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Detection of antiretroviral drug-resistant mutations and HIV-1 subtypes in circulation among men who have sex with men, SEM females and female sex workers: results of Vietnam's HIV Sentinel Surveillance Plus (HSS+) system, 2018 – 2020

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Abstract

Background: HIV drug resistance (HIVDR) can reduce the effectiveness of antiretroviral (ARV) drugs in preventing morbidity and mortality, limit options for treatment, and prevention. Our study aimed to assess HIV-1 subtypes and HIVDR among key populations in HIV Sentinel Surveillance Plus Behavior (HSS+) in 2018 and 2020.

Methods: One-stage venue-based cluster sampling was used to recruit participants at hotspots identified for Men who have sex with men (MSM) in 7 provinces and SEM females and female sex worker (FSW) in 13 provinces. Participants completed a standard questionnaire about risk and preventive behaviors, and ART history, and provided intravenous blood for HIV testing. HIVDR testing was conducted on HIV-positive samples with VL >1,000 copies/ml.

Results: A total of 185/435 (42.5%) HIV-positive samples had viral load ≥1,000 copies/ml, of which 130/136 from MSM and 26/49 from FSW, were successfully sequenced. Six HIV-1 subtypes were detected (CRF01_AE, A, CRF07/08_BC, B, C, CRF25_cpx), with CRF01_AE (82.7%, 129/156) the most common. Drug resistance mutations were detected in 16.7% of participants overall (26/156), in 15.4% (20/130) of MSM, and in 23.1% (6/26) of FSW. Mutations associated with resistance to NNRTI were the most frequently detected (73.1%, 19/26). The high level of resistance was presented in NNRTI and NRTI classes. There are 10 major resistance mutations detected with NRTI (M184VI-25.0%, K65KR-50.0%, Y115F-25%), NNRTI

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Conflicts of Interest

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(K103N-21.1%, E138A-10.5%, V106M-5.3%, K101E-5.3%, G190A-5.3%) PI (L33F-40.0%, M46L-20.0%).

Conclusions: Vietnam's HSS+ system identified an emerging strain of HIV-1 and mutations associated with resistance to multiple drug classes among MSM and FSW.

Keywords

Antiretroviral therapy; Drug resistance; Men who have sex with men; Sex workers; Vietnam

INTRODUCTION

By the end of 2020, a total of 322,897 people had been diagnosed with HIV in Vietnam, with 109,446 cumulative deaths [1]. To reduce the burden and incidence of HIV, Vietnam has scaled up the provision of antiretroviral therapy (ART). An estimated 155,973 persons living with HIV (PLHIV) are on ARV treatment by the end of 2020 [1], representing an estimated 70% coverage of treatment [2–4]. In 2017, the Vietnam Ministry of Health guideline for HIV treatment recommended first-line ART was tenofovir + lamivudine + efavirenz (TLE), the alternative regiment suggest TDF + 3TC (or EVF) + DTG; TDF + 3TC (or FTC) + NVP; AZT + 3TC + EFV; AZT + 3TC + NVP [5]. However, the ART program face with the financial burdens when the international funding resources which support approximately 95% of antiretroviral (ARV) drugs for Vietnam, previously speedily cut in the recent years [6].

The emergence of HIV drug resistance can compromise the effectiveness of ART in reducing morbidity and mortality, limit second- and third-line options for treatment, and reduce prevention of onward transmission[4,5,7–9]. As efforts to scale-up ART and HIV pre-exposure prophylaxis (PrEP) continue, the prevalence of HIV drug resistance is likely to increase. For example, it is projected that transmitted HIV drug resistance will increase to 16% prevalence and acquired drug resistance to 18% in Vietnam by 2030 in the absence of viral load monitoring[9,10].

Although data are scant for much of the world including Vietnam, the prevalence of HIV drug resistance may be higher for key populations, such as men who have sex with men (MSM), SEM females and female sex workers (FSW) who bear a disproportionate burden of HIV prevalence and incidence[4,5,7–11]. In addition, there is not national drug resistance surveillance in Vietnam in these high-risk groups thus there is limited information on drug resistance specific to these populations. Therefore, there is great need for systems or surveillance to track trends in HIV drug resistance among these key populations.

The HIV Sentinel Surveillance Plus (HSS+) in Vietnam presents an opportunity to detect and track trends in HIV drug resistance among key populations by person, place, and time. HSS+, as part of the monitoring and evaluation component of the National Strategy on Prevention and Control HIV/AIDS, is designed to measure HIV prevalence and related factors in MSM, SEM females and FSW, and other populations at high risk [9–12]. Samples from HSS+ participants who test HIV positive are sequenced to identify mutations associated with HIV drug resistance. In this paper, we present the first HSS+ program data

on HIV drug resistance collected from 2018 to 2020 among MSM, SEM females and FSW across the nine provinces from the North and the South of Vietnam.

METHODS

Study populations and overall design

The HSS+ comprises serial cross-sectional surveys of MSM, SEM females and FSW conducted in selected, sentinel study sites across Vietnam. HSS+ is implemented every two years. MSM participants were defined as men aged 16 years and older who are currently living or working in the province and self-report having anal sex with another man at least once in the last 12 months. SEM females who were from 16 years old to less than 18 years old and FSW participants were defined as females aged 18 years and older who are currently living or working in the province of data collection and self-report having exchange sex for money or other items of value at least once in the last 30 days. This paper includes data collected in 2018 and 2020 from MSM, SEM females and FSW testing HIV positive and for whom sufficient viral RNA was available for genetic sequencing.

Study procedures

Survey methods are detailed in a previous publication on HIV and syphilis prevalence in the HSS+ data for MSM in southern Vietnam[10–13]. In brief, sample sizes of 150–300 participants are recruited from sentinel provinces. A cluster sampling design was used. Within the selected sentinel districts, a sampling frame was built and updated every year by collecting data on where KP congregate in each cluster (e.g. venues and hotspots for SEM females and FSW and MSM). Clusters were randomly selected from the sampling frame. In each selected cluster, all eligible participants were invited to participate into HSS+. Local health staff, outreach workers, and peer educators were involved in participant recruitment process. Sentinel provinces included in HIV drug resistance testing were Lao Cai, Ha Noi, Hai Phong, and Nghe An in the north of Vietnam and An Giang, Can Tho, Dong Nai, Ho Chi Minh, and Kien Giang in the south. Within these provinces, three to five districts are chosen based on HIV prevalence, known hotspots and venues with MSM, SEM females and FSW, and the presence of governmental and community-based HIV prevention and care services. Using key informants, focus groups, and community guides, a sampling frame of hotspots and venues is created that include the locations where MSM, SEM females and FSW congregate (e.g., bars, clubs, parks, and other public spaces). A random sample of hotspots and venues is selected where outreach worker staff with community guides intercept persons present and assess their eligibility and willingness to participate. Eligible MSM, SEM females and FSW are given invitation cards for a brief, anonymous survey with HIV and syphilis testing at the site indicated on the card.

HIV testing and sequence analysis

HIV-positive cases were defined by the national testing strategy that follows WHO guidelines [11–15], for surveillance and diagnostic purposes, requiring three consecutive reactive tests to confirm an HIV-positive case. Study sites used combinations of the following tests[10–13,15]: SD Bioline HIV-1/2 3.0 (Standard Diagnostics Inc., Gyeonggi-do, Korea), Vikia HIV-1/2 (BioMerieux Shanghai Biotech Co., Shanghai, China), Determine

HIV-1/2 (Alere Medical Co., Matsudo, Japan), Alere HIV Combo (Alere Medical Co., Matsudo, Japan), Murex HIV Ag/Ab Combination (DiaSorin, Dartford, United Kingdom), or Abon HIV-1/2 (ABON Biopharm, Hangzhou Co., Hangzhou, China). Specimens confirmed positive were also tested for HIV recency (i.e., acquired infection within the preceding 12 months) using Asante recency assay. Following the Recent Infection Testing Algorithm (RITA), HIV viral load (VL) was performed using Roche COBAS AmpliPrep/ COBAS TaqMan v2.0 or Abbott m2000 sp[16]. Those who tested recent on the Asanté™ HIV-1 Rapid Recency® Assay (Sedia Biosciences) and had viral load ≥1,000 copies/mL were classified as RITA-recent.

HIV drug resistance testing was conducted on plasma specimens with VL ≥1,000 copies/ml at the National Institute of Hygiene and Epidemiology in Ha Noi and the Pasteur Institute in Ho Chi Minh. ABI 3130XL sequencer was used for sequencing HIV-1 *Pol* gene (reverse transcriptase and protease) with the Big-Dye Terminator v3.1 Cycle Sequencing Kit (Applied Biosystem). HIV subtype and HIV DR identification and interpretation was based on the HIVdb Program: Sequence Analysis in the Stanford University HIV Drug Resistance Database (https://hivdb.stanford.edu/hivdb/by-sequences/). HIVDR was classified as the detection of mutations associated with one or more of the following drugs used in Vietnam and level of resistance based on data analyzed from the HIVdb program: any non-nucleoside reverse transcriptase inhibitor (NNRTI) (nevirapine (NVP), efavirenz (EFV)), any nucleoside reverse transcriptase inhibitors (NRTI) (Tenofovir disoproxil fumarate (TDF), Lamivudine (3TC), Emtricitabine (FTC)), and any protease inhibitors (PI) (atazanavir (ATV), darunavir (DRV), or lopinavir (LPV)).

Data analysis

HIV drug resistance results were linked by code to participant survey responses, including demographic characteristics, risk and preventive behaviors, and clinical history for those self-reporting as HIV-positive.

Descriptive analysis was used to describe the detection of mutations associated with antiretroviral drug resistance among MSM, SEM females and FSW overall and by sub-groups. Proportions were calculated as the number of participants classified as having HIV drug resistance among individuals with interpretable sequences.

Ethical considerations

The study protocol and procedures were approved by the Research Ethics Committee of the National Institute of Hygiene and Epidemiology (IRB-VN01057). This project was reviewed in accordance with the US Centers for Disease Control and Prevention (CDC) human research protection procedures and was determined to be research, but CDC investigators did not interact with human subjects or have access to identifiable data or specimens for research purposes. All participants provided verbal informed consent. Participants received approximately $1.50 for the interview and $3.50 for providing a blood specimen. A non-identifying study code was given to each participant to provide their test results, counselling, and needed referrals at a follow-up visit. Participants under 18 years of age were given

information of where they can seek, when necessary, services to orphans, protection of women and girls, protection of children and adolescents.

RESULTS

A total of 435 samples were identified as HIV-positive and 185/435 (42.5%) had viral load ≥1,000 copies/ml, of which 130/136 samples from MSM and 26/49 samples from SEM females and FSW were successfully sequenced. The proportion of successfully sequenced samples were 84.3% (156/185). Figure 1 and Table 1 show the geographic distribution of the study sites in Vietnam and the variation of HIV-1 subtypes detected among MSM, SEM females and FSW. In the northern provinces, four subtypes were observed: A and CRF07/08_BC among MSM, and C and CRF01_AE among SEM females and FSW. In the southern provinces, subtypes A, B, and CRF25_cpx were observed among MSM and subtype CRF01_AE among MSM, SEM females and FSW. Among 9 MSM in the north, subtype B+C predominated (88.9%−8/9), while subtype CRF01_AE was most common among 121 MSM in the south (86.8%−105/121). Among 12 SEM females and FSW in the north, CRF01_AE was more commonly detected (83.3%−10/12) than C (16.7%−2/12). Only subtype CRF01_AE (100%−14/14) was detected among 14 SEM females and FSW in the south. Of note, the subtype CRF25_cpx, found in two MSM participants in the south, was detected for the first time in Vietnam.

Demographic, risk, and clinical characteristics of the 156 HIV-positive participants are shown in Table 2. Among the 130 HIV-positive MSM, most were 35 years and older (93.9%), unmarried (86.9%), and had a high school education or higher (72.3%). More HIV-positive MSM were identified in the southern provinces, particularly Can Tho, compared to the northern provinces. With respect to HIV-related risks, 10.8% had multiple partners at the same time (i.e., group sex), 5.4% had ever injected drugs, and 5.4% reporting having a sexual partner who was HIV-positive, although most (80.0%) did not know the serostatus of their partners. Many MSM had recent HIV infection (17.7%−23/130) and a majority of MSM said they were not on ART (56.2%−73/130) or declined to answer/didn't know (22.3%- 29/130). Among the five HIV-positive MSM who reported being on ART, 2 (40.0%) said they had ever forgotten to take their ARV. Among the 26 HIV-positive SEM females and FSW who provided sufficient samples for sequencing, the majority were under 35 years (57.7%), were married or living with a partner (80.8%) and had less than complete high school education (92.3%). 30.8% had ever injected drugs and had known HIV-positive partners (23.1%); none had recent HIV infection. Three (11.5%) reported taking ART; of whom 2 (66.7%) said they had ever forgotten to take their ARV.

Drug resistance mutations were detected in 16.7% of participants overall (26/156), in 15.4% (20/130) of MSM, and in 23.0% (6/26) of SEM females and FSW (Table 2). High levels of drug resistance were detected in MSM, SEM females and FSW who had ever injected drugs compared to the group non-injected drugs (28.6% (2/7) vs. 14.6% (18/123) and 37.5% (3/8) vs. 16.7% (3/18), respectively). Of the 23 MSM classified being recently infected, one (5.0%) had an HIV drug resistant strain. Half (50.0%) of the HIV drug resistant strains detected were among MSM who reported never taking ART and among one-third (33.3%) of SEM females and FSW reporting never taking ARV. However, many drug-resistant strains

were detected among MSM (25.0%), SEM females and FSW (66.7%) who declined to answer this question. Meanwhile, two out of two MSM (100%) and no case of SEM females and FSW who reported taking ARV and had ever forgotten to take their ARV had drug resistant strains.

Table 3 shows the distribution of mutations detected among MSM, SEM females and FSW in the HSS+ system by drug classes and resistance levels. Mutations associated with resistance to the non-nucleoside reverse transcriptase inhibitor (NNRTI) drug class were the most frequent (73.1%, n=19/26), detected in 13 of 18 (72.2%) MSM with any drug resistant strains and six of six (100%) SEM females and FSW with any drug resistant strains. The most common mutations associated with NNRTI resistance detected were V179T (n=7), K103N (n=4), and V106I (n=4). Mutations associated with resistance to nucleoside reverse transcriptase inhibitors (NRTIs) were detected in 23.1% (n=6/26) of MSM, SEM females and FSW with any resistant mutation, 22.2% among MSM and 33.3% among SEM females and FSW. The most common mutations detected that were associated with NRTI resistance were V75M and K65R. Mutations associated with resistance to protease inhibitors (PI) were detected in six MSM (23.1%) at eight mutation positions (L24F, V32L, L33F, M46L, I47S, G48S, I50S, I54IS). Mutations associated with dual-class resistance to NRTIs and NNRTIs were detected in two MSM participants and two SEM females and FSW participants, and dual-class resistance to PIs and NNRTIs were detected in one MSM. High level resistance was detected in NNRTI and NRTI classes with Efavirenz (EFV) (26.3%, n=5/19) Nevirapine (NVP) (10.5%, n=2/19),Stavudine (D4T) (50.0%, n=3/6), Didanosine (DDI) (33.3%, n=2/6), Emtricitabine (FTC) (33.3%n=2/6), Lamivudine (3TC) (33.3%n=2/6), and Tenofovir disoproxil fumarate (TDF) (33.3%n=2/6), respectively. There were 10 major resistance mutations associated with reduced susceptibility or virological response to first and second-line HIV treatment recommended in Vietnam in 2018 and 2020 detected, including for NRTIs (M184VI-25.0%, K65KR-50.0%, Y115F-25%) and NNRTIs (K101E-5.3%, K103N-21.1%, V106M-5.3%, E138A-10.5%, G190A-5.3%), and PIs (L33F-40.0%, M46L-20.0%) which reduced susceptibility or virological response to the current first-line HIV treatments TLE in Vietnam in 2018 and 2020.

DISCUSSION

Our study suggests that the HIV Sentinel Surveillance Plus (HSS+) can serve as an HIV molecular epidemiology surveillance system for key populations at risk for HIV in Vietnam [9–12,16]. Implemented in many provinces across the major regions of the country, HSS+ provides a wealth of data on HIV prevalence and incidence, HIV drug resistance, and related risk and preventive behaviors among key populations including MSM, SEM females and FSW. HSS+ addresses the challenge of MSM, SEM females and FSW status being incomplete in clinic-based data, as well as collecting data on people living with HIV who are outside of HIV care and treatment programs.

In our analysis of the genetic sequence data obtained from the 2018 and 2020 HSS+ surveys, we documented a total of six subtypes that were differentially distributed in the north and the south of Vietnam and across key populations. The most common subtype detected overall was CRF01_AE, accounting for 80% of cases sequenced in our study.

HSS+ was also able to detect the subtype CRF25_cpx with the low prevalence (1.7%). Very few CRF25_cpx sequences have been documented in the literature[15–19]. CRF25_cpx has a mosaic composition that consists of nine segments derived from subtypes A and G and unclassified (U) regions. The CRF25_cpx strain may have originated in Cameroon, although its epidemiological significance remains unclear. The detection of the HIV-1 CRF25_cpx strains should prompt further epidemic investigation of HIV transmission in Vietnam. Of note, these cases detected in Vietnam appeared among MSM in the south. A previous publication of HSS+ reported increasing HIV prevalence among MSM in the south[10–13,15] suggesting that emerging trends in the molecular epidemiology of HIV in Vietnam may be first detected in this disproportionately affected population with continuing rapid spread of infection. We emphasize the need for in-depth studies on the transmission networks of newly emerging strains of HIV-1 in Vietnam such as through index testing and partner notification. The HSS+ system can provide the first signal to trigger further investigations.

Other strains of HIV-1 detected reflect the regional molecular epidemiology[7]. CRF01_AE and B+C where the most common subtypes detected in northern provinces, while CRF01_AE was the predominant subtype in the southern provinces. CRF01_AE, CRF08_BC, and CRF07_BC are the three major circulating strains of HIV-1 in China's southwestern provinces of Yunnan and Guangxi, which directly border northern Vietnam, while CRF01_AE is common in the southern, highly industrial Chinese provinces of Guangdong and Fujian[16–20]. Vietnam's northern provinces and have extensive travel and trade relationships with these parts of China. Meanwhile, CRF01_AE is commonly reported from Cambodia and Thailand, countries closer to the southern part of Vietnam[21,22]. The similarities in circulating HIV-1 subtypes between areas of Vietnam and nearby countries may result from transmission within sexual networks that cross these international borders[23,24].

Our study also suggested the ability of the HSS+ system with HIVDR genotyping to detect a wide array of mutations associated with resistance to multiple classes of antiretroviral drugs. The proportion of study isolates with any HIV drug resistant-associated mutation was 16.7%, which did not differ overall from the 2012–2013 sentinel surveillance surveys conducted in central Vietnam (19.1%) and a multi-country survey that included 152 isolates from Vietnam (14.7%)[25,26]. However, the surveys from central Vietnam tended to have a lower proportion of HIV drug resistance among SEM females and FSW compared to MSM (8.3% vs. 33.3%, respectively) in contrast to our data (23.0% vs 15.4%, respectively)[21–25]. Earlier studies in Vietnam suggest our data show a recent increase in HIV drug resistance. For example, a nationally representative clinic-based study found the prevalence of HIV drug resistance among patients under ART to be 4.6% in 2014, and a second study conducted in 2017–2018 found pre-treatment resistance prevalence to be 5.8%[12–15,23–27]. The difference in prevalence for our study may be a result of data being collected from MSM, SEM females and FSW both pre- and post- treatment. Of note, high levels of transmitted HIV drug resistance are found among MSM in North America and Europe at 13.7% and 11.0%, respectively, while 7.8% among MSM in low to middle-income countries[24–28]. The differences in proportion of TDR between high-income and low- and middle-income countries may be the result of LMICs introducing potent combination therapy since the beginning of their ART programmes. Combination therapy is more

effective in suppressing in-vivo viral replication and limiting the selection of drug-resistant strains than the legacy single/dual therapies introduced in high-income settings in the early stages of their ART programmes [24–26].

Mutations associated with resistance to NNRTIs were the most commonly detected in our study, representing nearly three-fourths of drug-resistant cases among MSM and all (six of six) drug-resistant cases among SEM females and FSW. Data from WHO indicate prevalence of drug resistance to NNRTIs was up to 10% of adults starting HIV treatment and from 50% to 97% among persons failing NNRTI-based treatment regimens[3,4,7–9]. A systematic review and meta-analysis of 212 studies found the prevalence of transmitted resistance to NNRTIs increasing among MSM[24–28]. The high prevalence of drug resistance, particularly to NNRTIs, emphasizes the need to scale up viral load monitoring, enhance adherence counselling, and promptly switching individuals with treatment failure, as recommended by the WHO[11–14]. The high prevalence of NNRTI also suggest replacing NNRTIs with more optimized ARV drugs such as integrase inhibitor-containing regimens. From 2019, the Vietnam Ministry of Health recommended integrase inhibitor-containing regimens (dolutegravir-based) for PLHIV on ART.

We acknowledge limitations to our study. First, the sample size was small with respect to the number of isolates obtained, allowing for the detection of key mutations and strains, but not precisely estimating prevalence. Moreover, while detection in the HSS+ demonstrates the presence of a strain or mutation, non-detection does not prove its absence. The sample size can be increased in future HSS+ surveys by expanding recruitment at existing sites, adding new sites and provinces, and accumulating data over multiple years. Second, information collected on antiretroviral treatment history by self-report was uncertain. Many participants responded “don’t know” or declined to answer. Without complete treatment history, the HSS+ data cannot accurately determine if HIV drug resistance is transmitted or acquired. While stigma may contribute to non-response, enhanced training of interviews might improve data collection. Additionally, HSS+ could add ART metabolite testing to verify treatment status. Third, while the addition of recency testing holds promise to distinguish strains currently circulating, in the present analysis, there were too few recent infection cases for meaningful interpretation. The sample size for isolates from cases with recent infection can also be increased over time and with expansion of recruitment at sites and increasing the number of sites.

Despite limitations, the HSS+ in Vietnam shows promise as a system to detect and track HIV drug resistance and the emergence of new strains in community-recruited samples of key populations. With system strengthening with regards to sample size, quality of epidemiological data, and addition of testing for ART metabolites, HSS+ can provide more precise and accurate molecular epidemiological data. HSS+ data can help guide the public health response to the HIV epidemic, linking newly diagnosed cases to treatment, and helping Vietnam maintain a target for HIV drug resistance below 15%[25–29]. Finally, our study data suggests that HSS+ can act as an early warning system in identifying emerging trends in the epidemic among the populations most severely affected by HIV.

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REFERENCES

1. Vietnam Administration of HIV/AIDS Control (VAAC) - Ministry of Health. HIV epidemic data - 2020. https://vaac.gov.vn/bao-cao-tong-ket-cong-tac-phong-chong-hiv-aids-nam-2020.html
2. World Health Organization (WHO). HIV drug resistance report 2021. 2021.
3. Vietnam Administration of HIV/AIDS Control (VAAC) - Ministry of Health. Report on HIV/AIDS in 2020. 2021. 124/BC-BYT.
4. World Health Organization (WHO). Key facts HIV-2020. Accessed 09/10, 2022. https://cdn.who.int/media/docs/default-source/hq-hiv-hepatitis-and-stis-library/key-facts-hiv-2020.pdf?sfvrsn=582c3f6e_3
5. Vietnam MOH. Decision No. 5418/QD-BYT, Guideline for HIV/AIDS treatment and care. In: MOH, editor. 2017.
6. Mai HT, Le GM, Tran BX, et al. Adherence to antiretroviral therapy among HIV/ AIDS patients in the context of early treatment initiation in Vietnam. Patient Prefer Adherence. 2018;12:2131–2137. doi:10.2147/PPA.S175474 [PubMed: 30349207]
7. Paraskevis D, Hatzakis A. Global molecular epidemiology of HIV-1: the chameleon challenge. Lancet Infect Dis. Feb 2019;19(2):114–115. doi:10.1016/S1473-3099(18)30687-X [PubMed: 30509776]
8. Clutter DS, Jordan MR, Bertagnolio S, Shafer RW. HIV-1 drug resistance and resistance testing. Infect Genet Evol. Dec 2016;46:292–307. doi:10.1016/j.meegid.2016.08.031 [PubMed: 27587334]
9. Ministry of Heath. The HIV drug resistance preventive and monitoring plan in the period from 2019 to 2023. In: VAAC, editor. 6036/QD-BYT, 05/10/2018. Ha Noi: Ministry of Heath; 2018.
10. Pham QD, Wilson DP, Nguyen TV, et al. Projecting the epidemiological effect, cost-effectiveness and transmission of HIV drug resistance in Vietnam associated with viral load monitoring strategies. J Antimicrob Chemother. May 2016;71(5):1367–79. doi:10.1093/jac/dkv473 [PubMed: 26869689]
11. Garcia C, Rehman N, Lawson DO, Djiadeu P, Mbuagbaw L. Developing Reporting Guidelines for Studies of HIV Drug Resistance Prevalence: Protocol for a Mixed Methods Study. JMIR Res Protoc. May 13 2022;11(5):e35969. doi:10.2196/35969 [PubMed: 35559984]
12. Vietnam Administration of HIV/AIDS Control (VAAC) - Ministry of Health. Prevalence of HIV, Syphilis, and Related Risk Behaviors among Men Who Have Sex with Men, People Who Inject Drugs, and Female Sex Workers in Vietnam. 2021.
13. Nguyen TV, Tran HP, Khuu NV, et al. Increases in both HIV and syphilis among men who have sex with men in Vietnam: Urgent need for comprehensive responses. International journal of STD & AIDS. Dec 2021;32(14):1298–1307. doi:10.1177/09564624211036421 [PubMed: 34392717]
14. World Health Organization (WHO). Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. 2015.
15. Dat VQ, Duong BD, Nhan DT, et al. Viral load suppression and acquired HIV drug resistance in adults receiving antiretroviral therapy in Viet Nam: results from a nationally representative survey. Western Pac Surveill Response J. Jul-Sep 2018;9(3):16–24. doi:10.5365/wpsar.2018.9.1.008

16. UNAIDS. Recent infection testing algorithm technical update. 2018.
17. Luk KC, Holzmayer V, Ndembi N, et al. Near full-length genome characterization of an HIV type 1 CRF25_cpx strain from Cameroon. AIDS Res Hum Retroviruses. Oct 2008;24(10):1309–14. doi:10.1089/aid.2008.0124 [PubMed: 18851680]
18. Yamaguchi J, Badreddine S, Swanson P, Bodelle P, Devare SG, Brennan CA. Identification of new CRF43_02G and CRF25_cpx in Saudi Arabia based on full genome sequence analysis of six HIV type 1 isolates. AIDS Res Hum Retroviruses. Oct 2008;24(10):1327–35. doi:10.1089/aid.2008.0101 [PubMed: 18844465]
19. Yebra G, Frampton D, Gallo Cassarino T, et al. A high HIV-1 strain variability in London, UK, revealed by full-genome analysis: Results from the ICONIC project. PLoS One. 2018;13(2):e0192081. doi:10.1371/journal.pone.0192081 [PubMed: 29389981]
20. Xiao P, Li J, Fu G, Zhou Y, Huan X, Yang H. Geographic Distribution and Temporal Trends of HIV-1 Subtypes through Heterosexual Transmission in China: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health. Jul 24 2017;14(7)doi:10.3390/ijerph14070830
21. Winichakoon PT, Siripong. The Emerging of CRF01_AE: A Clinical Story and Future HIV/AIDS Situation in Thailand. Current HIV Research. 2020;18:11.
22. Piyanot Wirachsilp WK, Suporn Foongladda, Thippawan Chuenchitra, Surapol Kohriangudom, Niracha Athipanyasilp, Sombat Tanprasertsuk, Malee Gasitrongand Ruengpung Sutthent,. Surveillance of subtype and genetic variation ofthe circulating strains of HIV-1 in Thailand. Southeast Asian J Trop Med Public Health. 2007;38 [PubMed: 17539244]
23. Li J, Feng Y, Shen Z, et al. HIV-1 Transmissions Among Recently Infected Individuals in Southwest China are Predominantly Derived from Circulating Local Strains. Sci Rep. Aug 27 2018;8(1):12831. doi:10.1038/s41598-018-29201-3 [PubMed: 30150680]
24. Liang B, Huang Q, Ou Y, et al. Trends and associated factors in the uptake of HIV testing among female sex workers in Sino-Vietnam border areas in Guangxi, China: a cross-sectional study. BMC Infect Dis. May 19 2022;22(1):479. doi:10.1186/s12879-022-07459-3 [PubMed: 35590271]
25. Do HT, Nguyen DT, Nguyen LAT, et al. An Alarmingly High Proportion of HIV-1 Isolates Carrying Mutations Corresponding to Resistance to Antiretroviral Drugs among HIV-Positive High-Risk Groups in Central Vietnam: a Substudy of the National Sentinel Survey. Jpn J Infect Dis. Nov 22 2017;70(6):621–627. doi:10.7883/yoken.JJID.2016.512 [PubMed: 28890504]
26. Ngo-Giang-Huong N, Huynh THK, Dagnra AY, et al. Prevalence of pretreatment HIV drug resistance in West African and Southeast Asian countries. J Antimicrob Chemother. Feb 1 2019;74(2):462–467. doi:10.1093/jac/dky443 [PubMed: 30418575]
27. Dat VQ, Anh NTL, Van Nghia K, et al. The prevalence of pre-treatment and acquired HIV drug resistance in Vietnam: a nationally representative survey, 2017–2018. J Int AIDS Soc. Feb 2022;25(2):e25857. doi:10.1002/jia2.25857
28. Pham QD, Wilson DP, Law MG, Kelleher AD, Zhang L. Global burden of transmitted HIV drug resistance and HIV-exposure categories: a systematic review and meta-analysis. AIDS. Nov 28 2014;28(18):2751–62. doi:10.1097/QAD.0000000000000494
29. Ministry of Heath. The HIV drug resistance preventive and monitoring plan in the period from 2019 to 2023, Vietnam Administration of HIV/AIDS Control (VAAC). 2018.

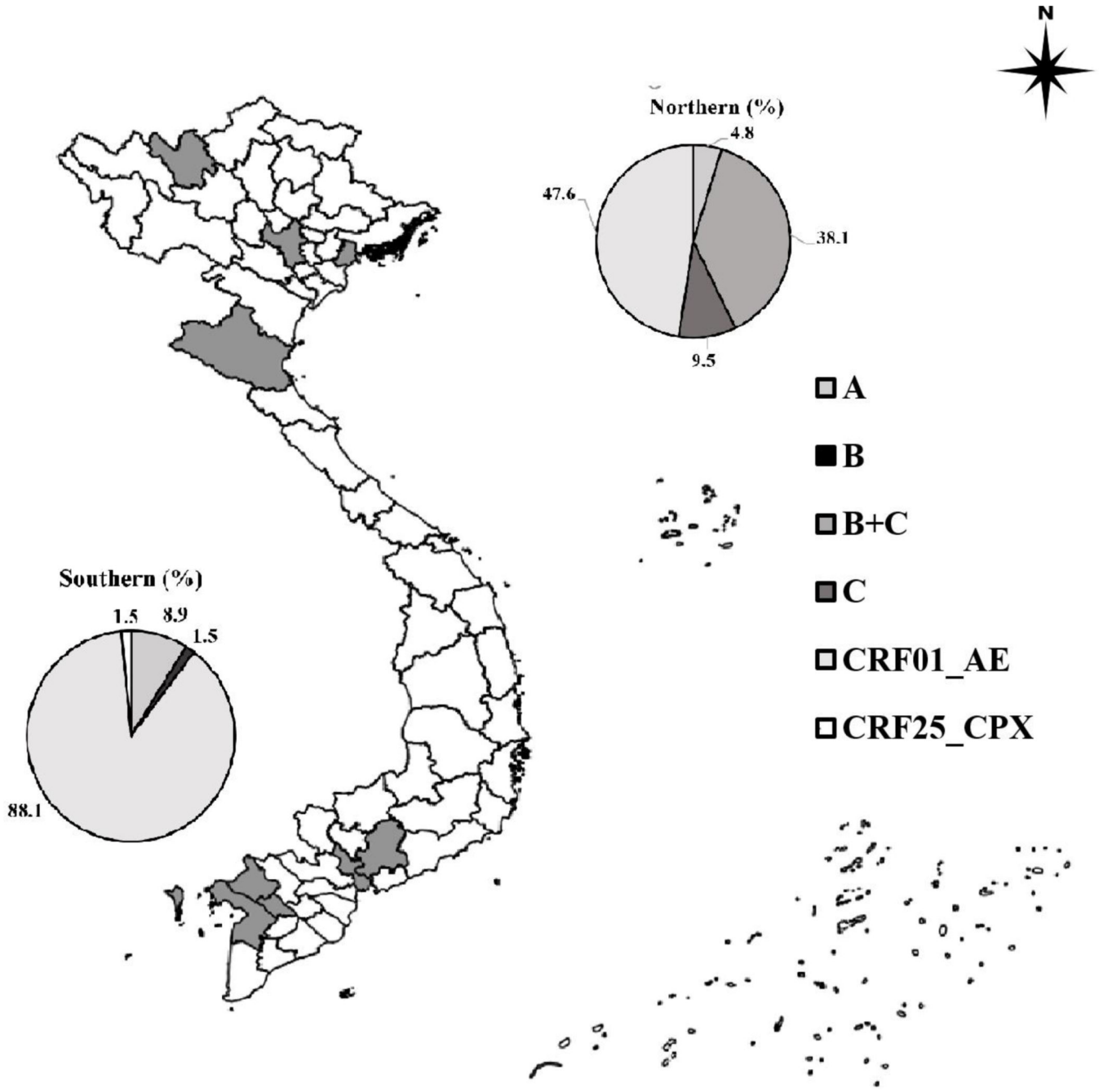

Figure 1.

Prevalence of HIV-1 subtypes among men who have sex with men, SEM females and female sex workers in Vietnam, 2018–2020 (n=156)

The map illustrates the provinces in Vietnam (grey) that participated in the HIV sentinel surveillance (HSS+) program. The pie chart shows the prevalence of each subtype that circulate within the northern (Subtype A - 4.8%, B+C - 38.1%, C - 9.5%, CRF01_AE - 47.6%) and southern regions (A - 8.9%, B – 1.5%, CRF01_AE – 88.1%, CRF25_cpx – 1.5%).

Table 1:

HIV-1 subtypes detected among men who have sex with men, SEM females and female sex workers in the Northern and Southern regions of Vietnam participating in the HIV sentinel surveillance (HSS+) program, 2018–2020.

Subtype	Men who have sex with men (N=130)		SEM females and female sex workers (N=26)	
	Northern n (%)	Southern n (%)	Northern n (%)	Southern n (%)
A	1 (11.1)	12 (9.9)	0	0
B	0	2 (1.7)	0	0
B+C	8 (88.9)	0	0	0
C	0	0	2 (16.7)	0
CRF01_AE	0	105 (86.8)	10 (83.3)	14 (100)
CRF25_cpx	0	2 (1.7)	0	0
Total	9 (100)	121 (100)	12 (100)	14 (100)

Table 2.

Demographic, risk, and clinical characteristics of men who have sex with men, SEM females and female sex workers tested for HIV drug resistance in regions of Vietnam participating in the HIV sentinel surveillance (HSS+) program, 2018–2020.

	Men who have sex with men (MSM)		SEM females and female sex workers (FSW)	
	Total HIV with VL >1000 copy/ml, N=130	HIV drug resistance detected n=20	Total HIV with VL >1000 copy/ml, N=26	HIV drug resistance detected n=6
	n (%)	n (%)	N (%)	N (%)
Total	130 *	20(15.4)	26	6 (23.0)
Age group in years				
<35	8 (6.1)	2 (10.0)	15 (57.7)	3 (50.0)
≥35	122 (93.9)	18 (90.0)	11 (42.3)	3 (50.0)
Current marital status				
Unmarried	113 (86.9)	14 (70.0)	5 (19.2)	3 (50.0)
Married	2 (1.5)	1 (5.0)	8 (30.8)	3 (50.0)
Living with male partner	15 (11.5)	5 (15.0)	13 (50.0)	0 (0)
Highest level of education				
Less than primary	0 (0)	0 (0)	2 (7.7)	1 (16.7)
Primary (Grade 1–5)	7 (5.4)	0 (0)	11 (42.3)	3 (50.0)
Secondary school (Grade 6–9)	29 (22.3)	6 (30.0)	11 (42.3)	2 (33.3)
High school (Grade 10 – 12)	36 (27.7)	6 (30.0)	2 (7.7)	0 (0)
College, university	58 (44.6)	8 (40.0)	0 (0)	0 (0)
Province				
Northern Vietnam				
Lao Cai	0 (0)	0 (0)	3 (11.5)	1 (16.7)
Ha Noi	4 (3.1)	--	1 (3.8)	0 (0)
Hai Phong	5 (3.8)	1 (5.0)	5 (19.2)	1 (16.7)
Nghe An	0 (0)	0 (0)	3 (11.5)	1 (16.7)

	Men who have sex with men (MSM)		SEM females and female sex workers (FSW)	
	Total HIV with VL >1000 copy/ml, N=130	HIV drug resistance detected n=20	Total HIV with VL >1000 copy/ml, N=26	HIV drug resistance detected n=6
	n (%)	n (%)	N (%)	N (%)
Southern Vietnam				
An Giang	22 (16.9)	3 (15.0)	8 (30.8)	2 (33.3)
Can Tho	60 (46.2)	6 (30.0)	0 (0)	-
Đồng Nai	--	--	1 (3.8)	0 (0)
Ho Chi Minh	26 (20.0)	7 (35.0)	1 (3.8)	1 (16.7)
Kien Giang	13 (10.0)	3 (15.0)	4 (15.4)	0 (0.0)
Ever had sex with multiple partners at the same time				
Yes	14 (10.8)	4 (20.0)	--	--
No	116 (89.2)	16 (80.0)	--	--
Ever injected drugs				
Yes	7 (5.4)	2 (10.0)	8 (30.8)	3 (50.0)
No	123 (94.6)	18 (90.0)	18 (69.2)	3 (50.0)
HIV status of partner (self-report)				
Positive	7 (5.4)	1 (5.0)	6 (23.1)	1 (16.7)
Negative	19 (14.6)	4 (20.0)	6 (23.1)	1 (16.7)
Missing	104 (80.0)	15 (75.0)	14 (53.8)	4 (67.7)
HIV recency				
Long term	102 (78.5)	17 (85.0)	24 (92.3)	4 (66.7)
Recent	23 (17.7)	1 (5.0)	0 (0)	0 (0)
Missing	5 (3.8)	2 (10.0)	2 (7.7)	2 (33.3)
Antiretroviral treatment (self-report)				
Yes	28 (21.5)	5 (25.0)	3 (11.5)	0 (0)
No	73 (56.2)	10 (50.0)	13 (50.0)	2 (33.3)

	Men who have sex with men (MSM)		SEM females and female sex workers (FSW)	
	Total HIV with VL >1000 copy/ml, N=130	**HIV drug resistance detected n=20**	**Total HIV with VL >1000 copy/ml, N=26**	**HIV drug resistance detected n=6**
	n (%)	**n (%)**	**N (%)**	**N (%)**
Don't know/Don't answer	29 (22.3)	5 (25.0)	10 (38.5)	4 (66.7)
Ever forgot to take medicine (self-report; n=5 MSM and n=3 SEM females and FSW with a history of ARV use)				
Ever forgot	2 (40.0)	2 (100)	2 (66.7)	0 (0)
Never forgot	3 (60.0)	0 (0)	1 (33.3)	0 (0)

*Some categories do not add up to total due to missing data. Note: "--" = no one recruited for the category, "0" = no one with detected drug resistance.

Table 3:

Resistance levels by HIV drug class among men who have sex with men, SEM females and female sex workers in regions of Vietnam participating in the HIV sentinel surveillance (HSS+) program, 2018–2020 (N=24)

Class/drug	Antiretroviral drug resistance mutations detected	Men who have sex with men resistance level (n=19)				SEM females and female sex workers resistance level (n=6)			
		Potential low	Low	Inter-mediate	High	Potential low	Low	Inter-mediate	High
Protease Inhibitor (PI) (major and accessory									
Atazanavir (ATV)	I54IS, M46L, G48S, V32L, L33F, I47S, I50S	1	2						
Lopinavir/ritonavir (LPV)	I54IS, M46L,G48S, V32L, L33F, I47S, I50S	1	2						
Nucleoside Reverse Transcriptase Inhibitor (NRTI)									
Abacavir/lamivudine (ABC)	A62AV, K65KR, D67DG, Y115YF, M184I **K70T*, V75M, M184V, T215A, K65R**		1		1			2	
Azidothymidine (AZT)	T215TS **K70T, V75M, M184V, T215A**		1				1		
Stavudine (D4T)	T215TS, A62AV, K65KR, D67DG, Y115YF **K70T, V75M, M184V, T215A, K65R**		1		1				2
Didanosine (DDI)	T215TS, A62AV, K65KR, D67DG, Y115YF, M184I **K70T, V75M, M184V, T215A, K65R**	2			1			1	1
Emtricitabine (FTC)	A62AV, K65KR, D67DG, Y115YF, M184I **K70T, V75M, M184V, T215A, K65R**			1	1			1	1
Lamivudine (3TC)	A62AV, K65KR, D67DG, Y115YF, M184I **K70T, V75M, M184V, T215A, K65R**			1	1			1	1
Tenofovir disoproxil fumarate (TDF)	A62AV, K65KR, D67DG, Y115YF **K70T, V75M, M184V, T215A, K65R**				1		1		1
Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI)									
Doravirine (DOR)	K103N, Y188H, V179T, Y318F, V106I, V106I, K103N, P225H **V106I, K103N, P225H, V179E, K101E, V106M, G190A**	3		2		2		1	1
Efavirenz (EFV)	K103N, Y188H, V179T, Y318F, K103N, P225H **K103N, P225H, V106I, V179E, K101E, V106M, G190A, V179D**	1			2	2			3
Etravirine (ETR)	V106I, E138A **V106I, V179E, K101E, V106M, G190A, V179D**	4				2	1		1

Class/drug	Antiretroviral drug resistance mutations detected	Men who have sex with men resistance level (n=19)				SEM females and female sex workers resistance level (n=6)			
		Potential low	Low	Inter-mediate	High	Potential low	Low	Inter-mediate	High
Nevirapine (NVP)	K103N, Y188H, V179T, Y318F, V106I, P225H **V106I, K103N, K103N, P225H, V179E, K101E, V106M, G190A, V179D**	2		1	2	2	1	3	
Rilpivirine (RPV)	V106I, E138A **V106I, V179E, K101E, V106M, G190A, V179D**	2	2			2	1		1

*Bold indicates mutations detected among SEM females and female sex workers.