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10-Year Cardiovascular Risk in Hypertensive Patients: Insights from Central Vietnam Using WHO 2019 Chart

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Abstract

Background: Assessing the 10-year cardiovascular disease (CVD) risk is crucial for effective prevention and management. Despite its significance, information is limited on CVD risk among hypertensive patients in primary care in Central Vietnam. We conducted this study to estimate 10-year CVD risk in primary care settings and explore its associated risk factors, using the 2019 WHO CVD risk chart.

Methods and Results: This cross-sectional study collected socio-demographic and clinical data through a standardized questionnaire. Cardiovascular risk was estimated using the WHO CVD risk charts for Southeast Asia. The prevalence of low, moderate, and high CVD risk was 52.1%, 38.9%, and 9.0%, respectively. Notably, men had significantly higher rates of moderate (48.6%) and high (17.6%) CVD risk than women (31.4 and 2.4%, respectively) ($P<0.001$). Age was a significant factor, with an increasing prevalence of moderate and high CVD risk as age advanced. Specifically, the 50-59 age group had a moderate risk of 18.6%, rising to 69.9% in the 70-74 age group. High CVD risk increased from 0.6% to 27.6% in the same age groups. Lower educational levels were associated with a higher proportion of moderate CVD risk. Smoking and excessive alcohol consumption were linked to elevated CVD risks (25.0% and 30.0%, respectively), surpassing those without these behaviors. Similar trends were observed for individuals with diabetes, high total cholesterol, and high blood pressure.

Conclusion: Approximately one-tenth of hypertensive patients face a high risk of developing CVDs within the next 10 years. A comprehensive approach, encompassing behavioral changes and the management of metabolic risk factors, is essential to reduce CVD risk effectively.**(International Journal of Biomedicine. 2024;14(2):246-252.)**

Keywords: blood pressure • hypertension • cardiovascular risk • risk chart

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Abbreviations

BP, blood pressure; **CVR**, cardiovascular risk; **CVD**, cardiovascular disease; **CV**, Central Vietnam; **TC**, total cholesterol.

Introduction

In 2019, CVDs accounted for 32% of global deaths, with more than 75% occurring in developing nations.[1] In Vietnam, the growing burden of heart-related issues stands out as a significant public health problem, reflecting the country's rapid economic growth and lifestyle changes. Over the past 10 years, CVDs have consistently been the leading cause of both death and disability in the country, with conditions like heart attacks and strokes contributing significantly. The prevalence of CVDs, including coronary artery disease and stroke, has consistently increased in recent years, making up 31% of all deaths in 2016, exceeding 170,000 fatalities.[2] Ischemic heart disease and stroke consistently ranked as leading causes of death in Vietnam.[3]

Predictable risk factors, such as age, gender, and lifestyle choices, significantly contribute to CVD development.[4-6] Among these, age is a non-modifiable factor, as the risk of CVD increases with advancing age. Age increases the risk of CVD, while gender differences tend to equalize post-menopause. Unhealthy dietary habits, tobacco use, family history, and physiological factors like hypertension, diabetes, and obesity further elevate cardiovascular risk (CVR). Awareness and management of these factors are vital for effective prevention.[4-6]

Calculating the 10-year CVD risk through risk prediction models proves to be a valuable tool for prevention and management.[7-9] This approach enables early identification of high-risk individuals, facilitating targeted interventions. Utilizing established charts assists healthcare providers in creating personalized treatment plans, optimizing resource allocation, and enhancing patient awareness. Given limited information on cardiovascular risk among hypertensive patients in CV's community health centers, we conducted this study to estimate 10-year CVD risk in primary care settings and explore its associated risk factors, using the 2019 WHO CVD risk chart.[8]

Materials and Methods

Study Design and Population

This analysis draws on data from an ongoing cross-sectional study, currently under peer review, aimed at evaluating medication adherence and hypertension knowledge among hypertensive patients in primary care settings across Central Vietnam. The dataset was obtained from community health centers in three provinces: Thua Thien Hue, Khanh Hoa, and Lam Dong, all situated in Central Vietnam. Within each province, one urban and one rural area were designated for inclusion in the study. Two to four community health centers in these areas were randomly selected to ensure a diverse participant pool. Recruitment followed a random process, selecting individuals at intervals of 5 from hypertensive patient lists at these community health centers, targeting 50 to 70 participants. Eligibility criteria encompassed individuals aged 40 to 74 diagnosed with primary hypertension, with exclusion criteria applied to those receiving treatment for less than six months or experiencing secondary hypertension or hypertension related to pregnancy.

Sample Size and Data Collection

To achieve a 5% margin of error and a study power of 99%, considering a reported medication adherence prevalence of 49.8% from a previous study, we calculated a sample size of 660 eligible subjects. To address potential non-response, we initially invited 792 patients, ultimately collecting data from 761 participants. Subsequently, we excluded 107 participants with a known history of cardiovascular events (e.g., stroke, coronary heart diseases), resulting in a sample size of 654 participants for CVD risk assessment using the WHO chart.[8]

Selected participants were asked to visit local community health centers on weekend mornings after refraining from eating or drinking. They were also requested to bring accurate blood pressure and cholesterol readings. A semi-structured, interviewer-administered questionnaire adapted from the WHO STEPS instrument was employed for data collection on CVD risk factors.[11] Information encompassed basic details, anthropometric measurements, personal behaviors, medication adherence, hypertension knowledge, and health metrics, including blood pressure (BP) and cholesterol levels. All team members underwent training to ensure a clear understanding of the study objectives and proper data collection procedures. The survey was conducted from March to June in the year 2023.

Variables

The study utilized the updated WHO CVD 2019 risk charts for Southeast Asia to estimate the ten-year risk of fatal or non-fatal cardiovascular events among hypertensive patients.[8] These laboratory-based charts incorporated parameters such as diabetes status, sex, age groups, smoking habits, blood cholesterol levels, and systolic BP, offering precise risk scores for individuals aged 40 to 74 without established CVDs, categorized into five groups. In our study, participants were further grouped into risk categories: low [very low and low] (<10%), moderate (10%–<20%), and high [high and very high] (≥20%). Current smokers were defined as those currently using or having quit smoking within the last 12 months, while diabetes was diagnosed by medical professionals or by the use of insulin or oral hypoglycemic drugs at the time of our survey. Hypercholesterolemia was identified as a blood TC value of ≥5.1 mmol/L. Blood pressure was measured using automatic sphygmomanometers, and controlled hypertension was defined as systolic BP <140 mmHg and diastolic BP <90 mmHg.[12]

Demographic information, personal medical history, and CVR factors were collected from participants. Education levels were stratified into three categories, depending on years of formal schooling: low (<6 years), middle (6-9 years), and high (>9 years). Occupations were grouped as manual workers (farmers, traders, housekeepers, and production roles), government staff, or other occupations (retirees, elderly, and unemployed). Most respondents belonged to the ethnic majority in Vietnam known as "Kinh." Urban and rural residences were determined based on administrative divisions within each province. Physical activity was assessed using metabolically equivalent tasks per minute per week (MET/min/week), with physical inactivity defined as having fewer than

600 MET/min/week of physical activity. Excessive alcohol consumption was categorized as more than 2 standard units per day or 14 standard units per week for men and more than 1 standard unit per day or 7 standard units per week for women.[11] Body mass index (BMI) was calculated as weight (kg) per height squared (m^2), with overweight defined as BMI from 23 to 24.9 kg/m^2 and obesity as BMI ≥25 kg/m^2.[13] Medication adherence was determined using the 5-item version of the self-report Medication Adherence Report Scale (MARS-5), where scores from 5 to 23 indicated non-adherence and scores of 24 to 25 were classified as adherent.[14]

Statistical analyses

We used EpiData Entry 3.1 to ensure precision in the data collection process. For descriptive and analytical purposes, we used SPSS 27.0. Inter-group comparisons were performed using the chi-square test. All analyses followed a two-sided approach; a probability value of $P<0.05$ was considered statistically significant.

Results

Table 1 outlines the socio-demographic characteristics of the 654 research participants. Among them, 370 were women, constituting 56.6% of the sample. Notably, individuals aged 60-69 represented half of the participants, with a higher proportion of women in this age group (53.0% vs. 44.4%). In the 70-74 age group, nearly one-fifth of the participants were men, showing a higher proportion than women (22.2% vs. 16.2%). Ethnic minorities constituted 7.3% of the participants. In terms of educational attainment, 40% of participants had a high level of education, with a higher prevalence among men than women. Manual workers comprised three-quarters of the participants, with a higher proportion of women in this category. Conversely, among employed or retired individuals, men outnumbered women.

The prevalence of smoking was 23.3%, with a significantly higher prevalence in men (45,8%) than in women (5.9%) ($P<0.001$).

Table 1.

Socio-demographic and clinical characteristics of the study population by gender.

Characteristics		Men n (%)	Women n (%)	Total n (%)	*P*-value
Overall (n)		284	370	654	
Age group	40-49	30 (10.6)	23 (6.2)	53 (8.1)	0.024
	50-59	65 (22.9)	91 (24.6)	156 (23.9)	
	60-69	126 (44.4)	196 (53.0)	322 (49.2)	
	70-74	63 (22.2)	60 (16.2)	123 (18.8)	
Residence	Urban	141 (49.6)	173 (46.8)	314 (48.0)	0.46
	Rural	143 (50.4)	197 (53.2)	340 (52.0)	
Ethnicity	Ethnic majority	263 (92.6)	343 (92.7)	606 (92.7)	0.95
	Ethnic minorities	21 (7.4)	27 (7.3)	48 (7.3)	
Educational level	Low	49 (17.3)	151 (40.8)	200 (30.6)	<0.001
	Medium	95 (33.5)	103 (27.8)	198 (30.3)	
	High	140 (49.3)	116 (31.4)	256 (39.1)	
Occupation	Manual worker	166 (58.5)	274 (74.1)	440 (67.3)	<0.001
	Governmental staff	28 (9.9)	17 (4.6)	45 (6.9)	
	Retired, Unemployed	90 (31.7)	79 (21.4)	169 (25.8)	
Health insurance	Yes	275 (96.8)	350 (94.6)	625 (95.6)	0.169
	No	9 (3.2)	20 (5.4)	29 (4.4)	
Smoking	Yes	130 (45.8)	22 (5.9)	152 (23.2)	<0.001
	No	154 (54.2)	348 (94.1)	502 (76.8)	
Excessive alcohol consumption	Yes	19 (6.7)	1 (0.3)	20 (3.1)	<0.001
	No	265 (93.3)	369 (99.7)	634 (96.9)	
Physical inactivity	Yes	156 (54.9)	237 (64.1)	393 (60.1)	0.018
	No	128 (45.1)	133 (35.9)	261 (39.9)	
Fruits & Vegetables	≥5 servings/day	176 (62.0)	236 (63.8)	412 (63.0)	0.634
	<5 servings/day	108 (38.0)	134 (36.2)	242 (37.0)	
BMI	Underweight	158 (55.6)	189 (51.1)	29 (4.4)	0.402
	Normal weight	13 (4.6)	16 (4.3)	347 (53.1)	
	Overweight,	52 (18.3)	88 (23.8)	140 (21.4)	
	Obesity	61 (21.5)	77 (20.8)	138 (21.1)	
Diabetes	Yes	37 (13.0)	48 (13.0)	85 (13.0)	1.00
	No	204 (71.8)	265 (71.6)	469 (71.7)	
	Unknown	43 (15.2)	57 (15.4)	100 (15.3)	
High TC	Yes	157 (55.3)	214 (57.8)	371 (56.7)	0.513
	No	127 (44.7)	156 (42.2)	283 (43.3)	
Hypertension control	Yes	220 (77.5)	319 (86.2)	539 (82.4)	0.004
	No	64 (22.5)	51 (13.8)	115 (17.6)	
Medication adherence	High	153 (53.9)	172 (46.5)	325 (49.7)	0.061
	Low	131 (46.1)	198 (53.5)	329 (50.3)	

Excessive alcohol consumption was found in 3.1% of the population, predominantly in men (6.7%), with a statistically significant difference ($P<0.001$). The prevalence of physical inactivity and overweight was higher in women than in men (64.1% vs. 54.9% and 23.8% vs. 18.3%, respectively). The prevalence of diabetes and high cholesterol stood at 13% and 56.7%, respectively, with no significant gender difference. Hypertension control was achieved in 82.4% of cases, with a higher proportion observed in women than in men (86.2% vs. 77.5%, $P=0.004$) (Table 1).

Table 2 displays the distribution of 10-year CVD risk across demographic factors. The prevalence of low, moderate, and high CVD risk was 52.1%, 38.9%, and 9.0%, respectively. Notably, men had significantly higher rates of moderate (48.6%) and high (17.6%) CVD risk than women (31.4 and 2.4%, respectively) ($P<0.001$). Age was a significant factor, with an increasing prevalence of moderate and high CVD risk as age advanced. Specifically, the 50-59 age group had a moderate risk of 18.6%, rising to 69.9% in the 70-74 age group. High CVD risk increased from 0.6% to 27.6% in the same age groups.

Table 2.

Distribution of 10-year risk for fatal or non-fatal cardiovascular events based on background characteristics.

Characteristics		CVD risk			*P*-value
		Low (<10%), n (%)	Moderate (10-20%), n (%)	High (>20%), n (%)	
Overall		341 (52.1)	254 (38.9)	59 (9.0)	
Gender	Men	96 (33.8)	138 (48.6)	50 (17.6)	<0.001
	Women	245 (66.2)	116 (31.4)	9 (2.4)	
Age group	40-49	51 (96.2)	2 (3.8)	0 (0.0)	<0.001
	50-59	126 (80.8)	29 (18.6)	1 (0.6)	
	60-69	161 (50.0)	137 (42.5)	24 (7.5)	
	70-74	3 (2.4)	86 (69.9)	34 (27.6)	
Residence	Urban	160 (51.0)	116 (36.9)	38 (12.1)	0.029
	Rural	181 (53.2)	138 (40.6)	21 (6.2)	
Ethnicity	Ethnic majority	310 (51.2)	240 (39.6)	56 (9.2)	0.188
	Ethnic minorities	31 (64.6)	14 (29.2)	3 (6.3)	
Educational level	Low	86 (43.0)	96 (48.0)	18 (9.0)	0.016
	Medium	117 (59.1)	65 (32.8)	16 (8.1)	
	High	138 (53.9)	93 (36.3)	25 (9.8)	
Occupation	Manual worker	251 (57.0)	162 (36.8)	27 (6.1)	<0.001
	Governmental staff	31 (68.9)	12 (26.7)	2 (4.4)	
	Retired, Unemployed	59 (34.9)	80 (47.3)	30 (17.8)	
Health Insurance	Yes	324 (51.8)	245 (39.2)	56 (9.0)	0.677
	No	17 (58.6)	9 (31.0)	3 (10.3)	
Home BP monitoring	Yes	137 (50.2)	107 (39.2)	29 (10.6)	0.429
	No	204 (53.5)	147 (38.6)	30 (7.9)	
Smoking	Yes	29 (19.1)	85 (55.9)	38 (25.0)	<0.001
	No	312 (62.2)	169 (33.7)	21 (4.2)	
Excessive alcohol consumption	Yes	7 (35.0)	7 (35.0)	6 (30.0)	0.004
	No	334 (52.7)	247 (39.0)	53 (8.4)	
Physical inactivity	Yes	196 (49.9)	157 (39.9)	40 (10.2)	0.253
	No	145 (55.6)	97 (37.2)	19 (7.3)	
Fruits & Vegetables	≥5 servings/day	223 (54.1)	152 (36.9)	37 (9.0)	0.380
	<5 servings/day	118 (48.8)	102 (42.1)	22 (9.1)	
BMI	Underweight	10 (34.5)	17 (58.6)	2 (6.9)	0.131
	Normal weight	173 (49.9)	137 (39.5)	37 (10.7)	
	Overweight	76 (54.3)	54 (38.6)	10 (7.1)	
	Obesity	82 (59.4)	46 (33.3)	10 (7.2)	
Diabetes	Yes	18 (21.2)	48 (56.5)	19 (22.4)	<0.001
	No	272 (58.0)	165 (35.2)	32 (6.8)	
	Unknown	51 (51.0)	41 (41.0)	8 (8.0)	
High TC	Yes	175 (47.2)	154 (41.5)	42 (11.3)	0.005
	No	166 (58.7)	100 (35.3)	17 (6.0)	
Hypertension control	Yes	309 (57.3)	196 (36.4)	34 (6.3)	<0.001
	No	32 (27.8)	58 (50.4)	25 (21.7)	
Medication adherence	High	164 (50.5)	127 (39.1)	34 (10.5)	0.398
	Low	177 (53.8)	127 (38.6)	25 (7.6)	

Urban areas exhibited a higher prevalence of high CVD risk (12.1%) than rural areas (6.2%). Lower educational levels were associated with a higher proportion of moderate CVD risk. Smoking and excessive alcohol consumption were linked to elevated CVD risks (25.0% and 30.0%, respectively), surpassing those without these behaviors. Similar trends were observed for individuals with diabetes, high TC, and high BP. However, no significant differences were found in terms of physical inactivity, fruit and vegetable consumption, BMI, hypertension knowledge, or hypertension medication adherence.

Distinct patterns in the prevalence of elevated CVD risk emerged across age groups stratified by gender. Among men, the prevalence of high CVD risk increased notably, escalating from 1.5% in the 50-59 age group to 17.5% in the 60-69 age group and 42.9% in the 70-74 age group. In contrast, this increase was more gradual among women, starting at 1% in the 60-69 age group and reaching 11.7% in the 70-74 age group. The proportion of moderate CVD risk in the 50-59 and 60-69 age groups was significantly higher in men than in women (36.9% and 60.3% vs. 5.5% and 31.1%, respectively). However, in the 70-74 age group, this proportion was higher in women (83.3% vs. 57.1%). Additionally, the proportion of low CVR in women exceeded that in men across all age groups (Table 3).

Table 3.
Variation in CVD risk levels across age and gender of participants.

Gender	Age group	CVD risk		
		Low (<10%) n (%)	Moderate (10-20%) n (%)	High (>20%) n (%)
Men	40-49	28 (93.3)	2 (6.7)	0 (0.0)
	50-59	40 (61.5)	24 (36.9)	1 (1.5)
	60-69	28 (22.2)	76 (60.3)	22 (17.5)
	70-74	0 (0.0)	36 (57.1)	27 (42.9)
Women	40-49	23 (100.0)	0 (0.0)	0 (0.0)
	50-59	86 (94.5)	5 (5.5)	0 (0.0)
	60-69	133 (67.9)	61 (31.1)	2 (1.0)
	70-74	3 (5.0)	50 (83.3)	7 (11.7)

Discussion

Using a 10-year CVR chart is crucial in both clinical practice and community health for prevention. Firstly, it provides a standardized and evidence-based tool to assess an individual's risk of developing CVDs over a specific timeframe. This allows healthcare professionals to stratify patients based on risk levels, facilitating targeted interventions and personalized preventive strategies. Secondly, risk charts, such as the WHO CVD risk chart for Southeast Asia, integrate various risk factors, including age, gender, smoking, diabetes, TC, and hypertension, providing a comprehensive evaluation. In hypertensive patients, the CVD risk could be much higher than in the general community. In resource-limited areas like community health centers in Central Vietnam, employing such a tool enables primary healthcare practitioners to make informed decisions, optimize resource allocation, and improve CVD prevention and management outcomes. Our study provides information on the 10-year CVD risk in hypertensive patients in primary care settings in Central Vietnam.

In the present study, the overall prevalence of low, moderate, and high CVD risk was 52.1%, 38.9%, and 9.0%, respectively. It is crucial to note that the distribution of CVD risk varies across different countries in Asia.[15-18] Mongolia, Malaysia, and Cambodia exhibit notably low CVD risk, ranging from 89.6% in Mongolia to 94.4% in Malaysia and 97% in Cambodia.[17] Notably, the percentage of the population at high CVD risk is highest in Mongolia at 6%, compared to 2.3% in Malaysia and 1.3% in Cambodia. Bangladesh and Oman show an increase in the proportion of high CVD risk. In Bangladesh,[16] the prevalence of low, moderate, and high CVD risk was 69.5%, 25.9%, and 1.7%, respectively, while in Oman,[19] these proportions were 68.0%, 19.1%, and 12.9%, respectively. These differences could be attributed to distinct participant characteristics in each country. It is worth highlighting that the moderate and high CVD risk observed in our study is comparatively higher, given that we focused on estimating the 10-year CVD risk in hypertensive patients.

In our study, the prevalence of moderate and high CVD risk was significantly higher in men than in women. Moreover, these proportions increased with age, although the trends varied between genders. Among men, the prevalence of high CVD risk exhibited a notable rise, escalating from 0% in the 40-49 age group to 17.5% in the 60-69 age group and 42.9% in the 70-74 age group. In contrast, the increase was more gradual among women, starting at 0% in the 40-59 age group, rising to 1% in the 60-69 age group, and reaching 11.7% in the 70-74 age group. Similar patterns were observed in other Asian countries.[16-18] For instance, in Bangladesh,[16] the proportion of persons with high CVD risk increased from 0% in the 40–49 age group to 12.3% in those aged 70+, with a higher prevalence in men (17.6%) than in women (2.4%). In Cambodia,[17] high CVD risk among men increased from 0.6% in the 40-49 age group to 6.8% in the 60-64 age group, while among women, it increased from 0.2% to 3.4% in the same age groups. The observed gender differences in CVD risk can be attributed to the interplay of biological, hormonal, and lifestyle factors. Lifestyle choices such as higher rates of smoking and excessive alcohol consumption are more common in men, contributing to an elevated risk of cardiovascular events. Estrogen, the predominant hormone in women, is believed to have protective effects on the cardiovascular system. Therefore, considering male patients in CVD prevention and management is crucial to reduce the overall burden on the community.

The association between CVD risk and educational levels was evident in our study, aligning with findings from prior research in Nepal [18] and Oman.[19] For example, 52.3% of participants with no formal education exhibited elevated CVD risk compared to 16.0% among those with higher education in Oman. Educational levels have a discernible impact on patient knowledge and health behavior, a significance underscored by the prevalence of high-risk CVD cases among elderly individuals with lower educational attainment in our study. Enhancing knowledge and awareness of risk factors is crucial for preventing and mitigating CVD risk, as emphasized by the study conducted by Kubota.[20] Risk factors such as smoking, diabetes, high BP, and high TC were identified as significant contributors to increased CVD risk, aligning with key elements in various risk charts predicting CVD and corroborating findings from previous studies.[4,5,7,9]

Strengths and Limitations

This study represents the pioneering effort to estimate the total 10-year CVD risk among hypertensive patients in primary care settings in Central Vietnam. Our research adopts a novel approach, employing the updated WHO CVD 2019 risk chart. This chart, rooted in extensive research and epidemiological data, establishes a robust foundation for accuracy and reliability. Its simplicity and user-friendly design enhance accessibility for a diverse range of healthcare professionals, allowing for a swift assessment of CVR without the need for intricate calculations. The evidence generated from our study holds significance for healthcare planners and researchers, offering valuable insights for the development of effective interventions.

Despite these strengths, our study has certain limitations. The risk charts are primarily designed based on data from specific populations in Southeast Asia, lacking specificity for the Vietnamese population. While these charts encompass common risk factors like age, gender, smoking status, BP, and cholesterol levels, they may not fully consider emerging risk factors or individual variations that could influence cardiovascular risk. Consequently, there is a potential for underestimating CVD risk, a general limitation inherent in almost all CVD risk charts. Recognizing these limitations is crucial for interpreting the findings and underscores the need for ongoing research to refine risk assessments for specific populations.

Conclusion

The 10-year CVR among hypertensive patients in primary care settings in Central Vietnam emerged as notably high. The distribution revealed that 52.1% had low risk, 38.9% moderate risk, and 9.0% high risk. Moreover, the incidence of high CVD risk was significantly higher in men than in women, rising with advancing age. Educational level, occupation, smoking, excessive alcohol consumption, diabetes, high TC, and high BP emerged as robust indicators strongly associated with CVD risk. These findings highlighted the imperative of formulating and implementing targeted interventions for hypertensive patients in primary care settings, aiming to reduce the burden of CVDs. Recognizing the multifactorial nature of CVD risk and addressing these modifiable risk factors through tailored interventions is paramount for enhancing preventive strategies and overall cardiovascular health in this population.

Ethical Approval

The research obtained ethical approval from the University of Medicine and Pharmacy, Hue University, with the reference number H2023/027. Additional approvals were secured from the health departments of the three respective provinces. Adhering strictly to ethical standards, detailed explanations of the study's objectives and procedures were provided to all potential participants, and written informed consent was obtained before participating in the research.

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Disclosure and Competing Interests

The authors declare that they have no competing interests. The views presented in this paper are the views of the authors and not of the organizations present.

Data Availability

The data set is owned by the University of Medicine and Pharmacy, Hue University, and the research partners. The data set underlying the study's findings is available on request to Hoang Anh Tien, the corresponding author of this study.

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