



**Karolinska
Institutet**

Department of Public Health Sciences

**Antiretroviral therapy among HIV-infected persons
in Northeastern Vietnam:**

*Impact of peer support on virologic failure and mortality in a
cluster randomized controlled trial*

ACADEMIC DISSERTATION

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Abstract

Background: Wide access to antiretroviral therapy (ART) has substantially improved the prognosis of patients living with HIV/AIDS (PLHIV). However, in resource-limited countries, sustaining ART programs to prevent drug resistance and treatment failure and to maximize the existing human resources is still challenging. In 2010, Vietnam had 254,000 PLHIV and 52,000 people accessed ART. Viral load (VL) testing has not been routinely performed for monitoring treatment failures due to the high cost and the necessity of advanced laboratory equipment. Peer support has been proven to improve quality of life, reduce stigma and to improve adherence to treatment. However, there is little known about the impact of peer adherence support on ART outcomes. The overall aim of this study was to assess the impact of peer support on virologic and immunologic treatment outcomes and mortality among HIV-infected patients by monitoring routinely a simple- and low- cost VL in a cluster randomized controlled trial in Quang Ninh, Vietnam. The primary outcome was virologic failure rate between intervention and control group.

Methods: A total of 640 HIV-infected patients recruited from 59 clusters (communes) were randomized into either intervention or control group. Both groups received first-line ART regimens according to the National Treatment Guidelines and were followed up for 24 months. Viral load (ExaVir™ Load) and CD4 counts were measured every 6 months. Patients in the intervention group received enhanced adherence support by 14 peer supporters. Survival analyses with Kaplan-Meier curve and Cox proportional hazard model were used to identify survival rate and risk factors for deaths. Causes of death were assessed through medical records and verbal autopsy questionnaire. Cluster longitudinal and survival analyses with intention-to-treat were used to study time to virologic failure and CD4 trends and to compare between the intervention and control groups. At baseline, we monitored the spread of infection and prevalence of transmitted drug resistance mutations (TDRMs) by analyzing 63 1000bp pol-gene sequences generated from 63 treatment-naïve HIV-1 CRF01_AE patients. Through the cohort, we determined the feasibility, sensitivity and specificity of ExaVir Load in 605 HIV treatment-naïve patients and compared the correlation and agreement of 60 samples between Roche Cobas TaqMan® VL and ExaVir Load.

Results: After 24 months of follow-up, 78% of the patients remained in the study, mortality rate was 11% (6.4/100 person-years), cumulative virologic failure rate (VL >1,000 copies/ml) was 7.2% and the median CD4 increase was 286 cells/μl. There were no significant differences between intervention and control groups in virologic failure rates (VL >1,000 copies/ml) [6.9% vs 7.5%, respectively, RR 0.93; (95%CI: 0.13-6.54), p=0.94], in the time to virologic failure [HR 1.0; (95%CI 0.5-1.7), p=0.94], in CD4 trends [Coeff. (95%CI: 0.2(-0.6;-0.9), p=0.69] and in mortality (Log-rank p=0.79). Risk factors for virologic failure were ART-non-naïve status [aHR 6.9;(95%CI 3.2-14.6); p<0.01]; baseline VL >100,000 copies/ml [aHR 2.3;(95%CI 1.2-4.3); p<0.05] and incomplete adherence (self-reported missing more than one dose during 24 months) [aHR 3.1;(95%CI 1.1-8.9); p<0.05]. From the cohort of 605 ART-treatment naïve patients, we found the virologic suppression rate (VL <200 copies/ml) after 24 months was 64% (intention-to-treat) and 94% among patients assessed with VL (on-treatment). Tuberculosis (TB) was the most common cause of death (40%). Risk factors for AIDS-related death were age ≥35 years, clinical stage 3 or 4, body mass index (BMI) <18 kg/m², CD4 count <100/μl, haemoglobin level <100 g/l, and plasma VL ≥100,000 copies/ml. The TDRMs including Y181C, L210W, L74I and V75M were found in 4/63 patients (6.3%). Phylogenetic analysis for calculating the time of the most recent common ancestor (tMRCA) was shown in two distinct groups: the small group (n=3) had tMRCA in year 1997.5 and the larger group had tMRCA in 1989.8. ExaVir Load and the Roche Cobas TaqMan showed a strong correlation ($r^2 = 0.97$), high agreement (log difference = 0.34; 95% CI -0.35;1.03), high sensitivity (98%) and high specificity (100%).

Conclusions: Enhanced adherence intervention by peer support had no impact on virologic failure and CD4 trends as well as on mortality after 24 months of ART initiation. Early deaths occurred among patients presented late to ART and majority of deaths were attributable to TB. Baseline VL ≥100,000 copies/ml was a predictive factor for virologic failure, CD4 changes and mortality. Transmitted drug resistance rate should be monitored regularly and prospectively in Vietnam. Using ExaVir Load is feasible to monitor efficacy of ART programs in resource-limited settings.

Keywords: HIV; AIDS; Vietnam; mortality; causes of death; peer support; antiretroviral therapy; viral load; ExaVir Load; virologic failure; virologic suppression; limited-resource settings; reverse transcriptase; CD4 count; CRF01_AE; transmitted drug resistance; tMRCA.

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