


# A 10-Years Risk of Cardiovascular Disease Among HIV-Positive Individuals Using BMI-Based Framingham Risk Score in Indonesia

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Linlin Lindayani, PhD<sup>1</sup> , Heni purnama, MNS<sup>2</sup>,  
Nunung Nurhayati, M.Kep<sup>3</sup>, Diwa Agus Sudrajat<sup>1</sup> and  
Taryudi Taryudi, PhD<sup>4</sup>

## Abstract

**Introduction:** Cardiovascular disease (CVD) is the primary cause of death in HIV patients. The number of HIV patients suffering from cardiovascular disease is almost twice as high as that of patients who are not HIV-positive.

**Objective:** The purpose of this study was to evaluate risk of cardiovascular disease among HIV-positive persons.

**Methods:** We conducted a cross-sectional study with HIV positive individuals at public health center and non-AIDS governmental organization. We enrolled people diagnosed with HIV, age over 30 years old, and on CVD medications. We collected data of demographic, anthropometric and clinical information, smoking history, and non-fasting cholesterol and blood glucose. Estimation of 10-years CVD risk was calculated using the BMI-based Framingham Risk Score.

**Results:** Of 150 participants enrolled, 66.7% were male and mean age was 38.09 (SD = 7.99) years. The mean current CD4 counts was 493.3 (SD = 139.8) cells/mm<sup>3</sup>. Female were younger, had a shorter duration living with HIV and a shorter duration of receiving ART than males. About 8.7% of respondents had a high risk of developing a CVD event in the next 10 years, and higher among females than males. The most common CVD risk factors were smoking, high blood pressure, and hypercholesterolemia.

**Conclusion:** Our study demonstrates that HIV positive persons who are at risk for developing CVD in the next 10-years. There is an increasing need for educational programs on CVD prevention for the HIV-positive person and to further facilitate the identification of persons at elevated risk in routine practice.

## Keywords

cardiovascular disease risk, early detection, Framingham risk score, HIV

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Cardiovascular disease (CVD) is the leading cause of non-acquired immunodeficiency syndrome (AIDS) related death among human immunodeficiency virus (HIV)-positive persons in the era of antiretroviral therapy (ART) (Farahani et al., 2016). Although total mortality had decreased dramatically from 1.5 million in 2000 to 1.1 million in 2015, CVD mortality has increased over time and contributes about 10% to 37% of all mortality causes (Farahani et al., 2016; Feinstein et al., 2016). CVD in people with HIV caused an increasing in-hospital mortality from 15% in 2015 to 20% in 2016 (Okeke et al., 2016). With additional life years of about 37.3 and 29.0 years when ART is initiated at age 20 and 35 years, respectively, many people are now

at elevated risk for aging-related diseases including CVD (Farahani et al., 2016; Teeraananchai et al., 2017). HIV-positive persons have been shown to have much higher

<sup>1</sup>Department of Medical Surgical Nursing, Sekolah Tinggi Ilmu Keperawatan PPNI Jawa Barat, Bandung, Indonesia

<sup>2</sup>Department of Community and Psychiatric Nursing, Sekolah Tinggi Ilmu Keperawatan PPNI Jawa Barat, Bandung, Indonesia

<sup>3</sup>Department of maternity Nursing, Sekolah Tinggi Ilmu Keperawatan PPNI Jawa Barat, Bandung, Indonesia

<sup>4</sup>Faculty of Engineering, Universitas Negeri Jakarta, Jakarta, Indonesia

## Corresponding Author:

Linlin Lindayani, STIKep PPNI Jawa Barat, Kampus I. Jalan Ahmad IV, No.32, Bandung, West Java, Indonesia.

Email: linlinlindayani@gmail.com



rates of CVD compared with the general population (11.13% versus 6.98%, respectively) (Triant et al., 2007). Previous study using heart rate variability indicator found means normal to normal (NN) that indicated instantaneous heart rate was significantly lower in HIV patients compared to controls (Lindayani, Darmawati, et al, 2019). The Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) study in 21 high-income countries reported the incidence rate of first cardiovascular events among persons with HIV was 5.8 per 1000 person-years (Sabin et al., 2013). CVD increases with age, from 3.65 per 1000 person-years in aged 40–45 years to 15.89 in those aged 60–65 years (Petoumenos et al., 2014). A meta-analysis of 20 studies reported the pooled relative risk of CVD was 2.0 fold-higher among HIV-positive persons on ART compared with the general population and 1.52 fold-higher compared with treatment-naïve ART (Islam et al., 2014). This urgently highlights the need for primary identification CVD prevention among HIV-positive individuals.

Several studies have highlighted the increased risk of CVD among HIV-positive persons, however, the type of CVD risk factors and duration of taking ART were varied among those studies (Bloomfield, 2011; De Socio et al., 2008; Muronya, 2011; Triant et al., 2007). Previous study suggested that long-term used of ART is associated with increased values of total cholesterol, low-density lipoprotein cholesterol (LDL-C) and triglycerides (TGs) and reduced values of high-density lipoprotein cholesterol (HDL-C) (Ballocca et al., 2016). Another study found that the risk of CVD was elevated in advanced naïve patients and tended to remain high in the first year of therapy as measured using brachial artery flow-mediated vasodilation (Maggi et al., 2017). In addition, patients with HIV infection exhibit higher rates of conventional CVD risk factors compared to the general population such as smoking or drink alcohol, dyslipidemia, hypertension, and metabolic syndrome (Glass et al., 2006; Vance et al., 2011). Furthermore, CVD risk factors may differs between countries according to ethnicity, environmental, genetic factors and populations' uptake of smoking cessation campaign (Clarke & Mousa, 2009; Elder, 2009; Jermendy et al., 2011).

Assessment of CVD risk for HIV population is fundamental to guide risk management. Limited research has been conducted predicting of CVD risk in low-income countries. Estimating CVD risk informs patients of their risk status and provides clinicians with tailored recommendations for lifestyle changes, specific medication therapy, or other preventive interventions. Therefore, early identification of the risk of CVD is important for identification of high-risk people who may be a candidate for primary prevention. The purpose of this study was to evaluate the risk of cardiovascular

disease among HIV-positive persons in a low-income country.

## Methods

### Study Design and Sample

This was a cross sectional study conducted at a Public Health Center and AIDS- non governmental organization in West Java, Indonesia. The population in this study were patients with HIV. The inclusion criteria were patients diagnosed with HIV confirmed by their medical records, aged more than 30 years old. The exclusion Criteria were diagnosed with heart disease or undergoing cardiac treatment. The sample technique used in this study was convenience sampling.

### Measurement

Demographic data and medical history were collected using standard online forms. Demographic data collected includes age, gender, education level, occupation, and marital status. Medical history including self-reported smoking status (current and previous), injecting drug use, family history of cardiovascular disease, diabetes, ART regimen and number of years, and years with HIV and Under ART. In addition, current CD4 counts were extracted from current laboratory values of patient's medical record.

Physical examination includes systolic and diastolic blood pressure, height, and weight. Blood pressure was measured by nurses through the brachial artery using a digital sphygmomanometer with an adult cuff on the day of data collection. The patient sits in an upright position in a quiet room; two consecutive blood pressure measurements were taken, and the average was recorded as the final result. Blood pressure was defined as high if systolic blood pressure  $\geq 140$  mmHg and diastolic blood pressure  $\geq 90$  mmHg (Pickering et al., 2005). Subjects were defined as thin if the BMI (body mass index)  $\leq 18.5$  kg/m<sup>2</sup>, normal (BMI ranging from 18.5 to 24.9), overweight (BMI starting from 25.0–29.9), and obesity (BMI  $\geq 30$ ). Non-fasting blood examinations were evaluated to measure total cholesterol and blood glucose.

Framingham Risk Score (FRS) is a CVD risk prediction model used to estimate the likelihood of people for developing CVD in the next 10-years. The 10-year risk estimate of CVD was the FRS using the formula based on BMI. The components of the BMI based were age, gender, and weight. FRS The formula for BMI is weight in kilograms divided by height in meters squared. The score based on BMI-based formula was introduced by D'Agostino et al. for an easier adoption in the field for public health use (Chia et al., 2015; D'Agostino et al., 2008).

## Procedure

Approval of the protection human subjects was obtained from the Institutional Review Board of the affiliated university. After obtaining written informed consent, the participant completed the questionnaire, completed a physical examination and lab work. Data collection was collected during patient visits in a public health center or AIDS-non governmental organization. Outcome measures and risk factors were collected at one time point. At the end, every participants was provided a leaflet that contained information of CVD prevention.

## Data Analysis

Descriptive statistic were used to describe participant characteristic and major variables using the means, standard deviation, or frequency. Differences between male and female on demographic and clinical information, and CVD risk factors were determined using independent t test and chi square test, p-values <0.05 were considered significant limits. Data was analyzed using statistical package for the social science (SPSS) version 22.00 for windows.

## Results

A total of 150 HIV-positive persons participated in this study. The mean age was 38.09 (SD = 7.99) years, and 66.7% were male (Table 1). The majority were married (77%), graduated from secondary education (80.7%),

and employed (87.7%). The mean years living with HIV was 9.47 (SD = 3.84), and the duration of receiving ART was 9.27 years (SD = 3.75). The mean (SD) CD4 cell count was 493.3 (SD = 139.8) cells/mm<sup>3</sup>. Female were younger (*p*-value = 0.001), had a shorter duration living with HIV (*p*-value = 0.001) and a shorter duration of receiving ART (*p*-value = 0.001) than males (Table 1).

Current smoking was higher among males than females respectively (90 vs 32%, *p* = 0.001) while more females than males were obese (42 vs 14%, *p* = 0.022), had hypercholesterol (more than 200 mg/dl) (52% vs 19%, *p* = 0.001), and had family history of CVD (44% vs 12%, *p* = 0.001). High blood pressure was present more often in males than in females (44% vs 24%, *p* = 0.001).

According to the Framingham estimation, about 8.7% of respondents had a high risk of developing a CVD event in the next 10 years, and higher among females than males (12% vs. 7%). Then, about 23.3% had a moderate risk and majority had a low risk (68%) (Figure 1).

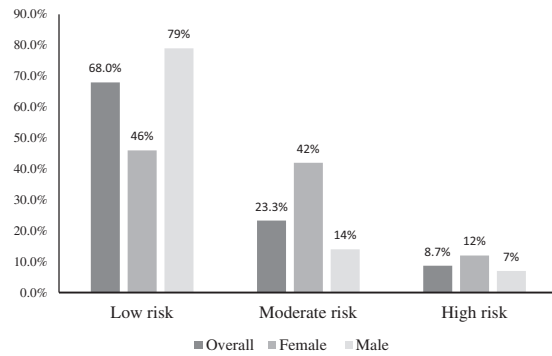
## Discussion

This study shows that approximately 8.7% of people with HIV in the low-income country were at high risk of cardiovascular disease, and 32% were at moderate risk (CVD). According to the World Health Organization (2018), 80% of non-communicable disease (NCD) death occurs in low-income countries, and CVD is the biggest burden. Globalization, rapid urban

**Table 1.** Demographics, HIV Information and CVD Risk Factors in HIV-Posit If Individuals Treated With ART by Gender.

	All participant N = 150, n (%)	Females N = 50, n (%)	Males N = 100, n (%)	p-value
<b>Demographic</b>				
Age (no.year)	38.09 ± 7.99	36.5 ± 8.57	40.9 ± 11.6	<i>0.001</i>
Married	115 (76.7)	50 (100)	65 (65)	<i>0.004</i>
Secondary education	121 (80.7)	37 (74)	84 (84)	<i>0.003</i>
Unemployed	20 (13.3)	5 (10)	15 (15)	0.358
<b>Clinical information</b>				
Years living with HIV, mean ± SD	8.03 ± 3.84	6.83 ± 4.21	9.24 ± 5.79	<i>0.001</i>
CD4 count (cells/mm <sup>3</sup> ), mean ± SD	493.3 ± 139.8	485.7 ± 112.4	499.6 ± 145.3	0.120
Duration of ART in months, mean ± SD	9.27 ± 3.75	6.54 ± 2.67	9.89 ± 4.13	<i>0.001</i>
<b>CVD risk factors</b>				
Diabetic mellitus (yes/no)	13 (8.7)	3 (6)	10 (10)	0.404
Family history of CVD (yes/no)	34 (22.6)	22 (44)	12 (12)	<i>0.01</i>
Current smoker (yes/no)	106 (70.6)	16 (32)	90 (90)	<i>0.001</i>
Previous smoker (yes/no)	14 (9.3)	4 (8)	10 (10)	0.350
Obesity (yes/no)	35 (23.3)	21 (42)	14 (14)	<i>0.022</i>
Cholesterol (mg/dl), mean ± SD	164.1 ± 45.37	178.9 ± 28.48	154.7 ± 21.67	<i>0.001</i>
Blood glucose (mg/dl), mean ± SD	197.5 ± 38.9	195.4 ± 31.4	201.8 ± 27.6	0.567
Systolic blood pressure (mmHg), mean ± SD	112.3 ± 9.37	114.6 ± 18.51	126.7 ± 15.13	0.605
Diastolic blood pressure (mmHg), mean ± SD	75.9 ± 5.79	74.37 ± 3.64	81.14 ± 6.69	<i>0.022</i>
Alcohol use (yes/no)	23 (15.3)	4 (8)	19 (19)	0.143

Significant values are in italic.



**Figure 1.** 10-Year Risk Estimate of CVD Based on BMI-Based Formula by Gender.

growth, sedentary living and unhealthy eating patterns and population-aged developments raise major challenges for government and public-health stakeholders (World Health Organization, 2011). In the low and middle-income countries, the prevalence of current regular smoking, low fruit and vegetables intake, lack of physical activity and high episode alcohol consumption were characterized by socioeconomic status (Hosseinpoor, 2012). Furthermore, barriers to CVD management arise at different healthcare levels, system-level barriers (especially the acute shortage of healthcare professionals) restrict the capability of low-income countries to manage CVD at primary care. Interventions at national level would benefit from the implementation of equity-focused interventions to minimize CVD risk, keeping in mind that demographic groups may vary in their ability to engage in such programs and/or experience of expected health advantages.

Although our study population was young, using the FRS risk equation 32% of participants had a 10-year moderate to high CVD risk. This finding is similar to a cross-sectional study conducted in Croatia ( $n = 254$ ) which reported that people with HIV have high risk of CVD, ranged from 27.2% as measured by FRS to 51.6% for the DAD score (Begovac et al., 2015). A study from Zimbabwe in HIV-positive individuals ( $n = 215$ , age ranged = 39.8-42.0, under ART = 3.9 years ( $SD = 3.4$ )) also highlighted 1.4% prevalence of high CHD risk within the next ten years using the Framingham risk estimation (Zhou et al., 2015). This estimation was lower than that in current study, it may due to the difference in duration of using ART, whereas in our study the mean duration of ART was more than 9 years. Interestingly, this study also found that females have a higher risk of CVD than males. This findings could be due to many females were obese, had family history of CVD, and hypercholesterol than males.

In our study, the common CVD risk factors were smoker, hypertension, and hypercholesterolemia. This was similar with previous study in Croatia and Serbia

reported that the most common traditional CVD risk factors among HIV-positive persons was hypertension and hypercholesterolemia (Begovac, 2015). Another study from Australia among adults with HIV infection found that the most common CVD risk factors were smoking (38%), hyperlipidaemia (16%) and hypertension (28%) (Chan, 2013). In the HIV outpatient study, at baseline, comorbid conditions were common, with high prevalence of overweight or obesity (50.0%), hypertension (47.8%), and hypercholesterolemia (16.9%), and 13.3% had been prescribed statins (Thompson-Paul, 2016). Different strategies to prevent CVD among HIV-positive persons is needed by referring to the common CVD risk factors.

We found that current smoking was the most common CVD risk factors. Prevalence of tobacco use among HIV positive reported higher than general population (Lindayani, Yeh, et al., 2019). A Data Collection on Adverse Events of Anti-HIV Drugs (D: A: D) study reported that HIV-positive smokers have a 1.43-fold increase in cardiovascular disease (CVD) events and 2.0-fold increase in of myocardia infarct compared with HIV-positive-non-smokers (Friis-Moller et al., 2016). Another study reported that menthol HIV-smokers were twice as likely to have hypertension and moderate to high CVD risk (Míguez-Burbano et al., 2014). Although health benefits of smoking cessation are well documented among HIV-positive individuals, there are no clinical practice guidelines to guide the provision of smoking cessation treatment in HIV-positive persons (Lindayani, Yeh, et al., 2019). Clinical evidence exists to support the use of a range of smoking cessation interventions in the general population. Innovative and effective interventions tailored to HIV population that will ultimately result in lower smoking prevalence and improved overall health.

One limitation of this study was due to the nature of its cross-sectional design, we could not determine causal effect of covariate on CVD risk factors. Furthermore, the information about tobacco and alcohol use were based on self-reported questions that may be limited by recall bias. We used non-random sampling to recruit participants with small sample size. Although this study may not represent whole population of HIV in Indonesia who receiving ART, this is probably the first in our country to explore CVD risk factors that could be useful information to raise awareness on non-communicable diseases prevention. In addition, we did not explore CVD risk among those who received cholesterol or hypertension medication. Thus, future studies may consider this issues in estimating CVD risk using FRS-BMI based.

In conclusion, the majority of our young HIV-population had low risk of CVD risk and one-third had moderate to high risk of CVD in the next



10 years. The most common traditional CVD risk factors were smoking, hypertension, and hypercholesterolemia. Future studies are needed to evaluate CVD risk factors by using specific tools for the HIV population with large sample size and using longitudinal design and CVD risk factors in HIV-positive persons.

### Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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### ORCID iD

Linlin Lindayani  <https://orcid.org/0000-0002-6153-7632>

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