

# Incidence and Associated Risk Factors of Hypertension among Apparently Healthy Adult Filipinos in the LIFECARE Philippine Cohort Study

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## ABSTRACT

**Objective.** This study aimed to estimate the incidence of hypertension and determine the risk factors for hypertension among apparently healthy adult Filipinos.

**Methods.** This observational prospective community-based study included apparently healthy adult individuals aged 20–50 years from the Life Course Study in Cardiovascular Disease Epidemiology (LIFECARE) Philippine cohort at baseline and followed-up after an average of four years. Sociodemographic data, psychosocial stress, and clinical and metabolic profiles were obtained and analyzed. Multivariable Cox regression analysis was performed to identify factors associated with the development of hypertension.

**Results.** A total of 2,089 non-hypertensive participants were included, with 59% women and average age of 35 years (SD = 8.4). The incidence rate of hypertension was 38.1 per 1,000 person-years. The cumulative incidence of hypertension over a mean follow-up time of four years was 15.4% (95% CI = 13.9–17.0%). The risk of incident hypertension was higher among males (aHR=1.3, 95% CI: 1.0–1.8;  $p=0.044$ ),  $\geq 40$  years old (aHR=3.9, 95% CI: 2.6–5.8;  $p<0.001$ ), family history of hypertension (aHR=1.4, 95% CI: 1.1–1.7;  $p=0.007$ ), abdominal obesity (aHR=1.4, 95% CI: 1.0–2.0;  $p=0.027$ ), baseline systolic blood pressure (SBP) of at least 130 mm Hg or diastolic blood pressure (DBP) of at least 80 mm Hg (aHR=5.1, 95% CI: 3.8–6.8;  $p<0.001$ ).

**Conclusion.** The 4-year incidence rate of hypertension among apparently healthy adult Filipinos is high. Increased age, male sex, family history of hypertension, abdominal obesity, and high normal blood pressure were significantly associated with the development of hypertension.

**Keywords:** hypertension, incidence, LIFECARE Philippines, Filipino

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## INTRODUCTION

Hypertension is the most common risk factor for the development of cardiovascular disease globally and in the Philippines.<sup>1,2</sup> It affects about 1 billion people worldwide; of these, two-thirds reside in developing countries such as the Philippines.<sup>3</sup> Approximately 12 million Filipinos had hypertension.<sup>4</sup> It is predicted that up to 1.58 billion adults worldwide will suffer from hypertension complications by 2025. It is primarily responsible for approximately 19% of all deaths and 9% of disability adjusted life years.<sup>5</sup> A three-year cross-sectional study conducted in Northern California, USA showed that Filipinos had the highest prevalence of hypertension compared to other racial and ethnic minority populations. Hypertension was more prevalent in male and female Filipinos than in their Japanese, Vietnamese, Korean, Mexican, Chinese, Asian Indian, and non-Hispanic white counterparts.<sup>6</sup> According to the PRESYON 4 trial, approximately 37% of Filipino adults have hypertension. Interestingly, only one in every five hypertensive patients (19%) was aware that they were hypertensive. Although the benefits of blood pressure treatment and control on cardiac and cerebrovascular outcomes are well established in the literature, one in three hypertensive Filipinos is not on anti-hypertensive medications; hence, they are at a significant risk for long-term cardiovascular complications. Despite these statistics, the level of hypertension awareness is low, especially in lower middle-income countries, such as the Philippines.<sup>7</sup>

Hypertension is usually defined as an office systolic blood pressure of  $\geq 140$  mm Hg and/or diastolic blood pressure of  $\geq 90$  mm Hg taken in two separate office visits.<sup>8</sup> This condition is caused by various mechanisms from disruption of the renal angiotensin aldosterone system in the young, leading to endothelial dysfunction and subsequent vascular remodeling that causes stiffening of the arterial tree, a feature of elderly hypertensive patients. Each increment in blood pressure by 20/10 mm Hg above 115/75 mm Hg showed a proportional doubling of coronary artery disease and stroke mortality.<sup>5</sup> In fact, high blood pressure accounts for approximately 54% of all strokes and 47% of ischemic heart disease events worldwide.<sup>9</sup> Projections have been made for the expected reduction in morbidity and mortality resulting from a 10-12 mm Hg reduction in systolic pressure and a 5-6 mm Hg reduction in diastolic pressure using data from multiple clinical trials performed over the past three decades. Although direct causality has not been proven, the estimated benefit from this magnitude of blood pressure reduction is a 38% risk reduction in stroke and a 16% risk reduction in coronary artery disease.<sup>10</sup>

Early and prompt intervention in hypertension treatment has the potential to diminish the detrimental effects and complications of chronic high blood pressure. Therefore, it is important to predict the development of hypertension in at-risk individuals.

Several international studies have explored possible predictors of hypertension development. Young adults with childhood hypertension, especially in combination with obesity are at a high risk of developing future hypertension.<sup>11</sup> Family history of hypertension and tachycardia is also a strong contributory risk factor.<sup>6</sup> Meanwhile, in a study done by Ursua et al., who examined the predictors of hypertension among Filipino immigrants in the US, they found out that older age, male sex, migration to the United States for over five years, a body mass index (BMI) greater than 23.0 kg/m<sup>2</sup>, an elevated glucose reading, a family history of hypertension, and fair to poor self-reported health status predicted the development of hypertension later in life.<sup>12</sup> According to the National Nutrition and Health Survey (NNHeS) 2013, the overall prevalence of high low density lipoprotein cholesterol (LDL-C) among Filipinos (defined as greater than 160 mg/dL) was at 47.2%, and the overall prevalence of low high density lipoprotein cholesterol (HDL-C) (defined as less than 40 and 50 mg/dL for males and females, respectively) was very high at 71.3%.<sup>2</sup> Hypercholesterolemia and low HDL-C levels were identified as predictors of hypertension.<sup>12</sup>

Interestingly, poor hypertension control among Filipinos in Hawaii was attributed to low medication adherence, lack of culturally and linguistically appropriate screening and educational materials, limited knowledge of health care systems, and lack of health insurance.<sup>13</sup> One of the less explored relationships is between stress and hypertension. Psychosocial stressors have been shown to predict hypertension in several cohorts. Low educational attainment, low occupational prestige, worry about job stability, feeling inadequate in one's job, social alienation, and depressive symptoms were found to be associated with the development of hypertension among Filipinos in California.<sup>14</sup> Specifically, multivariate analysis revealed that job insecurity, unemployment, and low self-reported job performance were independent predictors of hypertension in men. Low work status was an independent predictor of hypertension in women. The study highlights that in the general population, low occupational status and performance, and the threat or reality of unemployment increase the likelihood of developing hypertension independent of demographic and behavioral risk factors.

As a common risk factor for cardiovascular disease among Filipinos, it is important to determine its possible predictors to curb the prevalence of hypertension, and consequently, cardiovascular disease. Understanding and identifying the risk factors for hypertension that are unique to adult Filipinos will allow the design of more effective, holistic, and tailored community-based prevention strategies and interventions at the individual, community, and national levels. This study aimed to estimate the incidence of hypertension and determine the risk factors for hypertension among participants in the Philippine LIFECARE cohort. To the best of our knowledge, this is the first study to examine the incidence of hypertension in Filipino adults.

## METHODS

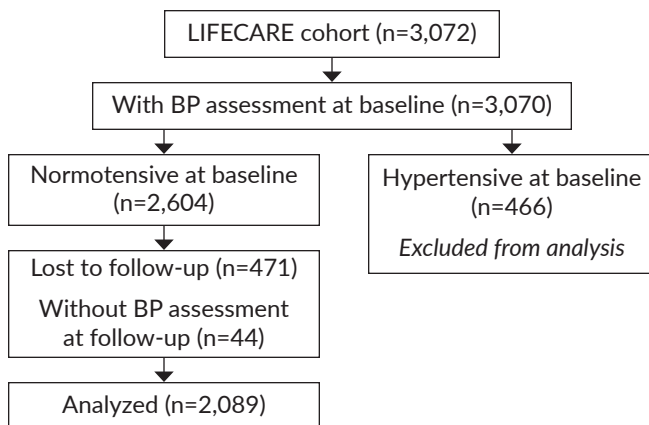
### Study Design and Participants

The LIFEcourse study in CARdiovascular disease Epidemiology (LIFECARE) is an international cohort study conducted in four Southeast Asian countries: the Philippines, Thailand, Malaysia, and Indonesia. The description of the cohort, manner of recruitment, and data collected have been previously published.<sup>15</sup> Over a span of nearly three years, the Philippine LIFECARE team was able to recruit 3,072 apparently healthy adults. The study was conducted in four provinces (Rizal, Batangas, Quezon, Bulacan) and one highly urban area (Metro Manila) in Luzon Island, the Republic of the Philippines.

Participants in the Philippine LIFECARE cohort were included in this analysis if they (1) were adult Filipinos aged 20-50 years old; (2) were free of previous cardiovascular diseases, such as stroke, myocardial infarction, or peripheral arterial disease; (3) had undergone baseline and follow-up examinations; and (4) were not classified as hypertensive at baseline. A total of 2,089 non-hypertensive participants with complete baseline and follow-up data after 3 to 5 years were included in the current analysis (Figure 1).

### Study Variables

The development of hypertension was determined in participants who were initially normotensive at baseline and were followed up after 3-5 years. The primary outcome variable used in the analysis was incident hypertension after follow-up, defined as a systolic blood pressure (SBP) measurement of at least 140 mm Hg and/or a diastolic blood pressure (DBP) measurement of at least 90 mm Hg, and/or self-reported anti-hypertensive medication use. Blood pressure was measured using an automated device (OMRON Model IA2) after at least five minutes of rest in the sitting position, using a cuff properly adapted to the arm size. Three BP measurements were obtained and the average of the readings was used for both SBP and DBP.



**Figure 1.** Flow diagram of the Philippine LIFECARE Cohort.

Body mass index (BMI) was computed as the weight in kilograms divided by the squared height in meters ( $\text{kg}/\text{m}^2$ ). The Asia-Pacific guidelines were used to classify BMI into four categories, underweight ( $<18.5 \text{ kg}/\text{m}^2$ ), normal ( $18.5\text{--}22.99 \text{ kg}/\text{m}^2$ ), overweight ( $23.0\text{--}24.99 \text{ kg}/\text{m}^2$ ), and obese ( $\geq 25.0 \text{ kg}/\text{m}^2$ ).<sup>16</sup>

Abdominal obesity using waist circumference was defined as waist circumference  $\geq 90$  cm for males and  $\geq 80$  cm for females. Abdominal obesity by waist-hip ratio was defined as  $\geq 0.9$  cm for males and  $\geq 0.85$  cm for females.

Using the World Health Organization (WHO) criteria for diabetes, participants were classified as diabetic if fasting plasma glucose was (FPG)  $\geq 7 \text{ mmol}/\text{L}$  ( $126 \text{ mg}/\text{dL}$ ) or self-reported intake of anti-diabetic medications.<sup>17</sup>

Metabolic syndrome was defined as the presence of any three of the following five component risk factors: (1) elevated BP with SBP  $\geq 130$  mm Hg or DBP  $\geq 85$  mm Hg or on drug treatment; (2) elevated triglyceride (TG)  $\geq 1.7 \text{ mmol}/\text{L}$  or on drug treatment; (3) elevated FBG  $\geq 5.5 \text{ mmol}/\text{L}$  or on drug treatment; (4) low HDL-C  $<1.0 \text{ mmol}/\text{L}$  for men,  $<1.3 \text{ mmol}/\text{L}$  for women or on drug treatment; and (5) abdominal obesity.<sup>18</sup>

Dyslipidemia was defined as any of the following: (1) high total cholesterol (TC)  $\geq 200 \text{ mg}/\text{dL}$ , (2) high triglyceride (TG)  $\geq 150 \text{ mg}/\text{dL}$ , (3) high LDL-C  $>130 \text{ mg}/\text{dL}$ , (4) low HDL-C  $<40 \text{ mg}/\text{dL}$  (male) or  $<50 \text{ mg}/\text{dL}$  (female), or (5) non-HDL-C (total cholesterol - HDL)  $>160 \text{ mg}/\text{dL}$ .

### Data Analysis

Frequencies and percentages were presented for categorical variables, whereas means and standard deviations were calculated for continuous variables. Time at risk was computed as the time elapsed between the baseline and follow-up visits. The incidence rate was expressed per 1,000 person-years and calculated as the number of incident cases of hypertension divided by the total number of person-years at risk. Bivariate test results with a *p-value*  $\leq 0.20$  were considered as candidates for the multivariable model. The full model included age, sex, civil status, employment status, family history of hypertension, BMI, waist circumference, total cholesterol, triglyceride, LDL-C, HDL-C, baseline BP, and fasting blood glucose. Multivariable Cox regression analysis was performed to determine risk factors associated with incident hypertension. Unadjusted and adjusted hazard ratios (HR), 95% confidence intervals, and *p-values* were presented. The Schoenfeld test was used to test for violation of proportional hazards. All statistical analyses were performed using Stata version 16 for Windows®.

## RESULTS

### Socio-demographic and Clinical Profile of Study Participants, and Bivariate Results

A total of 2,089 participants were included in the analysis, given that they were initially normotensive at baseline and

**Table 1.** Baseline Socio-demographic Characteristics of the Philippine LIFECARE Participants (N = 2,089)

	Frequency	%
<b>Age groups</b>		
20-29	604	28.9
30-39	779	37.3
40-50	706	33.8
<b>Age, mean (SD)</b>		
	35.1 (8.4)	
<b>Sex</b>		
Female	1,231	58.9
Male	858	41.1
<b>Civil status</b>		
Single/widow/separated	454	21.7
Married/live-in	1,635	78.3
<b>Educational attainment<sup>a</sup></b>		
Elementary level	434	20.8
High school level	1,152	55.2
College level	497	23.8
<b>Place of residence<sup>b</sup></b>		
Rural	1,086	52.0
Urban	1,003	48.0
<b>Employment status</b>		
Unemployed/student/retired	690	33.0
Employed	1,399	67.0
<b>Current smoker</b>		
Yes	570	27.3
No	1,519	72.7
<b>Alcohol drinker</b>		
Yes	1,178	56.4
No	911	43.6
<b>Perceived general health (SF-36 v2)<sup>c</sup></b>		
Excellent/very good	263	12.6
Good	1,320	63.2
Fair/poor	506	24.2
<b>EQ-5D pain subscale<sup>d</sup></b>		
No pain or discomfort	1,261	60.4
With moderate to extreme pain or discomfort	827	39.6
<b>Stress in the past 12 months</b>		
Never/some period of stress	1,785	85.4
Several periods to permanent	304	14.6
<b>Financial stress</b>		
None/little	703	33.7
Moderate	1,172	56.1
High/severe	214	10.2
<b>K10 score (depression)<sup>a</sup></b>		
Well	1,518	72.7
Mild mental disorder	382	18.3
Moderate mental disorder	139	6.7
Severe mental disorder	42	2.0

<sup>a</sup> Percentages may not add up to 100% due to missing data

<sup>b</sup> Rural/Urban classification was based on 2010 Census of Population and Housing, Philippine Statistics Authority

<sup>c</sup> Actual question was, "In general, would you say your health is excellent, very good, good, fair, poor?"

<sup>d</sup> Answer to the question, "Please indicate which statements best describe the state of your health today." I have no pain or discomfort; I have moderate pain or discomfort; I have extreme pain or discomfort

were followed-up within a period of five years. Approximately 59% were women, and the average age was 35 (SD =8.4) years old. Most (78%) of the participants were married or had a domestic partner, 79% had at least a high school level of education, a little more than half were residing in rural areas, and 67% reported to be employed. Over a quarter (27%) of the participants were current smokers and over half (56%) reported alcohol consumption (Table 1). Four out of ten participants were overweight or obese by the Asia-Pacific guidelines, 48% had family history of hypertension, and almost a fifth found to have metabolic syndrome (Table 2).

The cumulative incidence of hypertension over a mean follow-up time of four years was 15.4% (95% CI = 13.9 – 17.0%). The incidence rate of hypertension was 38.1 per 1,000 person-years (322 events out of 8,452.3 total person-time).

Sociodemographic characteristics associated with the development of hypertension included older age, male sex, marital status, a domestic partner, and employment status. Other factors associated with hypertension included family history of hypertension, higher BMI, baseline blood pressure, abdominal obesity measured by waist circumference, total cholesterol, triglyceride, LDL, fasting blood glucose, and metabolic syndrome. Increasing blood pressure levels at baseline were likely to develop hypertension after an average of four years (Table 3).

## Multivariable Cox Regression Results

Table 3 presents the crude and adjusted hazard ratios (HR) and 95% CIs for the development of incident hypertension. Males were 1.3 times more likely to develop hypertension compared to females (aHR=1.3, 95% CI: 1.0 – 1.8;  $p=0.04$ ), and participants at least 40 years old were 3.9 times more likely to have hypertension compared to participants aged 20-29 years old (aHR=3.9, 95% CI: 2.6 – 5.8;  $p<0.001$ ). Furthermore, participants with family history of hypertension were 1.4 times more likely to have the disease (aHR=1.4, 95% CI: 1.1 – 1.7;  $p=0.007$ ), and those who had baseline SBP of at least 130 mm Hg or DBP of at least 80 mm Hg tended to increase the risk of having hypertension by more than 5 times (aHR=5.1, 95% CI: 3.8 – 6.8;  $p<0.001$ ). Obese individuals were found to be 1.4 times more likely to have hypertension (aHR=1.4, 95% CI: 1.0 – 2.0;  $p=0.027$ ) compared to individuals with normal waist circumference.

## DISCUSSION

Prevalence of hypertension among Filipinos is decreasing from 23.9% (2014) to 19.2% (2018) according to the Philippines' National Nutrition and Health Survey (NNHeS) which is conducted every 4 to 5 years.<sup>2</sup> There have been many publications on its prevalence, and this is the first time that the incidence of hypertension was measured in a population-based longitudinal study among Filipinos with no pre-existing cardiovascular disease. In our LIFECARE study, the incidence rate was 38.1 per 1,000 person-years,

**Table 2.** Baseline Cardiovascular Risk Factors of the Philippine LIFECARE Participants (N = 2,089)

	Frequency	%
<b>Family history of hypertension</b>		
Yes	997	47.7
No	1,092	52.3
<b>BMI (Asia Pacific)</b>		
Normal	956	45.8
Underweight	230	11.0
Overweight	340	16.3
Obese	563	26.9
<b>Waist circumference</b>		
<90 cm (M), <80 cm (F)	1,429	68.4
≥90 cm (M), ≥80 cm (F)	660	31.6
<b>Waist-hip ratio</b>		
<0.9 cm (M), <0.85 cm (F)	200	9.6
≥0.9 cm (M), ≥0.85 cm (F)	1,889	90.4
<b>Total cholesterol (mmol/L)</b>		
Normal (<5.2)	1,475	70.6
Borderline high (5.2–6.1)	451	21.6
High (≥6.2)	163	7.8
<b>Triglyceride (mmol/L)</b>		
Normal (<1.7)	1,601	76.6
Borderline high (1.7–2.25)	271	13.0
High (≥2.26)	217	10.4
<b>LDL-C (mmol/L)</b>		
Normal (< 2.6)	791	37.9
Near or above optimal (2.6–3.3)	693	33.2
Borderline high (3.4–4)	430	20.6
High (≥4.1)	175	8.4
<b>HDL-C (mmol/L)</b>		
Low (<1.03)	1,194	57.2
Normal (1.03–1.54)	659	31.6
High (≥1.55)	236	11.3
<b>Diabetes<sup>a</sup></b>		
Yes	87	4.2
No	2,000	95.7
<b>Metabolic syndrome (modified NCEP)<sup>a</sup></b>		
Yes	397	19.0
No	1,690	80.9

<sup>a</sup> Percentages may not add up to 100% due to missing data

and the cumulative incidence was 15.4% over a mean follow-up time of four years in the Filipino cohort. There are sparse data on incidence rates and varied time frames for follow-ups, making it difficult to make direct comparisons across different populations.

The first reported incidence rate for hypertension was from the Framingham cohort, with the longest follow-up of 30 years. Two-year incidence rates were computed and showed 3.3% in males and 1.5% in females among those between aged 30 to 39 years, but higher among those 70–79 years of age at 6.2% in males and 8.6% in females.<sup>19</sup> Another US study, the Atherosclerosis Risk in Communities (ARIC), a multi-ethnic cohort that included Caucasians, African Americans, and a few Hispanics and Asians that looked into annual incidence over a 9-year period showed 3.5% in white males and 3.2% in white females but a higher rate in blacks

(5.8% in males and 6.4% in females). In Europe, the Polish Monitoring of Trends and Determinants of Cardiovascular Disease (Pol-MONICA) had an annual incidence rate over a 5-year period of 5.8% in both sexes.<sup>20</sup> In Asia, there are only two reports on the incidence of hypertension in China and India. The cardiometabolic risk reduction in South Asia (CARRS) cohort of India reported that one in six individuals developed hypertension over a period of two years (82.6 per 1,000 patient years, 95% CI: 80.8–84.4).<sup>21</sup> The Kailuan cohort of China reported an overall incidence rate of 44.3% over a period of 5.8 years which is nearly thrice higher than the Filipino cohort.<sup>22</sup>

Aging is a continuous process of decline in bodily function. The older a person becomes, the more co-morbid conditions that appear later in life. In NNHeS, the prevalence of hypertension increased 5-fold from an age group of 20–29 to 50–59 years. It has been postulated that aging leads to an increase in pro-inflammatory biomarkers, namely interleukin-6 (IL-6), C-reactive protein (CRP), and tumor necrosis alpha (TNF- $\alpha$ ), which are linked to an increase in intracellular oxidative stress and, eventually, endothelial dysfunction, the precursors of atherosclerosis.<sup>23</sup>

As stated above, males generally have a higher incidence of hypertension compared to their female counterparts in the early years of life. It has been postulated that this is due to circulating estrogen during the female reproductive years. This sex hormone promotes nitric oxide production and reduces endothelin-1 receptor levels resulting to vasodilatation. It upregulates angiotensin II type 2 receptor levels which reduces sodium reabsorption in the proximal tubule of the kidneys.<sup>24</sup>

Abdominal obesity was more strongly associated with the development of hypertension than was general obesity in our cohort. This was also observed in two large cohort studies, namely, the U.S. National Health and Nutrition Examination Survey (NHANES) and the China Health and Nutrition Survey (CHNS), even after adjusting for general obesity.<sup>25,26</sup> In a study by Seven et al., it was shown using abdominal ultrasound that an increase in visceral adipose tissue was associated with incident hypertension.<sup>27</sup> It was postulated to be mediated by physical compression of the kidneys by fat, which leads to the activation of the renin-angiotensin-aldosterone system and increased activation of the sympathetic nervous system.<sup>28</sup>

Family history has long been recognized as a risk factor for the development of hypertension, particularly parental hypertension. These findings have been observed in multiple cohorts in the USA.<sup>29–31</sup> This was postulated to be attributable to the shared environmental exposure and genetic susceptibility. However, our questionnaire did not particularly focus on parental history but on any member of the family from whichever generation they could recall. This may need to be validated in future studies among Filipinos if relatives beyond the parental level can be a factor in the development of hypertension.

**Table 3.** Risk Factors of Incident Hypertension among the Philippine LIFECARE Cohort<sup>a</sup>

	Total N 2,089	Hypertensive n (%) 322 (15.4)	Non-hypertensive n (%) 1,767 (84.6)	Crude HR (95%CI)	Adjusted HR (95% CI) <sup>b</sup>
<b>Age groups</b>					
20-29	604	36 (6.0)	568 (94.0)	1.0 (Ref)	1.00 (ref)
30-39	779	112 (14.4)	667 (85.6)	2.6 (1.8 – 3.8)**	2.3 (1.6 – 3.4)**
40-50	706	174 (24.6)	532 (75.4)	4.8 (3.4 – 6.9)**	3.9 (2.6 – 5.8)**
<b>Sex</b>					
Female	1,231	160 (13.0)	1,071 (87.0)	1.0 (Ref)	1.00 (ref)
Male	858	162 (18.9)	696 (81.1)	1.5 (1.2 – 1.9)**	1.3 (1.0 – 1.8)*
<b>Civil status</b>					
Single/widow/separated	454	53 (11.7)	401 (88.3)	1.0 (Ref)	1.00 (ref)
Married/live-in	1,635	269 (16.4)	1,366 (83.6)	1.5 (1.1 – 2.1)*	1.0 (0.7 – 1.3)
<b>Educational attainment</b>					
Elementary level	434	72 (16.6)	362 (83.4)	1.0 (Ref)	
High school level	1,152	170 (14.8)	982 (85.2)	0.8 (0.6 – 1.1)	
College level	497	79 (15.9)	418 (84.1)	0.8 (0.6 – 1.1)	
<b>Employment status</b>					
Unemployed/student/retired	690	83 (12.0)	607 (88.0)	1.0 (Ref)	1.00 (ref)
Employed	1,399	239 (17.1)	1,160 (82.9)	1.5 (1.2 – 2.0)**	1.0 (0.7 – 1.3)
<b>Place of residence</b>					
Rural	1,086	165 (15.2)	921 (84.8)	1.0 (Ref)	
Urban	1,003	157 (15.7)	846 (84.4)	1.0 (0.8 – 1.3)	
<b>Current smoker</b>					
No	1,519	234 (15.4)	1,285 (84.6)	1.0 (Ref)	
Yes	570	88 (15.4)	482 (84.6)	1.1 (0.8 – 1.4)	
<b>Alcohol drinker</b>					
No	911	129 (14.2)	782 (85.8)	1.0 (Ref)	
Yes	1,178	193 (16.4)	985 (83.6)	1.1 (0.8 – 1.3)	
<b>Perceived general health (SF-36 v2)</b>					
Excellent/very good	263	38 (14.4)	225 (85.6)	1.0 (Ref)	
Good	1,320	199 (15.1)	1,121 (84.9)	1.2 (0.8 – 1.7)	
Fair/poor	506	85 (16.8)	421 (83.2)	1.3 (0.9 – 1.8)	
<b>EQ-5D pain subscale</b>					
No pain or discomfort	1,261	192 (15.2)	1,069 (84.8)	1.0 (Ref)	
With moderate to extreme pain or discomfort	827	130 (15.7)	697 (84.3)	1.0 (0.8 – 1.2)	
<b>Stress in the past 12 months</b>					
Never/some period of stress	1,785	278 (15.6)	1,507 (84.4)	1.0 (Ref)	
Several periods to permanent	304	44 (14.5)	260 (85.5)	0.9 (0.6 – 1.2)	
<b>Financial stress</b>					
None/little	703	103 (14.6)	600 (85.4)	1.0 (Ref)	
Moderate	1,172	188 (16.0)	984 (84.0)	1.0 (0.8 – 1.2)	
High/severe	214	31 (14.5)	183 (85.5)	0.9 (0.6 – 1.4)	
<b>K10 score (depression)</b>					
Well	1,518	237 (15.6)	1,281 (84.4)	1.0 (Ref)	
Mild mental disorder	382	57 (14.9)	325 (85.1)	0.9 (0.7 – 1.3)	
Moderate mental disorder	139	21 (15.1)	118 (84.9)	1.0 (0.6 – 1.5)	
Severe mental disorder	42	6 (14.3)	36 (85.7)	0.8 (0.3 – 1.8)	
<b>Family history of hypertension</b>					
No	1,092	136 (12.4)	956 (87.6)	1.0 (Ref)	1.00 (ref)
Yes	997	186 (18.7)	811 (81.3)	1.4 (1.2 – 1.8)**	1.4 (1.1 – 1.7)*
<b>BMI (Asia Pacific)</b>					
Normal	956	99 (10.4)	857 (89.6)	1.0 (Ref)	1.00 (ref)
Underweight	230	11 (4.8)	219 (95.2)	0.5 (0.3 – 0.9)*	0.6 (0.3 – 1.2)
Overweight	340	70 (20.6)	270 (79.4)	2.0 (1.5 – 2.7)**	1.1 (0.8 – 1.6)
Obese	563	142 (25.2)	421 (74.8)	2.4 (1.9 – 3.1)**	1.0 (0.7 – 1.4)
<b>Waist circumference</b>					
<90 cm (M), <80 cm (F)	1,429	163 (11.4)	1,266 (88.6)	1.0 (Ref)	1.00 (ref)
≥90 cm (M), ≥80 cm (F)	660	159 (24.1)	501 (75.9)	2.1 (1.7 – 2.6)**	1.4 (1.0 – 2.0)*

**Table 3.** Risk Factors of Incident Hypertension among the Philippine LIFECARE Cohort<sup>a</sup> (continued)

	Total N 2,089	Hypertensive n (%) 322 (15.4)	Non-hypertensive n (%) 1,767 (84.6)	Crude HR (95%CI)	Adjusted HR (95% CI) <sup>b</sup>
<b>Total cholesterol</b>					
Normal	1,475	194 (13.2)	1,281 (86.8)	1.0 (Ref)	1.00 (ref)
Borderline high	451	93 (20.6)	358 (79.4)	1.4 (1.1 - 1.8) <sup>*</sup>	0.8 (0.6 - 1.1)
High	163	35 (21.5)	128 (78.5)	1.4 (1.0 - 2.0) <sup>*</sup>	0.7 (0.4 - 1.2)
<b>Triglyceride</b>					
Normal	1,601	206 (12.9)	1,395 (87.1)	1.0 (Ref)	1.00 (ref)
Borderline high	271	58 (21.4)	213 (78.6)	1.9 (1.4 - 2.5) <sup>**</sup>	1.2 (0.9 - 1.6)
High	217	58 (26.7)	159 (73.3)	2.2 (1.6 - 2.9) <sup>**</sup>	1.1 (0.8 - 1.5)
<b>LDL-C</b>					
Normal	791	96 (12.1)	695 (87.9)	1.0 (Ref)	1.00 (ref)
Near or above optimal	693	98 (14.1)	595 (85.9)	1.2 (0.9 - 1.6)	1.0 (0.7 - 1.3)
Borderline high	430	88 (20.5)	342 (79.5)	1.8 (1.4 - 2.4) <sup>**</sup>	1.4 (1.0 - 1.9) <sup>*</sup>
High	175	40 (22.9)	135 (77.1)	2.1 (1.4 - 3.0) <sup>**</sup>	1.2 (0.7 - 2.0)
<b>HDL-C</b>					
Normal	659	104 (15.8)	555 (84.2)	1.0 (Ref)	1.00 (ref)
Low	1,194	192 (16.1)	1,002 (83.9)	1.2 (1.0 - 1.5)	1.1 (0.9 - 1.5)
High	236	26 (11.0)	210 (89.0)	0.6 (0.4 - 0.9) <sup>*</sup>	0.6 (0.4 - 1.0) <sup>*</sup>
<b>Baseline BP</b>					
SBP<120 and DBP<80	1,297	74 (5.7)	1,223 (94.3)	1.0 (Ref)	1.00 (ref)
SBP (120-129) and DBP <80	404	82 (20.3)	322 (7.7)	3.4 (2.5 - 4.6) <sup>**</sup>	2.9 (2.1 - 4.0) <sup>**</sup>
SBP (130-139) or DBP (80-89)	388	166 (42.8)	222 (57.2)	7.0 (5.3 - 9.2) <sup>**</sup>	5.1 (3.8 - 6.8) <sup>**</sup>
<b>Diabetes</b>					
No	2,000	298 (14.9)	1,702 (85.1)	1.0 (Ref)	1.00 (ref)
Yes	87	23 (26.4)	64 (73.6)	2.1 (1.4 - 3.3) <sup>**</sup>	1.1 (0.7 - 1.6)

<sup>a</sup> Numbers may not sum to the total sample size due to missing data.

<sup>b</sup> Adjusted analysis included N=2,087 due to missing data for some of the covariates.

HRs were adjusted for age, sex, civil status, employment status, family history of hypertension, BMI, waist circumference, total cholesterol, triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, baseline BP, and diabetes.

CI - confidence interval, HR: Hazard Ratio, BP - blood pressure, SBP - systolic BP, DBP -: diastolic BP.

<sup>\*</sup>p<0.10; <sup>\*</sup>p<0.05; <sup>\*\*</sup>p<0.001.

Our study used the Philippine guidelines defining hypertension as  $\geq 140/90$  mm Hg and excluded these participants from our analysis. Blood pressure classifications for hypertension have changed over the years. The cut-off for staging hypertensive blood pressure levels decreased. Currently, a systolic blood pressure <120 mm Hg and/or <80 mm Hg is considered the optimal blood pressure level. European guidelines have classified systolic blood pressure of 120-129 mm Hg and/or diastolic blood pressure of 80-84 mm Hg as normal, and systolic blood pressure of 130-139 mm Hg and/or diastolic blood pressure of 85-89 mm Hg as high normal.<sup>8</sup> However, the American guidelines further lowered their cut-offs, wherein a systolic blood pressure of 120-129 mm Hg was defined as elevated blood pressure, while a systolic blood pressure of 130-139 mm Hg and/or diastolic blood pressure of 80-89 mm Hg was already classified as stage 1 hypertension.<sup>32</sup> Indeed, these aforementioned blood pressure measurements were earlier coined as prehypertension. Cohorts of normotensive individuals from Japan and Korea showed a high rate of progression to hypertension over a 3-year period among those with a high normal blood pressure at baseline.<sup>33-35</sup> Although

it enrolled an older population compared to our cohort, the Systolic Blood Pressure Intervention Trial (SPRINT) showed that initiating anti-hypertensive therapy among elevated cardiovascular patients with systolic blood pressure as low as 130 mm Hg and targeting a goal systolic blood pressure of <120 mm Hg achieved a significant reduction in its primary composite cardiovascular outcomes by 25% and all-cause mortality by 27%.<sup>36,37</sup> Therefore, Filipinos with these blood pressure levels should be closely monitored to identify and treat them early in their disease.

The findings of this study should be interpreted with caution, owing to several limitations. First, adult participants were recruited from selected *barangays* (villages) in the Luzon Region of the Philippines. Therefore, the findings of this study cannot be considered generalizable to all Filipinos in other areas of the country. Second, selection bias may have been introduced due to the loss to follow-up of some participants, although it may be considered non-differential with respect to the incidence of hypertension and exposures included in this study. Lastly, blood pressure measurements were taken only during a single visit due to the nature of the study being conducted in several remote areas in the main island of Luzon

which makes follow-up measurement difficult to satisfy the definition of blood pressure in an office setting.

We believe that any resulting bias is likely to be minimal and would not systematically favor one outcome over another. If there is any bias, we expect it to be towards the null, potentially underestimating the strength of the associations. Another limitation of this study is we also relied on self-reported use of antihypertensive medications. This may have introduced recall bias or misclassification, as some participants might not accurately report their medication use.

The Philippines is experiencing a change in healthcare access through the Universal Health Care Act (Republic Act No. 11223). In the authors' view, all adults should be offered an opportunity to have their blood pressure checked in public and private healthcare facilities, pharmacies, and even in workplaces and transportation hubs, and commercial establishments. Healthcare workers should be reminded to check for possible hypertension among older male patients, especially those with a family history of hypertension, above normal blood pressure levels, and abdominal obesity. Easy access to prompt and early diagnosis, appropriate treatment, and adequate management of hypertension among adults is essential throughout life. Programs and services which focus on health concerns of males can be further developed as part of universal healthcare.

## CONCLUSION

There is a high 4-year incidence rate of hypertension among these apparently healthy adult Filipinos wherein high normal blood pressure is the strongest associated risk factor. Other factors such as increasing age, male sex, family history of hypertension, and abdominal obesity were also significantly associated risk factors in the development of hypertension.

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## Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

## Author Disclosure

All authors declared no conflicts of interest.

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