counselling and support across the regions.

In the present study, the majority (94.1%) of the participants were adults (≥15 years) and they had a higher VL suppression than children (78.1% vs 48.5%). These results are consistent with those of previous studies in Zimbabwe [27] and Swaziland [28] which found that adults are more likely to be virally suppressed than children. Studies have also demonstrated that VL suppression in children across many countries in sub-Saharan Africa is low [29] [30] and adults are more likely to have higher rates of VL suppression because they are more adherent to treatment than children. Data used in this study were collected at a time when achieving viral suppression in children was challenging due to a number of reasons including the lack of optimal antiretrovirals with suitable pediatric formulations, pharmacokinetic challenges, long duration of therapy, adherence problems due to poor palatability of drugs, dependence on caregivers and pretreatment HIV drug resistance due to prior exposure to drugs as part of prevention of mother-to-child transmission (PMTCT) interventions.[31] [32] [33] [34] However, with the recent introduction of optimal pediatric formulations across many countries (e.g., dolutegravir-based regimens) for children, adherence to ART and VL suppression among children is expected to improve.[35] [36]

In the study, the majority of the patients were female (73.3%), and they had a higher VL suppression than male patients (77.4% vs 73.6%). These findings are similar to those of a population-based study conducted across Eswatini, Lesotho, Malawi, Zambia, and Zimbabwe which found that men were less likely, compared to women, to have VL suppression.[37] There are limited and inconclusive studies on association of gender and VL suppression. One study in Zambia found that women were less likely to be virally suppressed compared to men but the

difference was not statistically significant.[38] Nonetheless, targeting VL suppression among women may also have a vital added benefit of significantly reducing the risk of mother-to-child transmissions, thereby averting new infections.

Also, in our study, the majority of the patients (98.9%) had HIV subtype-1 (HIV-1) but patients with HIV subtype-2 (HIV-2) had a higher VL suppression rate (81.7% vs 76.3%) compared to those with HIV-1. HIV-1 is the most common subtype of HIV globally, with HIV-2 being more commonly found in west Africa.[39] Our finding contrasts that of a study conducted in Senegal which reported that VL suppression rate was lower among patients with HIV-2 than those with HIV-1.[40] Another study in rural Guinea-Bissau showed that HIV-2 patients with low VL levels maintained these stable VL levels and overall survival over prolonged periods.[41] Differences in VL between the HIV subtypes may be explained by the genetic components of each virus but further studies may be indicated to investigate pathogenicity and relationships between VL in HIV-1 and HIV-2.

Surprisingly, there was a statistically significant association between the period of blood specimen collection and VL suppression. Patients whose blood specimens were collected and tested between 2017-2018 were significantly more likely to be virally suppressed compared to those whose samples were collected and tested earlier between 2015-2016 (76.6% vs. 75.1% respectively). This finding may be explained by the fact that Côte d'Ivoire started implementing the WHO recommended 'Test and Start' [42] strategy in 2017. This strategy was characterized by patient centered care with close monitoring of patients on ART, regular adherence counselling and retention in care.

Undetectable VL

In our study, the overall undetectable VL was at 69.1% among the subsample of those who were virally suppressed leaving 30.9% with detectable but suppressed VL. This finding is encouraging as it shows that more than half of the patients in the sample with suppressed VL had undetectable VL, a cornerstone for the Undetectable=Untransmissible, U=U concept. This concept is based on evidence which demonstrated that an ART patient who has an undetectable VL does not transmit HIV to their sexual partners.[43] [44] The U=U messaging has the potential to reduce stigma towards people living with HIV, increase demand for HIV testing, ART initiation and improve adherence. The concept can also strengthen advocacy efforts for universal access to effective treatment and care. Moreover, messaging around U=U should be well-integrated into HIV prevention, care and treatment programs.[45] It is therefore imperative for HAI and other stakeholders in the HIV care arena in Côte d'Ivoire, to continue further accelerated efforts to increase early ART initiation and strong campaign for treatment adherence among PLHIV.

Adults ≥15 years of age who made up the majority of the VL suppressed subsample (96.2%) had a higher prevalence of undetectable VL (69.6% vs 55.2%). In a study conducted in southern Brazil, the prevalence of undetectable VL increased with age, although there was a weak statistical significance.[46] In our study, older participants were more likely to be virally suppressed which could also denote that age may be associated with undetectable VL. Though our study suggested age as a predictor of undetectable VL, more studies are needed to assess this relationship.

Also, virally suppressed female participants had a higher undetectable VL prevalence than their male counterparts (70.7% vs 64.4%). In the southern Brazil study, there were no gender effects on undetectable VL.[46] Another study conducted in Tanzania showed that females had a higher levels of undetectable VL than males who also had a higher likelihood of increased poor clinical outcomes and higher mortality.[47] This may suggest that increased focus needs to be placed on ensuring that men diagnosed with HIV are promptly initiated on ART and supported to be adherent to their treatment.

Undetected VL in the 4 health districts among those virally suppressed was higher in Gbeke (75.5%) than in Hambol (72.1%), Bounkani-Gontougou (70.3%) and Poro-Tchologo-Bagoue (56.5%). This disparity in undetectable VL across the regions goes in line with the differences also noted in VL suppression across HAI-supported regions which may indicate some areas needing more concentrated efforts in HIV management interventions.

A key strength of this VL suppression study was that the sample was relatively large and the database included patients receiving treatment across various types of health facilities (i.e. rural, semi-urban and urban areas). However, the results should be interpreted with caution given some limitations. A major limitation was that the data used for the study came from routine program activities that were not developed with such an assessment in mind. Another limitation was that the database had many missing values, although this was controlled for during data analysis. Third, the database did not contain variables that the research team would have liked to examine in the study. For example, there was no data available on key variables such as ART

regimen, chronic comorbidities, CD4 counts at ART initiation, duration on ART etc., which would have enabled the team to expand the analysis. Furthermore, only one VL value was used for this study (the most recent VL), which does not reflect an individual patient's VL trends for predicting clinical outcome. Despite these limitations, this study has generated relevant information on VL suppression across HAI-supported health facilities in Côte d'Ivoire. This information is vital and will enable HAI and partners to develop and implement context-specific interventions that will optimize VL suppression and undetectability among patients. The study results can be used as a tool to inform HAI and other stakeholders in Côte d'Ivoire on assessing areas of need and adeptly target interventions towards fighting HIV and hasten efforts to meet the updated 95-95-95 treatment targets by 2030. It may also inform HAI on regions that require prioritization of program efforts geared towards ART scale up and VL monitoring. Further implementation research is required to address the challenges associated with optimal VL suppression in HAI-supported health facilities.

5. Conclusions

The overall VL suppression rate found in this study was below the expected initial UNAIDS-90 targets. Although a substantial proportion of patients with VL suppression had undetectable VL levels, such levels were below the UNAIDS targets for 2020. Viral suppression also varied by certain demographic and relevant characteristics such as age and gender. The findings suggest that more efforts are needed to help patients on ART achieve viral suppression and improve their quality of life. Identifying the causes of poor adherence and systematically addressing them has the potential to improving VL suppression. It is important for strategies to be implemented that are aimed at sustaining adherence counselling of patients, close monitoring and follow-up of

patients and increased access to VL testing. When carefully designed and implemented, these strategies would significantly lead towards optimizing VL suppression rates at country level and contribute towards attaining the UNAIDS treatment goals.

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References

[1] M. K. Grabowski *et al.*, "Migration, hotspots, and dispersal of HIV infection in Rakai, Uganda," *Nat. Commun.*, vol. 11, no. 1, Dec. 2020, doi: 10.1038/s41467-020-14636-y.

[2] L. Dwyer-Lindgren *et al.*, "Mapping HIV prevalence in sub-Saharan Africa between 2000 and 2017," *Nature*, vol. 570, no. 7760, pp. 189–193, Jun. 2019, doi: 10.1038/s41586-019-1200-9.

[3] UNAIDS, "Global HIV statistics," *2020 Fact Sheet*, 2020. https://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf (accessed May 07, 2020).

[4] F. Maldarelli, "Biology of Human Immunodeficiency Viruses," in *Goldman-Cecil Medicine*, 26th ed., Elsevier - Health Science, 2020, pp. 2248-2252.e3.

[5] R. Baggaley *et al.*, "Beyond the 90-90-90: refocusing HIV prevention as part of the global HIV response," *J. Int. AIDS Soc.*, vol. 19, no. 1, p. 21348, Jan. 2016, doi: 10.7448/IAS.19.1.21348.

[6] UNAIDS, "AIDS and the sustainable development goals," *Sustainable Development Goals*, 2020. https://www.unaids.org/sites/default/files/media_asset/SDGsandHIV_en.pdf (accessed Apr. 20, 2020).

[7] M. Griesbeck, E. Scully, and M. Altfeld, "Sex and gender differences in HIV-1 infection," *Clin. Sci.*, vol. 130, no. 16, pp. 1435–1451, Aug. 2016, doi: 10.1042/CS20160112.

[8] HIV.gov - US Dept. of Health and Human Services, "HIV care continuum," *What Is the HIV Care continuum*, 2020. https://www.hiv.gov/federal-response/policies-issues/hiv-aids-care-continuum (accessed Apr. 20, 2020).

[9] UNAIDS, "90-90-90 An ambitious treatment target to help end the AIDS epidemic." UNAIDS Information Production Unit, 2014, Accessed: Nov. 30, 2019. [Online]. Available: https://www.unaids.org/en/resources/documents/2017/90-90-90#:~:text=Documents-,90%E2%80%9390%E2%80%9390%20%2D%20An%20ambitious%20treatment%20target%20to,help%20end%20the%20AIDS%20epidemic&text=By%202020%2C%2090%25%20of%20all,will%20receive%20sustained%20antiretroviral%20therapy.

[10] C. T. Rentsch *et al.*, "Non-disclosure of HIV testing history in population-based surveys: implications for estimating a UNAIDS 90-90-90 target," *Glob. Health Action*, vol. 11, no. 1, p. 1553470, Jan. 2018, doi: 10.1080/16549716.2018.1553470.

[11] HAI, "Where we work: Côte d'Ivoire," *Health Alliance International*, 2019. https://www.healthallianceinternational.org/ci/ (accessed Nov. 30, 2019).

[12] UNAIDS, "Country: Côte d'Ivoire," *Where we work: Western and Central Africa*, 2019. https://www.unaids.org/en/regionscountries/countries/ctedivoire (accessed Nov. 30, 2019).

[13] UNAIDS, "UNAIDS DATA 2019." UNAIDS, 2019, Accessed: Mar. 07, 2021. [Online]. Available: https://www.unaids.org/sites/default/files/media_asset/2019-UNAIDS-data_en.pdf.

[14] PHIA, "Cote d'Ivoire Population Based HIV Impact Assessment (CIPHIA)." ICAP at Columbia University, 2018, Accessed: Apr. 20, 2020. [Online]. Available: https://phia.icap.columbia.edu/wp-content/uploads/2018/08/CIPHIA_Cote-DIvoire-SS_FINAL.pdf.

[15] UNAIDS, "90-90-90: The Western and Central Africa catch-up plan. Putting HIV treatment on the fast-track by 2018." 2016, Accessed: Mar. 20, 2020. [Online]. Available: https://www.unaids.org/sites/default/files/media_asset/WCA-catch-up-plan_en.pdf.
[16] T. Gaolathe *et al.*, "Botswana's progress toward achieving the 2020 UNAIDS 90-90-90 antiretroviral therapy and virological suppression goals: a population-based survey," *Lancet HIV*, vol. 3, no. 5, pp. e221–e230, May 2016, doi: 10.1016/S2352-3018(16)00037-0.
[17] HAI, "Our History," *Health Alliance International*, 2019. https://www.healthallianceinternational.org/our-history/ (accessed Dec. 01, 2019).
[18] HAI, "Intergrating HIV service delivery," *Health Alliance International*, 2019. https://www.healthallianceinternational.org/project/hiv-integration/ (accessed Dec. 01, 2019).
[19] WHO, "HIV molecular diagnostic toolkit to improve access to viral load testing and infant diagnosis." World Health Organization, Switzerland, 2019, Accessed: Jan. 20, 2020. [Online]. Available: https://apps.who.int/iris/bitstream/handle/10665/325961/9789241516211-eng.pdf?ua=1.
[20] CDC, "HIV treatment as prevention," *HIV risk and prevention*, 2020. https://www.cdc.gov/hiv/risk/art/index.html (accessed Dec. 07, 2019).
[21] S. J. Reynolds *et al.*, "HIV-1 transmission among HIV-1 discordant couples before and after the introduction of antiretroviral therapy:," *AIDS*, vol. 25, no. 4, pp. 473–477, Feb. 2011, doi: 10.1097/QAD.0b013e3283437c2b.
[22] CDC, "Scale-up of HIV viral load monitoring – seven sub-saharan African countries," CDC, Atlanta, GA. USA, Morbidity and Mortality Weekly Reports (MMWR), 2015. Accessed: Jan. 20, 2020. [Online]. Available: https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6446a3.htm#Tab2.
[23] UW-ITECH, "Viral Load (CI)," MSHP, Cote d'Ivoire, Dashboard, 2018. Accessed: Mar. 06, 2021. [Online]. Available: https://chargevirale.openelisci.org/vl_dashboard/.
[24] UW-ITECH, "EID," MSHP, Cote d'Ivoire, Dashboard, 2019. Accessed: Mar. 06, 2021. [Online]. Available: https://chargevirale.openelisci.org/eid_dashboard/fr/.
[25] PHIA, "Cameroon Population Based HIV Impact Assessment (CAMPHIA)." ICAP at Columbia University, 2018, Accessed: Jan. 06, 2021. [Online]. Available: https://phia.icap.columbia.edu/cameroon-summary-sheet/.
[26] PHIA, "Kenya Population Based HIV Impact Assessment (KENPHIA)." ICAP at Columbia University, 2018, Accessed: Jan. 06, 2021. [Online]. Available: https://phia.icap.columbia.edu/kenya-preliminary-report/.
[27] E. Sovershaeva *et al.*, "Patterns of detectable viraemia among children and adults with HIV infection taking antiretroviral therapy in Zimbabwe," *Int. J. Infect. Dis.*, vol. 78, pp. 65–71, Jan. 2019, doi: 10.1016/j.ijid.2018.10.019.
[28] K. Jobanputra *et al.*, "Factors Associated with Virological Failure and Suppression after Enhanced Adherence Counselling, in Children, Adolescents and Adults on Antiretroviral Therapy for HIV in Swaziland," *PLOS ONE*, vol. 10, no. 2, p. e0116144, Feb. 2015, doi: 10.1371/journal.pone.0116144.
[29] M. B. Shiferaw *et al.*, "Viral suppression rate among children tested for HIV viral load at the Amhara Public Health Institute, Bahir Dar, Ethiopia," *BMC Infect. Dis.*, vol. 19, no. 1, p. 419, Dec. 2019, doi: 10.1186/s12879-019-4058-4.

[30] R. S. Boerma *et al.*, "Suboptimal Viral Suppression Rates Among HIV-Infected Children in Low- and Middle-Income Countries: A Meta-analysis," *Clin. Infect. Dis.*, vol. 63, no. 12, pp. 1645–1654, Dec. 2016, doi: 10.1093/cid/ciw645.
[31] Peter L Havens, Diana M Gibb, "Increasing Antiretroviral Drug Access for Children With HIV Infection," *PEDIATRICS*, vol. 119, no. 4, pp. 838–845, Apr. 2007, doi: 10.1542/peds.2007-0273.
[32] S. Lockman *et al.*, "Response to Antiretroviral Therapy after a Single, Peripartum Dose of Nevirapine," *N. Engl. J. Med.*, vol. 356, no. 2, pp. 135–147, Jan. 2007, doi: 10.1056/NEJMoa062876.
[33] K. C. Sigaloff, J. C. Calis, S. P. Geelen, M. van Vugt, and T. F. R. de Wit, "HIV-1-resistance-associated mutations after failure of first-line antiretroviral treatment among children in resource-poor regions: a systematic review," *Lancet Infect. Dis.*, vol. 11, no. 10, pp. 769–779, Oct. 2011, doi: 10.1016/S1473-3099(11)70141-4.
[34] M. Penazzato, A. J. Prendergast, L. M. Muhe, D. Tindyebwa, and E. Abrams, "Optimisation of antiretroviral therapy in HIV-infected children under 3 years of age," *Cochrane Database Syst. Rev.*, May 2014, doi: 10.1002/14651858.CD004772.pub4.
[35] E. Bruzzese *et al.*, "Dolutegravir-based anti-retroviral therapy is effective and safe in HIV–infected paediatric patients," *Ital. J. Pediatr.*, vol. 44, no. 1, p. 37, Dec. 2018, doi: 10.1186/s13052-018-0469-x.
[36] N. I. Paul and R. O. Ugwu, "Dolutegravir (DTG) Based Fixed Dose Combination (FDC) of Tenofovir/Lamivudine/Dolutegravir (TLD) and Viral Load Suppression in Children in Port Harcourt, Nigeria," *J. Sci. Res. Rep.*, pp. 52–59, Mar. 2020, doi: 10.9734/jsrr/2020/v26i230224.
[37] A. D. Haas *et al.*, "Prevalence of nonsuppressed viral load and associated factors among HIV-positive adults receiving antiretroviral therapy in Eswatini, Lesotho, Malawi, Zambia and Zimbabwe (2015 to 2017): results from population-based nationally representative surveys," *J. Int. AIDS Soc.*, vol. 23, no. 11, Nov. 2020, doi: 10.1002/jia2.25631.
[38] L. Andronescu, P. M. Zulu, S. S. Jackson, L. Hachaambwa, C. W. Claassen, and K. A. Stafford, "The association between gender and HIV viral suppression on third-line therapy in Zambia: a retrospective cohort study," *Int. J. STD AIDS*, vol. 30, no. 5, pp. 453–459, Apr. 2019, doi: 10.1177/0956462418817645.
[39] S. Requena *et al.*, "Treatment outcome in dually HIV-1 and HIV-2 coinfected patients living in Spain," *AIDS*, vol. 33, no. 14, pp. 2167–2172, Nov. 2019, doi: 10.1097/QAD.0000000000002338.
[40] S. J. Popper *et al.*, "Lower Human Immunodeficiency Virus (HIV) Type 2 Viral Load Reflects the Difference in Pathogenicity of HIV-1 and HIV-2," *J. Infect. Dis.*, vol. 180, no. 4, pp. 1116–1121, Oct. 1999, doi: 10.1086/315010.
[41] M. van der Loeff *et al.*, "Undetectable plasma viral load predicts normal survival in HIV-2-infected people in a West African village," *Retrovirology*, vol. 7, no. 1, p. 46, 2010, doi: 10.1186/1742-4690-7-46.
[42] WHO, "Prevent HIV, Test and Treat All (Progress Report 2016)." World Health Organization, Switzerland, 2016, Accessed: Mar. 20, 2020. [Online]. Available: https://apps.who.int/iris/bitstream/handle/10665/251713/WHO-HIV-2016.24-eng.pdf?sequence.
[43] WHO, "Viral suppression for HIV treatment success and prevention of sexual transmission of HIV." World Health Organization, Jul. 2018, Accessed: Jan. 06, 2021. [Online].

Available: https://www.who.int/hiv/mediacentre/news/viral-supression-hiv-transmission/en/.
[44] National Institute of Health (NIH), “The science is clear: with HIV, undetectable equals untransmittable.” NIH, Jn 2019, Accessed: Jan. 04, 2021. [Online]. Available: https://www.nih.gov/news-events/news-releases/science-clear-hiv-undetectable-equals-untransmittable.
[45] Linkages, “Undetectable=Untransmittable.” 2019, Accessed: Mar. 17, 2021. [Online]. Available: https://www.fhi360.org/sites/default/files/media/documents/linkages-u-equals-u-english.PDF.
[46] M. P. T. Silveira, M. de L. Draschler, J. C. de C. Leite, C. A. T. Pinheiro, and V. L. da Silveira, “Predictors of undetectable plasma viral load in HIV-positive adults receiving antiretroviral therapy in Southern Brazil,” *Braz. J. Infect. Dis.*, vol. 6, no. 4, Aug. 2002, doi: 10.1590/S1413-86702002000400003.
[47] F. Mosha, “Gender Differences in Human Immunodeficiency Virus (HIV) Disease Progression and Treatment Outcomes,” in *AIDS Updates - Recent Advances and New Perspectives [Working Title]*, IntechOpen, 2020.