

# Factors associated with HIV viral load suppression on antiretroviral therapy in Vietnam

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## Abstract

**Background:** Limited data are available on HIV viral suppression rates among men and women on antiretroviral therapy (ART) and factors associated with HIV RNA viral load (VL) suppression in Vietnam.

**Methods:** We conducted a cross-sectional survey of 1255 adult patients on ART for at least 1 year across four provinces in Vietnam. Data collection included a standardised questionnaire, routine laboratory testing, and an HIV VL assay. Bivariate and logistic multivariate analyses were conducted to assess viral suppression rates and factors associated with unsuppressed HIV VL.

**Results:** The median age was 34.5 years and the median time on ART was 46 months. Gender was 66% male ( $n=828$ ) and 34% female ( $n=427$ ). HIV viral suppression below 1000 copies/mL was 93%. Viral suppression among woman was not significantly different than among men (93.7% vs 92.9%;  $P=0.59$ ). On multivariate analysis, unsuppressed HIV VL was independently associated with lower CD4 cell count, social isolation, high stigma, not receiving a single-tablet daily regimen, multiple late appointments in past year, and immunological failure.

**Conclusion:** On-treatment viral load suppression rates in Vietnam are high and already exceed the UNAIDS 90% target for viral suppression on ART. Gender does not impact viral suppression rates of patients on ART in Vietnam. Access to routine viral load testing should be improved, adherence monitoring and counselling streamlined, and ART regimens simplified to maintain viral suppression rates, as more people start ART. Psychological and social factors are also associated with unsuppressed HIV VL, necessitating treatment support interventions to address social isolation and stigma among people living with HIV in Vietnam.

**Keywords:** HIV, antiretroviral therapy, gender, single-tablet regimen, adherence, HIV viral load suppression, Vietnam

## Introduction

The goal of early antiretroviral therapy (ART) for patients with HIV infection is to completely suppress viral replication, thus preventing further damage to the immune system, decreasing AIDS-associated morbidity and mortality, allowing immune function to return to normal, and reducing the risk of transmitting HIV infection to others [1–7]. However, the rate of viral suppression among patients on ART in many resource-poor settings is not known because routine laboratory monitoring of HIV viral load is not performed in the public treatment programme.

Although numerous studies have demonstrated lower HIV viral load among untreated women, gender does not appear to impact viral suppression rates once on ART [8–16]. However, regardless of gender, adherence to ART is essential for viral suppression and barriers to adherence are numerous [17]. The World Health Organization (WHO) cites poor access to services, complex drug regimens, pregnancy, mental health disorders, substance abuse,

weak social support networks and incarceration as major barriers to adherence [18]. A study conducted in Vietnam using a visual analogue scale (VAS) and an audio computer-assisted self-interview (ACASI) method identified a number of factors for sub-optimal adherence, including heavy alcohol use in the previous month, depressive symptoms, a greater number of medication side effects, unclear source for routine HIV care site for patients, a low perceived quality of information from healthcare providers, low satisfaction with received support and low social connectedness [19].

Other studies conducted in Vietnam also cite social stigma, structural and individual behavioural factors, including alcohol and injection drug use, as associations with low utilisation of healthcare services [20–24]. Moreover, a recent study that examined why PLHIV in Vietnam delay initiation of treatment after testing positive found significant associations with feeling healthy, injection drug use history, work/school conflicts, detention or imprisonment, and perceived distance to clinic with late entry into care [25].

Vietnam has actively engaged in the expansion of its national methadone maintenance treatment (MMT) programme to treat addiction, reduce incidence of HIV among persons who inject drugs (PWID), and improve adherence to treatment and retention in HIV care [26,27]. A number of studies have highlighted improved HIV treatment adherence and viral suppression during early years of opioid substitution therapy. However, whether these gains can be

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sustained over time remains a key research question. Multiple studies highlight the importance of combining MMT with psychosocial support to improve adherence and sustainability of treatment outcomes [27–30].

Single-tablet regimens (STRs) as initial ART have demonstrated improved patient satisfaction, adherence and maintenance of viral suppression when compared to multiple-tablet regimens [31–35]. The use of STRs when initiating ART is now recommended if they have comparable efficacy and tolerability among all available regimens [18,36]. However, there may not be much additional benefit of switching to once-daily regimens when patients are already virally suppressed. It also is likely that adherence in virally suppressed patients is more dependent on overall daily pill burden and not necessarily on dosing schedule [37]. Currently, Vietnam has only one STR, a fixed-dose combination of efavirenz (EFV), tenofovir (TDF) and lamivudine (3TC). This once-daily STR is also the preferred WHO recommended first-line regimen for ARV-naïve adults [18].

The primary purpose of the study was to determine the rate of HIV virological suppression among Vietnamese men and women on antiretroviral treatment (ART) for at least 1 year. The result will be useful in assessing the effectiveness of the national HIV treatment programme among patients retained in care and in informing future clinical quality and health system improvement initiatives.

## Methods

### Study settings

ART in Vietnam is provided to PLHIV through a network of more than 300 public clinics throughout the country. All services at the clinics, including drugs, examinations and routine blood testing, are provided free. These services are primarily delivered at the provincial and district levels and are supported through funding from PEPFAR, the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM), and the national HIV/AIDS treatment programme.

All PLHIV with CD4 counts  $<350$  cells/mm<sup>3</sup> or WHO clinical stage III/IV were eligible for ART in the Vietnam national HIV treatment program at the time of this study [38]. ART patients are followed clinically every month for the first 6 months and then every 2–3 months thereafter. However, patients must return to the clinic pharmacy every month to pick up their medicine. Routine laboratory testing is performed every 6 months, including a CD4 cell count. Although annual viral load monitoring is recommended in the Vietnam national HIV treatment guidelines, it is not currently included in the routine laboratory monitoring due to lack of funding. However, clinic doctors can order targeted viral load testing if patients are suspected of having treatment failure and meet WHO criteria for clinical or immunological treatment failure.

The study was conducted in HIV outpatient clinics (OPCs) in four provinces: Ho Chi Minh City (HCMC), An Giang (AG), Quang Ninh (QN) and Dien Bien (DB). These four provinces were chosen to represent geographic diversity (HCMC and AG in the south, QN and DB in the north), a mix of urban (HCMC, QN) and rural (AG, DB, QN) clinic locations, and to include locations supported by both PEPFAR and GFATM, the two largest international donors for HIV programmes in Vietnam.

### Study design

Inclusion criteria for the study were age 18 years and over, HIV infected, continuing on ART for more than 1 year, and returning to clinic for a regular follow-up visit that included laboratory testing. Patients who were unable or unwilling to give informed

consent, or had no visits and no record of receiving any ART medication within the previous 90 days were excluded. Within each clinic, subjects were randomly selected from the total number of patients who met inclusion criteria. In order to recruit a sufficient number of patients on MMT for data analysis, MMT patients were stratified and recruited separately at four clinics in HCMC that provided both ART and MMT services.

The original study design planned for a total sample size of 1600 subjects, which had  $>80\%$  power to detect an absolute difference of 10% in viral suppression rates between major demographic categories such as gender, urban/rural, donor and PWID on MMT versus PWID not on MMT. Due to budget constraints, the final target sample size was reduced to 1250, but the sample size in each clinic was adjusted to maintain a minimum power of 80% for all major factors.

### Data collection and study measures

During the recruitment period, consented participants completed a structured survey questionnaire (SQ) administered by clinic staff who had been trained on good clinical research practices and survey collection. The SQ included questions on demographics, clinical symptoms, adherence and risk behaviour characteristics. Depression was assessed using the Centers for Epidemiological Studies Depression Scale (CES-D), a 20-item measure that assesses symptoms of depression over the previous 7 days [39]. Major depression was defined as having a total CES-D score  $\geq 16$ . Stigma was measured through a six-question internalised AIDS-related stigma scale [40]. High stigma was defined as a stigma score  $\geq 5$ . Experienced discrimination and fear of disclosure were assessed by two standardised questions [40].

Alcohol and drug use were assessed for the previous 30 days. Binge alcohol use was defined as drinking more than five alcoholic beverages on at least one occasion within the past 30 days. PWID was defined as persons reporting ever injecting heroin.

Clinical variables included both patient report and data extracted from the medical record. Information including ART regimens, WHO stages, and opportunistic infections was extracted from the medical record. ‘Single-tablet regimen’ was defined as those patients who reported taking EFV/TDF/3TC with a fixed-combination once daily. Clinical failure was defined as any WHO stage III or IV illness in the past 12 months. Immunological failure was defined as current CD4 cell count less than CD4 cell count at time of ART initiation.

Patient and medically recorded levels of adherence are reported separately and coded as ‘good’ if consistently  $\geq 95\%$  in the medical record and ‘poor’ if there was any record of adherence  $<95\%$ . ‘ART interruption’ was defined as a treatment interruption for at least 1 week during the previous 12 months. ‘Multiple late appointments’ was defined as being 1 or more days late for a scheduled ART follow-up appointment more than once during the previous 12 months.

After completing the questionnaire, patients underwent routine follow-up and blood work with the addition of a single viral load test. The test required an additional blood draw of 5 mL of whole blood preserved in an EDTA tube and stored at appropriate temperatures for processing. Samples were transported following the current standard national protocol [41] and HIV viral load testing was performed at two sites. Samples from the southern provinces (HCMC, AG) were tested at the Pasteur Institute in HCMC, which used either a Biocentric HIV-1 RNA PCR platform (Biocentric, Inc., Collingswood, New Jersey, USA) with a limit of detection of 250 copies/mL or a CAP-CTM/Roche platform (Roche Diagnostics, Basel, Switzerland) with a limit of detection of 20 copies/mL. Samples from the northern provinces of QN and DB

were processed at the National Institute of Hygiene and Epidemiology (NIHE) in Hanoi using an Abbott Real-Time HIV-1 RNA PCR platform (Abbott Laboratories, Abbott Park, Illinois, USA) with a level of detection of 151 copies/mL. Both facilities have external quality assurance programmes with international partners (NIHE: NRL-Australia; Pasteur Institute: CDC-USA, National Institute of Health-Thailand, NRL-Australia) and routinely transport specimens to other in-country institutions to monitor quantitative HIV RNA viral load quality standards.

### Statistical analysis

Bivariate analyses were conducted on the entire analysis population to assess the associations of biological markers and demographical and behavioural characteristics with HIV viral suppression. These analyses were completed with viral load as a dichotomous variable (< or ≥1000 copies/mL). Chi-squared tests were used for testing the association with other categorical variables. For comparing continuous variables between the HIV RNA viral load groups, we used *t*-tests or ANOVA tests. In addition, we conducted a trend analysis examining the relationship between viral suppression and 'Category Time Year on ART' as well as 'Categorised Current CD4 Count' using the Cochran–Armitage trend test.

Items for the depression, stigma and social support scales were assessed considering the extent of missing values and lack of variability. In addition, Cronbach's alpha was computed to assess reliability of the scales across the study participants. Alpha >0.70 was considered adequate. If a scale did not meet the adequacy threshold, we used only individual items within the scale instead of the whole scale. These decisions were made before association analysis against the outcome of interest, viral suppression, was conducted.

A multivariate analysis was conducted to assess adjusted associations between selected variables and viral suppression across the entire analysis population. A logistic regression model was used for examining the dichotomous viral load suppression variable to identify factors associated with viral suppression. The results of the descriptive and the bivariate analysis on the entire sample population were used to select an initial set of variables to be included in the multivariate model. All variables significantly associated with viral suppression at the 0.05 level based on bivariate analysis were considered for inclusion in the multivariate model.

Variables including METRO (metropolitan area), PWID (ever IDU), single-tablet regimen, previous ART and CD4 category were included, regardless of significance in the multivariate model, based on theoretical association with HIV viral load. However, province or north/south were not included due to collinearity with metropolitan area. HCV and marital status were not included due to collinearity with PWID. Once-daily ARV regimen was not included due to collinearity with single-tablet regimen. Stage IV condition in past 12 months and clinical stage at ART initiation were excluded due to collinearity with clinical failure. WBC and lymphocyte count were not included due to collinearity with CD4 category.

After an initial set of variables was selected in the above process, the multivariate model was fitted and variables were dropped based on collinearity assessments (e.g. tolerance and variance inflation factor) and a backward variable selection strategy. The variables identified theoretically as mentioned in the preceding paragraph were not part of the backward selection process. Other variables with *P* value <0.10 were kept in the model in each step of backward selection. Variables with variance inflation factor (VIF) >10 or correlation coefficient >0.3 were investigated and were

dropped due to collinearity. Goodness of fit of the models was also assessed and model specification modified as appropriate. The Hosmer and Lemeshow goodness-of-fit test area under the ROC curve was used to assess goodness of fit of the model. Adjusted odds ratios (OR) along with 95% confidence intervals (CI) and *P* values from the final logistic model are presented.

### Ethical considerations and patient confidentiality

The study was approved by the Research Ethical Committee of the Hanoi School of Public Health and FHI 360's Office of International Research Ethics and the Protection of Human Subjects Committee. All data was coded by a unique identifier to maintain participant confidentiality. Unique identifier numbers were linked to medical record numbers solely through a paper-based log maintained at each study clinic. The logs were destroyed after data collection and verification was completed.

## Results

The analysis population included all subjects who provided informed consent, met inclusion criteria (ART>12 months) and for whom viral load data were available. A total of 1435 patients were screened and 1261 (88%) agreed to participate in the study. Among this group, two participants did not have documented viral load and four participants had been on treatment less than 12 months. The final analysis included the remaining 1255 participants.

### Demographic and clinical characteristics

Demographics of the study sample are shown in Table 1. The median age was 34.5 years (range 18–74). Women accounted for 34% of participants. The majority of participants were married (63%), and employed (76%).

Median time on ART was 46 months (IQR 28–70 months). Previous ARV use prior to ART at the current OPC was reported by 19% and the majority (64%) reported a change in ARV regimen at some time. The most common ARV regimen was TDF/3TC/EFV (52%) followed by zidovudine/lamivudine/nevirapine (ZDV/3TC/NVP) (23%). Of those patients taking TDF/3TC/EFV, 98% were taking a daily single-tablet regimen.

Clinical information is listed in Table 2A. Overall viral suppression, defined as an HIV viral load below 1000 copies/mL, was 93% (95% CI 91.6–94.5%). Median CD4 cell count was 443 cells/mm<sup>3</sup> (interquartile range [IQR] 297–613). Baseline CD4 cell count was available for 1147 (91%) participants. Median baseline CD4 count was 136 cells/mm<sup>3</sup> (IQR 39–247), and was not significantly different between those with viral suppression (140 cells/mm<sup>3</sup>) and those with HIV viral load above 1000 copies/mL (112 cells/mm<sup>3</sup>) (*P*=0.19). Mean change in CD4 cell count while on ART was an increase of 304 cells/mm<sup>3</sup>, while 5.6% of those with both current and baseline CD4 tests available had a fall in CD4 cell count below baseline while on ART, meeting the definition for immunological treatment failure. Clinical treatment failure was experienced by 7.2% within the previous 12 months, but only 41 (3.3%) were WHO clinical stage III or IV at the time of the interview.

Viral suppression among women (93.7%) was no different than among men (92.9%) (Table 2A). The proportion of women and men who were married was not significantly different, but women were significantly more likely to be divorced or widowed (30% vs 11%) and less likely to be single (6% vs 27%; *P*<0.001). In addition, women reported a higher proportion of HIV-infected primary sex partners than men (48% vs 22%; *P*<0.001).

**Table 1.** Demographic characteristics of patients on antiretroviral therapy >1 year (n=1255)

	Total n (%)
<b>Sex</b>	
Male	828 (66)
Female	427 (34)
<b>Age</b>	
<35	582 (46)
≥35	673 (54)
<b>Highest education level</b>	
Never went to school	93 (7)
Primary (1–5)	294 (23)
Secondary (6–9)	491 (39)
High school (10–12)	308 (25)
College/university	68 (5)
<b>Marital status</b>	
Married	788 (63)
Divorced/widowed	220 (18)
Single	247 (20)
<b>Currently lives with other people</b>	
Alone	80 (6)
With other people	1175 (94)
<b>Employment</b>	
Working	956 (76)
Unemployed	299 (24)
<b>HIV status of regular sex partner</b>	
Negative/unknown	502 (40)
Positive	384 (31)
No regular partner	343 (27)
Refuse to answer	26 (2)
<b>Time on antiretroviral therapy</b>	
<3 years	345 (28)
3–5 years	551 (44)
>5 years	359 (29)
<b>Antiretroviral regimen</b>	
TDF/3TC/EFV	647 (52)
TDF/3TC/NVP	97 (8)
ZDV/3TC/EFV	164 (13)
ZDV/3TC/NVP	289 (23)
2 NRTI+LPV/r	39 (3)
others	19 (2)
<b>Single-tablet regimen</b>	
Yes	637 (51)
No	618 (49)

TDF, tenofovir; 3TC, lamivudine; EFV, efavirenz, NVP, nevirapine; ZDV, zidovudine; NRTI, nucleoside reverse transcriptase inhibitor; LPV/r, lopinavir/ritonavir.

Adherence to ART was assessed in several different measurements. Adherence recorded by physicians or nurses in the medical record showed that 95.5% of patients had good adherence defined as taking at least 95% of doses. Patients self-reported a lower rate of adherence using a visual analogue scale (VAS): only 89% reported adherence of at least 95%. However, 20.6% of study participants had two or more late appointments in the past year and 6.2% had treatment interruptions for more than 1 week in the past year; both of these measurements of adherence were significantly associated with unsuppressed viral load on the bivariate analysis.

### Alcohol and drug use

Alcohol and drug use are shown in Table 2B. In the previous 30 days, 40% of patients recorded alcohol use and 30.4% had binge alcohol use of five or more drinks at one time. PWID were 42.4% of the sample, although only 57/532 (10.7%) of PWID reported injecting in the previous 30 days. Of the PWID, 43% were currently

on MMT for a median of 37 months (range 1–76 months). The mean dose of methadone was 191 mg/day (range 20–450 mg/day).

### Psychosocial factors

Psychosocial factors are listed in Table 2B. One-quarter of patients (24.9%) met the criteria for major depression, but this was not associated with unsuppressed viral load. The three-question social support scale did not meet adequacy based on the Cronbach's alpha threshold of 0.70. As a result, each of the three questions included in the scale was analysed separately. Factors with a positive association with unsuppressed viral load were higher internalised HIV stigma score, disclosure of HIV status and social isolation.

### Multivariate analysis

Results of the multivariate logistic regression are shown in Table 3. Factors independently associated with HIV viral load  $\geq 1000$  copies/mL were CD4 cell count  $< 200$  cells/mm<sup>3</sup>, social isolation, multiple late appointments in the previous year, not on a single-tablet regimen, high-internalised HIV stigma and immunological treatment failure. Age  $< 35$  and fear of disclosure demonstrated a trend toward associations with unsuppressed viral load approaching statistical significance.

### Discussion

Viral load suppression in the four provinces studied was 93% overall and ranged from 88 to 100%. This high rate of suppression already exceeds the UNAIDS 90–90–90 target. Although the WHO 2013 treatment guidelines currently define viral suppression as an HIV RNA VL below 1000 copies/mL [18], we also found a viral suppression rate of 89% with the lower threshold of 250 copies/mL, suggesting that most patients maintained on ART for at least 12 months have very low VL.

These findings provide critically important data on HIV clinical service delivery performance across Vietnam. On-treatment viral suppression rates across the study population were relatively high compared to other low- and middle-income settings and are likely to reflect a high level of adherence among those patients retained in care.

The United States Centers for Disease Control reported that among adult patients who received continuous treatment during the preceding 12 months between 2008 and 2010, approximately 77% of patients in the United States were suppressed with HIV viral loads less than 200 copies/mL [42]. A systematic review of low- or middle-income countries by McMahon found that 84% of the pooled on-treatment population had HIV VL less than 1000 viral RNA copies/mL [43]. A multi-country study that included three sites in Ho Chi Minh City, Vietnam found an on-treatment viral suppression rate ( $< 1000$  copies/mL) of 88.5% after 12 months of treatment [44]. A small study that enrolled 100 male patients with history of IDU receiving ART for at least 6 months at a large urban OPC in Hanoi Vietnam found that 73% of patients who continue in care had viral loads less than 1000 copies/mL [45].

In this study, viral suppression rates were slightly lower in the HCMC metropolitan area, where many of the first public ARV clinics in Vietnam were established in 2004 and participants have longer histories of ART use. The ARV regimens most commonly used prior to 2010 included ZDV, d4T and NVP, drugs which have significantly higher rates of side effects than current regimens, and which may have had an adverse effect on adherence.

Gender was not a significant factor for viral suppression in this study, consistent with other studies that demonstrate similar rates of HIV treatment efficacy between male and female patients [10,14,15]. Compared to men, women were less likely to be single

**Table 2A.** Clinical characteristics and bivariate analysis with HIV viral load

	HIV RNA <1000 copies/mL (n=1169) n (row %)	HIV RNA ≥1000 copies/mL (n=86) n (row %)	P value
<b>Gender</b>			
Male	769 (93)	59 (7)	
Female	400 (94)	27 (6)	0.59
<b>Current HIV clinical stage</b>			<0.01
Stage 1	1075 (94)	69 (6)	
Stage 2	63 (90)	7 (10)	
Stage 3	17 (77)	5 (23)	
Stage 4	14 (74)	5 (26)	
<b>Current CD4 cell count</b>			<0.01
0–199 cells/mm <sup>3</sup>	96 (71)	39 (29)	
200–349 cells/mm <sup>3</sup>	259 (94)	17 (6)	
≥350 cells/mm <sup>3</sup>	813 (96)	30 (4)	
<b>Single-tablet regimen</b>			<0.01
Yes	614 (96)	23 (4)	
No	555 (90)	63 (10)	
<b>Ever changed ARV since starting at this clinic</b>			0.46
Yes	753 (94)	52 (6)	
No	416 (92)	34 (8)	
<b>Reported previously receiving ARV from another clinic</b>			0.10
Yes	204 (91)	21 (9)	
No	965 (94)	65 (6)	
<b>Admitted to the hospital in past year for OI</b>			0.03
Yes	50 (86)	8 (14)	
No	1119 (93)	78 (7)	
<b>Clinical failure in past 12 months</b>			0.01
Yes	78 (87)	12 (13)	
No	1091 (94)	74 (6)	
<b>Immunological failure in past 12 months</b>			<0.01
Yes	43 (67)	21 (33)	
No	1028 (95)	54 (5)	
<b>Recorded adherence in chart</b>			0.92
Good	1114 (93)	81 (7)	
Poor	52 (93)	4 (7)	
<b>Multiple late appointments in last year</b>			0.02
Yes	232 (90)	26 (10)	
No	937 (94)	60 (6)	
<b>Patient reported VAS adherence past 3–4 weeks</b>			0.21
Good	1042 (93)	73 (7)	
Poor	125 (91)	13 (9)	

ARV, antiretroviral drug; OI, opportunistic infection; VAS, visual analogue scale.

and more likely to report having a primary partner with HIV infection, indicating that for most women the source of HIV transmission was from their primary sex partners.

PWID were more likely to have unsuppressed viral loads but this association was not significant on the multivariate analysis. Other studies have identified structural and psychosocial barriers to treatment compliance among this vulnerable population in Vietnam [19,20,25,46].

Interestingly, MMT did not have a significant impact on viral suppression rates among PWID. The cross-sectional nature of our study makes it difficult to evaluate factors that may mitigate the effect of MMT on adherence over time. In addition, it is likely

that PWID enrolled in MMT programmes have different characteristics than PWID not taking MMT, which may complicate comparisons of adherence or viral suppression rates between the two groups.

We did not find a difference in suppression based on donor funding. Apart from funding source, our study did not control for site-specific characteristics including assessment of previously provided technical assistance, time with HIV and ART service provision, facility structure and human resources, and the availability of social services including community-based treatment supporters.

Routine adherence measures including physician documentation in the medical record or patient responses to visual analogue scales were not associated with viral suppression. However, multiple late appointments were significantly associated with unsuppressed VL in the multivariate analysis. Systematic reviews have found that traditional adherence measures are likely to be inaccurate and that more simple and objective adherence tools should be developed [36]. Missed or late appointments could easily be tracked with paper or electronic appointment or logbook systems currently used in Vietnam. They could facilitate early identification of those patients who are more likely to have worsening adherence to ART and allow for intensive and targeted adherence education, counselling and community-based support to those patients in most need.

Nearly half of our study population was maintained on a single-tablet regimen of EFV/3TC/TDF and the use of this STR was significantly associated with viral suppression. This finding is consistent with a growing body of literature highlighting the benefits of STRs on patient satisfaction, adherence and viral suppression [31–35].

Viral suppression rates in our study population did not vary between NNRTI- and PI-based regimens or with duration of treatment. Less than 4% of our participants were on second-line PI-based treatment. Participants with CD4 cell counts less than 200 cells/mm<sup>3</sup> or immunological failure as defined by a current CD4 cell count below baseline were significantly more likely to have unsuppressed

viral loads. Under current Vietnam clinical guidelines, patients with suspected clinical or immunological failure are able to receive targeted viral load testing to diagnose treatment failure and access second-line ART [41]. Of concern, we found that 5.6% of our study population had immunological failure as defined by a current CD4 cell count below baseline, with 32% of these patients having unsuppressed viral loads. These patients could immediately benefit from adherence support, follow-up repeat viral load testing, and switching to a second-line ART regimen.

High internalised HIV stigma and social isolation were associated with unsuppressed viral load. Previous studies have reported that Vietnamese people living with HIV feel stigma and experience

**Table 2B.** Substance use and psychosocial factors and bivariate analysis with HIV viral load

	HIV RNA VL <1000 copies/mL (n=1169) n (row %)	HIV RNA VL ≥1000 copies/mL (n=86) n (row %)	P value
<b>Alcohol in last 30 days</b>			0.58
Yes	470 (94)	32 (6)	
No	699 (93)	54 (7)	
<b>Binge alcohol use in last 30 days</b>			0.48
Yes	352 (92)	29 (8)	
No	817 (93)	57 (7)	
<b>Ever injection drug use (IDU)</b>			0.02
Yes	485 (91)	47 (9)	
No	683 (95)	39 (5)	
<b>PWID on MMT</b>			0.70
Yes	210 (92)	19 (8)	
No	275 (91)	28 (9)	
<b>Major depression</b>			0.50
Yes	288 (92)	24 (8)	
No	880 (93)	62 (7)	
<b>Stigma score ≥5</b>			0.03
No	919 (94)	59 (6)	
Yes	248 (90)	27 (10)	
<b>I have been treated differently since I disclosed my HIV status to friends and family (discrimination)</b>			0.98
Disagree or N/A	867 (93)	64 (7)	
Agree	300 (93)	22 (7)	
<b>There are people I have not told that I am HIV positive out of fear of negative consequences (non-disclosure)</b>			0.03
Disagree or N/A	384 (91)	38 (9)	
Agree	783 (94)	48 (6)	
<b>If I were sick and needed someone to take me to a doctor, I would have trouble finding someone (lack of social support)</b>			0.65
Completely true	329 (94)	22 (6)	
Somewhat true	184 (94)	11 (6)	
Somewhat false	55 (95)	3 (5)	
Completely false	599 (92)	50 (8)	
<b>I feel that there is no one I can share my most private concerns and fears with (social isolation)</b>			<0.01
Completely true	244 (88)	34 (12)	
Somewhat true	304 (95)	15 (5)	
Somewhat false	155 (94)	10 (6)	
Completely false	464 (95)	27 (5)	
<b>I feel a strong emotional bond with at least one other person (emotional support)</b>			0.12
Completely true	760 (94)	50 (6)	
Somewhat true	199 (94)	12 (6)	
Somewhat false	27 (87)	4 (13)	
Completely false	181 (90)	20 (10)	

PWID, people who inject drugs; MMT, methadone maintenance treatment.

discrimination due to HIV [20,21,24]. These factors may contribute to delayed HIV testing, delayed entry into HIV care, and lower levels of ART adherence once on treatment [19,25]. Patients may benefit from the use of expanded outreach and community-based testing, mobile technologies, treatment buddies and additional community-based support to continue receiving care [47–52].

This study has a number of limitations. The cross-sectional, on-treatment methodology does not account for patients who have

been lost to follow-up or died while on ART. As a result, the estimate of viral suppression may be significantly higher than would be found in other studies with either lower loss to follow-up or reduced mortality. In addition, we expect that a significant number of women in our study were infected by their partners and may be more likely to adhere to therapy than in other study settings in which more women receive money for sex or have multiple partners. It is also possible that both male and female patients who were retained in care were more likely to adhere to treatment with minimal treatment support. For these reasons, it is possible that viral suppression rates will fall in the future as a greater proportion of patients are enrolled at higher CD4 cell counts under the revised national guidelines and more patients, particularly male patients, with suboptimal adherence to ART are retained in care through adherence support interventions [53].

The study was conducted at district level OPCs and only a very small percentage of participants were on second-line ART. In Vietnam, patients requiring second-line ART are usually referred to provincial or central-level hospitals. As a result, these findings may not represent viral suppression rates of patients managed in higher-level clinical settings. The study was conducted in only four provinces and may not be generalisable to provinces with limited ART access or lacking international donor support. However, we feel the findings are robust as the vast majority of patients in Vietnam receive HIV care at the district level and the four provinces chosen represent roughly 37% of patients on ART in the country [54].

Lastly, although the psychosocial scales and measures were validated in previous studies outside Vietnam, there may be some interpretation or translation bias for these questions when administered in the Vietnamese context.

## Conclusions

VL suppression rates in Vietnam are high relative to other settings and already exceed the UNAIDS 90% target for on-treatment viral suppression. These rates could possibly fall as more patients are enrolled in care at earlier stages of disease, retained in care and sustained on ART. Gender did not impact viral suppression rates on ART.

Based on the findings of this study, the Vietnam HIV programme can maintain and potentially improve virological treatment outcomes by improving access to targeted viral load testing, including a routine viral load for all patients on ART after 12 months of treatment, streamlining adherence monitoring and counselling, proactively switching patients to the available single-tablet EFV/3TC/TDF daily regimen, and mobilising treatment support interventions to address issues of social isolation and high stigma among PLHIV.

**Table 3.** Multivariate analysis of factors associated with HIV viral load  $\geq 1000$  copies/mL

	Adjusted OR (95% CI)	P value
<b>Age</b>		
<35	1.7 (0.99, 2.92)	0.05
$\geq 35$	Reference	
<b>Current CD4 cell count</b>		
0–199 cells/mm <sup>3</sup>	8.75 (4.5, 17)	<0.01
200–349 cells/mm <sup>3</sup>	1.78 (0.87, 3.62)	0.11
$\geq 350$ cells/mm <sup>3</sup>	Reference	
<b>I feel that there is no one I can share my most private concerns and fears with (social isolation)</b>		
Completely true	2.09 (1.06, 4.11)	0.03
Somewhat true	0.89 (0.43, 1.83)	0.74
Somewhat false	1.44 (0.57, 3.63)	0.43
Completely false	Reference	
<b>There are people I have not told that I am HIV positive out of fear of negative consequences (non-disclosure)</b>		
Disagree or N/A	1.81 (0.99, 3.28)	0.05
Agree	Reference	
<b>Metropolitan area</b>		
Yes	1.11 (0.55, 2.24)	0.77
No	Reference	
<b>Multiple late appointments in last year</b>		
Yes	2.61 (1.43, 4.78)	<0.01
No	Reference	
<b>PWID (ever)</b>		
Yes	1.31 (0.74, 2.3)	0.35
No	Reference	
<b>Previous ART</b>		
Yes	Reference	
No	1.08 (0.51, 2.31)	0.84
<b>Single-tablet regimen</b>		
Yes	Reference	
No	3.13 (1.7, 5.77)	<0.01
<b>Stigma score greater than 5</b>		
No	Reference	
Yes	2.34 (1.22, 4.5)	0.01
<b>Immunological failure</b>		
No	Reference	
Yes	4.18 (2.09, 8.34)	<0.01

PWID, people who inject drugs; ART, antiretroviral therapy.

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### Conflict of interests

The authors report no conflict of interests.

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