Prevalence and Predictors of Hypertensive Blood Pressure in Rural Farmers in Madagascar

by

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Randall Kramer

Thesis submitted in partial fulfillment of
the requirements for the degree of
Master of Science in the Duke Global Health Institute
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ABSTRACT

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Abstract

Introduction: Hypertension, the primary risk factor for the leading cause of mortality, cardiovascular diseases, is increasing in all parts of the world, including low-income countries. This thesis explores the prevalence and predictors of elevated blood pressure in rural farmers in northeastern Madagascar. The prevalence of hypertensive blood pressure was compared as defined by two commonly used hypertension standards, the World Health Organization (WHO), and the American College of Cardiology & the American Heart Association (ACC/AHA). The hypothesized drivers of systolic and diastolic blood pressure were investigated, focusing specifically on age, gender, body mass index (BMI), salt intake, and stress. Methods: Over 1,200 surveys were conducted from 2019 to 2022 in four villages in the Sava Region of Madagascar, where blood pressure readings were obtained on each participant. A subset of the sample in the last field season, participated in additional questions related to salt consumption and a measurement of salt taken over the course of seven days. A subsample of forty-eight participants completed an additional survey regarding stress. Generalized linear mixed models were run to assess associations involving blood pressure, salt intake and stress, and other predictions involving age, gender, and BMI. Results: The different standards of hypertension, as defined by the WHO and the ACC/AHA, changed the respective prevalence of elevated blood pressure for this population markedly, nearly doubling the prevalence of hypertension if the more stringent American standard was used (WHO=29.7%, ACC/AHA=59.6%). Age was found to be a strong predictor of blood pressure as well as BMI, while salt intake, stress, and gender had weaker associations.

Conclusion: The prevalence of elevated blood pressure in this population was markedly higher than that found in other studies conducted in this region and globally. Findings regarding lifestyle factors, salt intake and stress, as individual drivers of blood pressure were found to be inconclusive. Further research should be performed in this population to determine the predictors and lifestyle factors associated with blood pressure and the extent of their influence in this region. Consideration for standards of practice and diagnosis should be carefully considered in this population, as the burden of hypertension would potentially increase with a change in practice standard.

Dedication

This thesis is dedicated to my family and friends who have supported me in my endeavors and to the people of Madagascar who welcomed me as a friend into their homes and their community.

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Acknowledgements

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1. Introduction

1.1 Background

Recent reports have identified an unexpectedly high prevalence of hypertension in rural populations in multiple African countries [1-2]. Given reports that include Madagascar [3-4], the author aims to assess the prevalence of high blood pressures in four villages in Madagascar and what factors, if any, are associated with elevated blood pressure among individuals in these villages. Hypertension is a medical condition affecting a person's cardiovascular system, specifically the blood vessels [5]. It is directly linked to and is the highest risk for cardiovascular disease (CVD) [6], the leading cause of mortality worldwide [7]. According to the World Health Organization, approximately 1.28 billion people have hypertension globally and less than a fifth have it under control [8]. In lower- and middle-income countries (LMICs) it is estimated that 31.5% of adults over the age of 19 have hypertension [7] and of those, only 25% are receiving treatment [9].

1.2 First Objective

The diagnosis of hypertension is made primarily on consistent or consecutive elevated blood pressure readings [10]. Different standards exist for classifying blood pressure readings into “elevated” or “hypertensive” categories [11]. The two standards or definitions of hypertension explored in this paper are those provided by the American College of Cardiology & the American Heart Association (ACC/AHA) guideline [12] and the World Health Organization (WHO) [10]. The ACC/AHA standard was developed in 2017 [13] after a number of studies revealed that treatment of hypertensive levels between 130/80mmHg and 140/90mmHg decreased levels of CVD events and all-around mortality rates [14]. The WHO standard uses the traditional threshold of 140/90mmHg with readings above being considered hypertensive; it is the more globally accepted standard [13]. Using the more stringent threshold of the ACC/AHA over the WHO threshold will inevitably increase the number of people classified as hypertensive.

The first objective of this study is to investigate the magnitude of difference in hypertension under the two standards and to explore the implications this difference could have for this community, its healthcare system, and the standards of care. Any change in the standard of defining the hypertension threshold might impact the healthcare system in Madagascar by possibly increasing the overall burden of hypertension. Recent calls to action globally have been made to evaluate the practicality of standardized hypertension measurements, especially in LMICs [13, 15-16].

1.3 Second Objective

Hypertension, or the "silent killer" [10], has many risk factors, including genetics, environment influences, and behavioral and lifestyle factors [17]. Salt consumption and stress are both common drivers of heart health outcomes [18-20]. In this specific population, the author seeks to understand the extent that stress and salt intake have on individual blood pressures that possibly influence the unexpected high hypertension rates in Madagascar [3]. Recent studies have shown that hypertension occurs in rural Madagascar despite the population having a low mean body mass index (BMI), with more people falling within the acceptable range of BMI than being above it [3]. If high BMI, a known risk associated with CVD [21], is not widespread in this population, other factors may be contributing to elevated blood pressure. Salt, a common household commodity, is a chemical compound found in almost every diet around the world and has known effects on the cardiovascular system [20]. It is predicted that in this study sample, blood pressure increases with age, higher BMI, and in men compared to females, and that living in a household with higher measured salt intake per week is associated with higher blood pressure, independent of age, gender, and BMI.

Madagascar is also experiencing economic changes related to market integration and crop dependency [3], potentially influencing stress levels and diet. Stress, whether mental, emotional, or physical, puts significant strain on the cardiovascular system, which in turn leads to increased blood pressure and risk of CVD [22]. It is further predicted that higher levels of stress, as measured by the Perceived Stress Scale (PSS) [23], a questionnaire based on the findings of Cohen et al. [24], are positively associated with hypertension, independent of age, gender, and BMI.

2. Methods

This cross-sectional study is based on survey data, clinical status measurements, and salt usage data from residents of four farming villages in Madagascar. Statistical analyses for this study, to determine predictor relationships and hypertensive prevalence were conducted using R. All procedures and measurements were done and collected in accordance with the approval of ethical review boards of Duke University and Madagascar.

2.1 Setting

Data collection was performed[1] in four farming villages in the Sava Region of Madagascar. The four villages included Mandena, Sarahandrano, Andatsakala, and Ampandrana; the latter two are neighboring villages located within three kilometers of one other. This area is adjacent to Marojejy National Park and approximately 547 kilometers from Antananarivo, the capital of Madagascar. Agriculture is a main economic activity in all four villages and most healthcare is delivered by local clinics, generally provided by a nurse and/or midwife.

Data were collected over the course of eight field seasons from 2019-2022. In Mandena, fieldwork occurred from October 2019 to March 2020, stopping prematurely due to the COVID pandemic. Fieldwork occurred in Sarahandrano from November 2020 with adjustments due to COVID until September 2021. In Andatsakala, surveys were

[1] The author participated in data collection during the final season in Andatsakala and Ampandrana, June to August 2022.

completed between October 2021 and August 2022. Ampandrana was sampled in addition to Andatsakala in the final season from June 2022 to August 2022. Measurements of stress and salt intake were only taken in the final season in Andatsakala and Ampandrana (see Table 1 for further data collection details).

Table 1: Data Collection From Each Village

Category	Mandena	Sarahandrano	Andatsakala & Ampandrana
Total Participants	n=263	n=435	n=600
Dates for Data Collection	October 2019 - March 2020	November 2020 - September 2021	October 2021 - August 2022
Number of Seasons	2	3	3*
Weeks of Data Collection	8	16	21
Blood Pressure and BMI	Yes	Yes	Yes
Salt Intake	No	No	Yes^
Perceived Stress Scale	No	No	Yes^

*Ampandrana included in the final season with Andatsakala, June 2022-August 2022
^Data collected only during the final season (June 2022 - August 2022) and PSS only done in Andatsakala

2.2 Participants

A participant in this study was required to be a resident of the village being surveyed, capable of answering for themselves, and 18 years or older. Men and women were both included in the study, and ages ranged from 18 to 100 years-old (see Table 3 in the Appendix A for sample characteristics). Many participants were farmers or part of farming families, and many lived in close proximity to neighbors.

2.3 Sampling

The data obtained for this study is part of a larger study that used snowball sampling [25] to recruit participants and create social networks, a key objective of this larger study. In the snowball sampling, five landowners in each village were initially recruited and surveyed. They answered a series of questions and were asked to name five people with which they had various degrees of contact. The people named by the landowners were then found and invited to participate in the survey. If they decided to participate, they were also surveyed and asked to name five people with whom they were in contact. The cycle for finding and recruiting participants continued in this manner.

A "gatekeeper" was established in each village, who was a resident of the village and well-known by most or all the other residents of the village. Participants, or those named by previous participants, were invited to participate in the survey through the "gatekeeper." Compensation, in the form of phone credits, was given to those who elected to participate in the survey.

In the final season in Andatsakala and Ampandrana, 191 of the survey participants were invited to participate in a study of salt intake. Of those invited, many agreed to participate in the additional measurement of salt. In Andatsakala during the same season, an additional survey regarding stress was conducted. A subsample of men and women older than 18 years who were part of the survey were invited to answer an additional ten-question survey regarding perceived stress and coping abilities [23].

2.4 Field Measurements

All surveys were administered by an experienced social survey team based in Madagascar. Surveys were performed in the Malagasy language and in person with the participant, either near or inside the participant's home.

Blood pressure readings were taken three times on each participant throughout the 45-minute survey, once at the beginning, then halfway through the survey, and then at the end of the survey. The blood pressure measurements were performed by the local healthcare worker partnering with the Malagasy social survey team. Each reading was done in accordance with best known practices [26-28] with the participant sitting, legs uncrossed, and not talking during the reading [28]. It was taken using the Omron 10 Series Upper Arm sphygmomanometer (Omron Healthcare, Inc.). It is important to note that this study only measured blood pressure three times in one day; to diagnose hypertension, a person needs consistently elevated blood pressure measured over multiple days [10].

Demographics including age and gender were collected during the survey, which also included questions regarding healthcare utilization and barriers to healthcare (see survey questions regarding healthcare utilization in Appendix B). Height and weight were also collected on each participant and used to generate an individual BMI score, using the formula: BMI = kg/m^2 where weight is measured in kilograms (kg) and height measured in meters (m) [29]. Salt intake was measured in grams using the YONCON 3000g/0.1g High Accuracy Mini Pocket Scale and was measured by weighing the participant's household salt container (See Figure 1 below). Participants agreed to have their household salt measured twice: at baseline and seven days later. They also agreed to not add any additional salt to the container during the week between measurements. Salt intake for the household over one week was calculated by taking the difference between the baseline measurement and the final measurement of salt.

The additional stress questionnaire used was the ten-question standardized PSS [23], which was translated into the Malagasy language. The ten questions in the questionnaire are about perceived stress, with questions such as, "In the last month, how often have you felt nervous and stressed?" and "In the last month, how often have you felt that you were unable to control the important things in your life?" (The full PSS questionnaire is provided in Appendix B). The PSS score was calculated based on the participants' answers and then categorized into levels of low, moderate, and high stress.

Figure 1: Image of Salt Container Being Weighed at Baseline

2.5 Analysis

2.5.1 Prevalence Analysis

To calculate hypertensive prevalence in all four villages, the mean was taken of the last two blood pressure readings (second and third readings) of each participant, which follows similar procedures used in other hypertension studies [30]. The prevalence of hypertensive blood pressure readings was first calculated based on the two different standards or definitions of hypertension.

The ACC/AHA standard was categorized[2] into two groups: “Normal” and “Hypertensive.” “Normal” was defined as having a systolic blood pressure (SBP) less than 130mmHg and/or a diastolic blood pressure (DBP) less than 80mmHg. “Hypertensive” was defined as having a SBP of greater than or equal to 130mmHg and/or DBP greater than or equal to 80mmHg (130/80mmHg) [12].

The WHO definition was also categorized into two groups: “Normal” and “Hypertensive” where “Normal” was defined as having a SBP of less than 140mmHg and/or a DBP less than 80mmHg. “Hypertensive” was defined as having a SBP of greater than or equal to 140mmHg and/or a DBP greater than or equal to 90mmHg (140/90mmHg) [10]. The difference between the ACC/AHA and WHO standards is 10mmHg.

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[2] The ACC/AHA standard is originally separated into 4 groups: “normal” “elevated” “hypertension 1” and “hypertension 2”. The standard is made dichotomous for comparison purposes: normal & elevated = “normal”, hypertension 1 & hypertension 2 = “hypertensive” [12]

The prevalence was then stratified by gender, age, BMI, and village of residence. BMI categories were defined according to the BMI standards used by the Centers for Disease Control and Prevention. Those categories include “underweight” (BMI <18.5 kg/m^2), “normal” (BMI ≥18.5 kg/m^2 and <25 kg/m^2), “overweight” (BMI ≥25 kg/m^2 and <30 kg/m^2), and “obese” (BMI ≥30 kg/m^2) [29]. Prevalence difference estimates between strata were performed for additional insight (see Table 5 in Appendix A).

2.5.2 Blood Pressure and Predictors Analyses

For analyses of the predictors of blood pressure, the author ran generalized linear mixed models (GLMMs) to investigate the relationships between blood pressure and salt intake and PSS score. Each blood pressure reading, first, second, or third, was treated as one data point (i.e., persons with three readings had three data points). Rather than taking means of the last two readings as in the prevalence analyses, all blood pressure readings recorded were included in these analyses, controlling for read number. This approach makes use of all the data and statistically captures expected declines from the first to the second reading. It also follows methods used in a previous study of this population [3]. The mixed models included both random and fixed effects. The random effects included individual ID, blood pressure reading number (first, second, or third), and household ID when the model included the variable of salt intake. Fixed effects were salt intake, PSS score, BMI, age, and gender, with different variables included depending on the model tested. The author used binomial models for relationships between blood pressure defined as “hypertensive” or “normal” according to the two standards of hypertension, and predictors salt intake and PSS score, with additional variables that incorporated age, gender, and BMI.

After GLMMs were generated and using the MuMIn package in R [31], model selection and model averaging were used to predict blood pressure more precisely [32]. Using this package generates all possible versions of the GLMM to include the outcome and potential predictors, and then produces estimates based on the averaging of these models to control for any overestimation or underestimation in individual models. This process was done with both the SBP and DBP used as responses and represented as continuous variables. Additionally, model averaging was used to predict the hypertensive level as a categorical variable according to both the WHO and ACC/AHA standards. The process of model averaging was done on the full sample of 3,784 readings or data points, and then on a subset of samples that included data with either salt intake or PSS score. The model averaging process was then done on a sample that included both salt intake and PSS score as variables (see Figure 2 below). The estimates reported in this study are based on the 'full' average of the models which is a "type of shrinkage estimator" and does not tend to bias the estimate away from zero as is done in 'subset' averages [31].

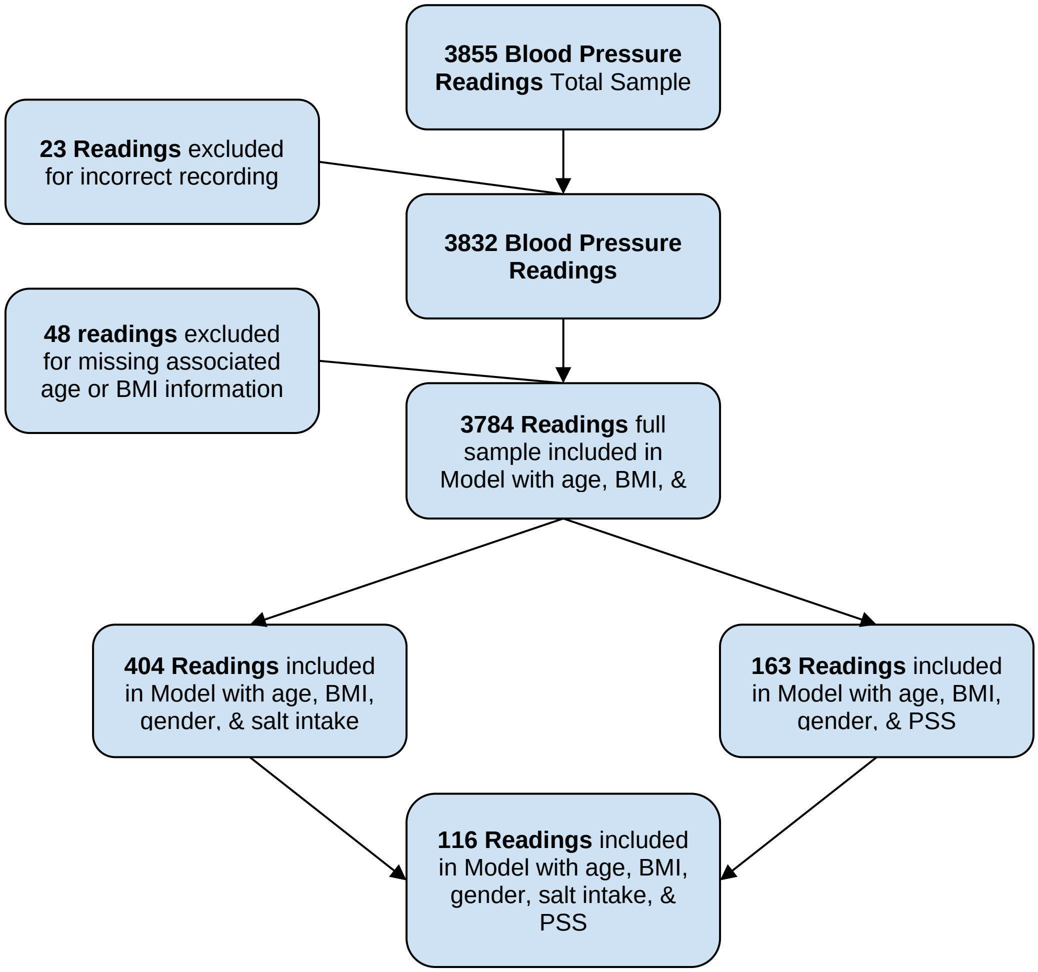


Figure 2: Model Samples Flowsheet

3. Results

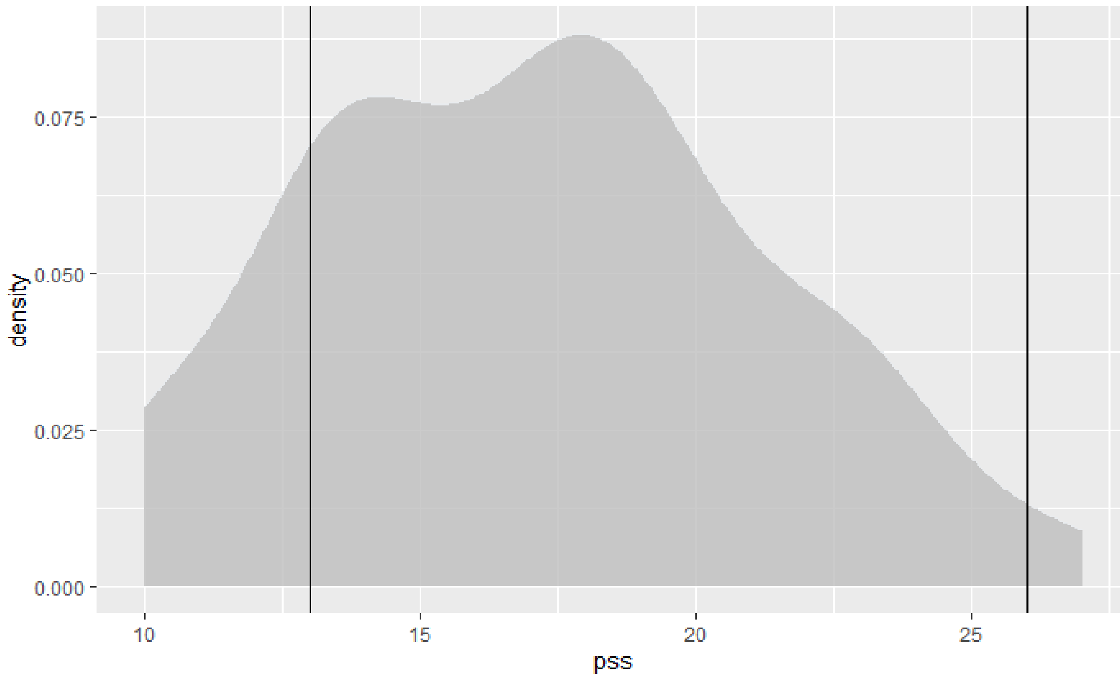
The findings of this study are presented in this section as sample results, and prevalence and model averaging results. The sample results include the sample characteristics and health measurements, overall findings of the various questions and measurements in which residents participated and include data on healthcare utilization and barriers. The prevalence and model averaging results are the outcomes of the different statistical analyses and models performed to understand the prevalence of high blood pressure and relationships between blood pressure and predictors.

3.1 Sample Results

Blood pressure readings were obtained on 99% of participants (45.7% female, 54.3% male) in all four villages, and 97.5% of participants had three complete blood pressure readings recorded. The median age was 33 years (females=34 years, males=33 years), with ages of participants ranging from 18 to 100 years old. The average BMI was 21.5 kg/m2 (SD=3.0 kg/m2) (females=22.4 kg/m2, males=20.8 kg/m2). Most participants were in the "normal" BMI category (n=949, 73.9%), with 152 participants (11.8%) in either the "overweight" or the "obese" categories. (See Table 3 in Appendix A for further details).

In the last season in Andatsakala and Ampandrana, 105 of 191 (55.0%) participants completed salt measurements (8.2% of all 1,285 participants). Forty-eight participants in Andatsakala (25.1% of 191 participants, and 3.7% of all 1,285 participants) completed the additional stress questionnaire, and thirty-nine participants completed both the stress questionnaire and the household salt measurement (20.4% of

191 participants, and 3.0% of all 1,285 participants). The mean amount of salt intake over the course of a week was 70.7 grams per person, or 10.1 grams per person per day (2.3 teaspoons per person per day). Salt was mainly used in cooking, with 65.4% of participants reporting that they “always” added salt or salty sauce to food while cooking, whereas 22.5% reported “always” adding salt or salty sauce to food while eating. In surveys asking participants how frequently in the previous week had they consumed packaged foods, 26.5% responded “always” and 30.7% responded “never” (see Table 6 in Appendix A). Based on the stress survey, the mean PSS score was 17.2 (SD=4.1), with 77.1% of the 48 participants categorized as having moderate or high stress (see Figure 3).



Notes: Solid black lines indicate separation between PSS categories of low (1-13), moderate (14-26), and high (27-40) stress levels.

Figure 3: PSS Distribution

3.2 Prevalence with WHO Guidelines versus Prevalence with ACC/AHA Guidelines

In the prevalence analysis for comparing the ACC/AHA and WHO standards, eight of the 1,285 surveys were excluded from blood pressure analysis due to missing the second and/or third reading(s) due to recording errors of the blood pressure monitors, leaving a total of 1,277 averaged blood pressure readings. All 1,277 were included for overall prevalence estimates and in groups stratified by age, gender, BMI, and village where possible. Three blood pressures were excluded from the age strata and thirteen from the BMI strata, due to missing data, but all 1,277 averaged blood pressure readings were included in the gender and village strata (see Figure 4).

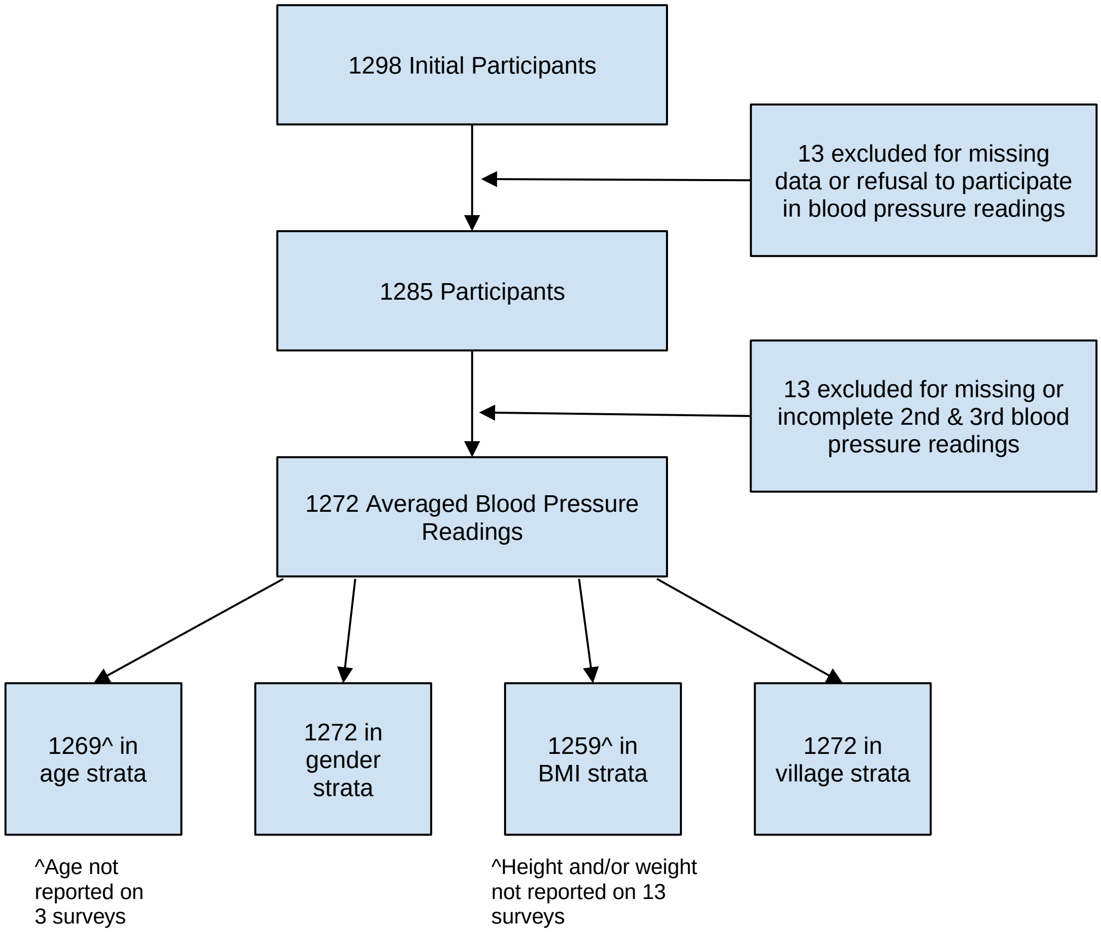


Figure 4: Flowchart of Inclusion of Participants and Averaged Blood Pressure Readings for Prevalence Analysis

According to the WHO guidelines of 140/90mmHg constituting hypertensive blood pressure, 27.4% of the 1,272 participants included in the prevalence analysis had a hypertensive blood pressure reading. However, 56.8% of participants had hypertensive blood pressure readings according to the ACC/AHA standard (130/80mmHg), more than doubling the prevalence (see Figure 5). The prevalence difference between the two standards was 29.3% (373 of 1,272 participants). This prevalence difference estimate is roughly the same throughout all the stratified groups of age, gender, BMI, and village, where about a third of each group falls between the two blood pressure thresholds (see Figure 6 below and Table 5 in Appendix A).

Figure 6 below shows the percentage of all participants, total and by strata, whose averaged blood pressure reading fell between the two standard hypertensive thresholds (130/80mmHg and 140/90mmHg). This is also known as the prevalence difference between the two standards. The age group[3] with the highest prevalence difference between the standards was the "33-46 years old" age group with a prevalence difference of 34.4% (or 34.4 per 100 people). In the "47 and above" age group, the prevalence of hypertensive blood pressure according to both the ACC/AHA and WHO standards was over 50% within the group and had the lowest group prevalence difference of only 22%. The median age for participants whose blood pressure fell between the two thresholds was 31 years (IQR: 18 years). The prevalence difference between the standards for each gender was almost equal, 30.2 per 100 among females and 28.5 per 100 among males.

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[3] Age was divided into 4 groups as defined by the sample's age quartiles.

With regards to BMI, the prevalence difference was similar throughout except for those with a BMI greater than 30, representing only 14 individuals where the prevalence difference equaled 50%. The difference between standards as stratified by village was also uniform throughout, reflecting the overall prevalence difference estimates. (See Table 5 in Appendix D for complete prevalence estimates).

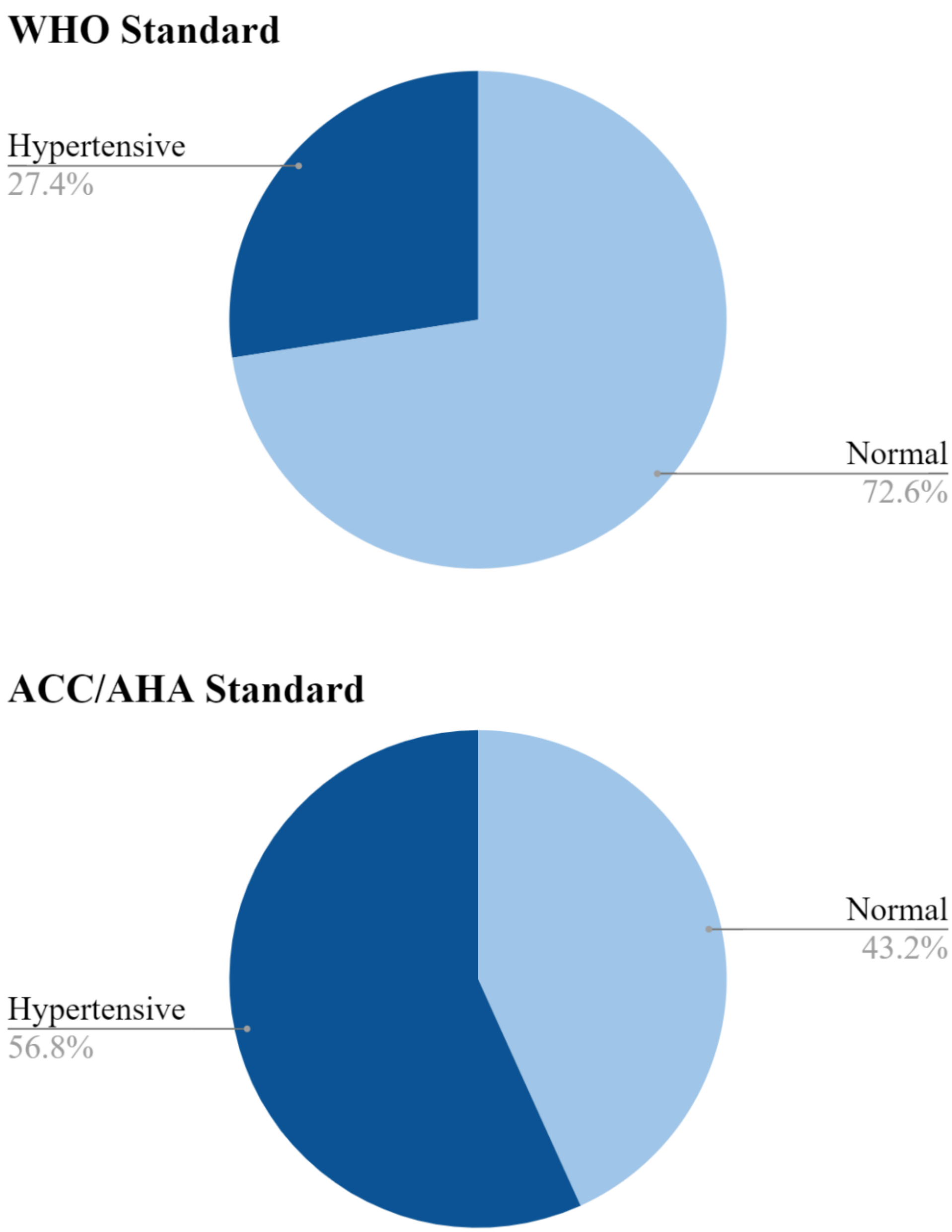

Figure 5: Comparison Between the Two Standards for All 1,277 Participants

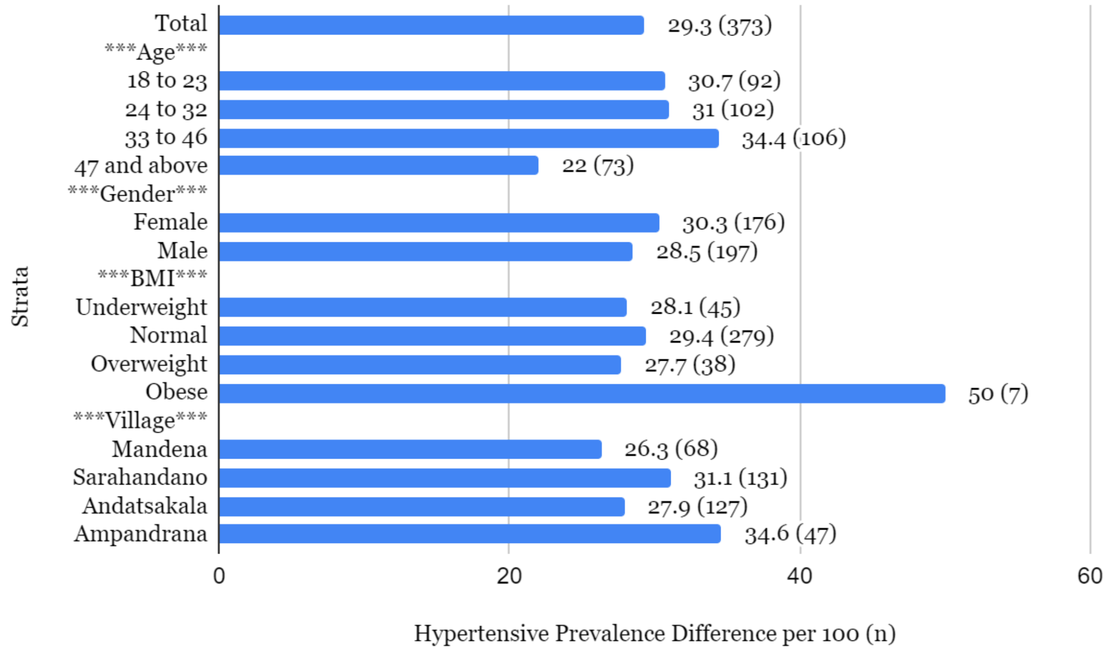

Figure 6: Bar Chart of Prevalence Difference Between WHO and ACC/AHA Standards, Total and By Strata

3.3 Model Averaging Results

3.3.1 SBP and DBP, and Predictors

Of the 1,298 participants surveyed, thirteen declined to have their blood pressure measured and were therefore excluded. Three blood pressure readings were taken on each of the remaining 1,285 participants, resulting in 3,855 blood pressure measurements with the systolic blood pressure mean of 127.1 mmHg (SD=20.5 mmHg) and 82.5 mmHg (SD=12.2 mmHg) for the diastolic blood pressure. Twenty-three measurements were excluded for being recorded only partially or incorrectly, leaving 3,832 blood pressure readings for statistical analysis. Of the remaining readings, 3,784 had complete age and BMI data (refer to Figure 2).

The only significant predictors found after running GLMM and model averaging of blood pressure were age and BMI (significance level α=0.05). This was true in both models where SBP and DBP were the outcomes and only age, BMI, and gender were included as predictors (see Table 2). In models where both salt intake and PSS score were included as potential predictors, age was found to be the only significant predictor of SBP, with older individuals having higher readings. When DBP was the outcome of interest, age was non-significant in the models that included both salt intake and PSS score as predictors. However, age was a significant positive predictor for both SBP and DBP in models that included salt intake and not PSS score or vice versa. In all models, gender, salt intake, and PSS score were non-significant as predictors for increased SBP and DBP. (See Table 2 for summary of results, or for all full model averaging estimates, see Table 7 in Appendix C).

3.3.2 Hypertensive State and Predictors

Similar to the models with systolic and diastolic blood pressure as outcomes, age was the only positive predictor for hypertensive state as defined by the WHO and ACC/AHA (see Table 2). This was true in models that only included age, BMI, and gender as predictors and in models that included salt intake and not PSS score. Age was not a significant predictor of hypertensive state for either the WHO definition or the ACC/AHA guideline in the models that included both salt intake and PSS score which may be due to decreased sample sizes. As the number of variables in the models increased the sample size decreased (see Figure 2). BMI was a positive predictor of hypertensive state as defined by ACC/AHA only in the model that included only age, gender, and BMI as predictors. In all models, gender, salt intake, and PSS score were non-significant predictors of hypertensive state defined by either the WHO or the ACC/AHA. (See Table 2 for summary of results, or for all full model averaging estimates, see Table 7 in Appendix C).

Table 2: Model Averaging Results Summary

Predictors:	Outcomes:															
	Systolic				Diastolic				WHO				ACC/AHA			
Age	+S	+S	+S	+S	+S	+S	+S	+N	+S	+S	+N	+N	+S	+S	+S	+N
BMI	+S	+N	+N	-N	+S	+N	+N	-N	+N	+N	+N	-N	+S	+N	+N	+N
Gender	+N	+N	+N	-N	-N	-N	+N	-N	+N	-N	+N	-N	-N	+N	+N	-N
Salt Intake		+N		+N		+N		+N		+N		+N		+N		+N
PSS			-N	-N			-N	-N			-N	-N			-N	-N

<u>Notes</u>: Significance is indicated as "S" signifying the result was significant and "N" signifying the result was non-significant, based on the significance level ($\boldsymbol{\alpha}$=0.05). (+/-) symbols represent the direction of relationship between predictor and outcome. Each sub-column under each outcome represents a different model and blank cells indicate when a variable was not included in the model. (1st column: Model with Age, Gender, & BMI only, n=3,784. 2nd column: Model with Age, Gender, BMI, & Salt Intake only, n=404. 3rd column: Model with Age, Gender, BMI, & PSS only, n=163. 4th column: Model with Age, Gender, BMI, Salt Intake, & PSS, n=116.) See table 7 in Appendix C for a full list of estimates and confidence intervals.

3.4 Healthcare Utilization and Barriers to Care

Most participants reported that they seek healthcare in government facilities (63.7%) and from traditional practitioners (45.7%), with 28.3% reporting seeking care in private hospitals (participants were able to select more than one option) (see Table 4 in Appendix A). Between money, distance, and going alone as barriers for obtaining care, money was most frequently reported as “a big problem” (55.2%), whereas 20.8% reported distance as “a big problem” and 21.0% reported going alone as “a big problem.” A small number of participants preferred not to answer if money, distance, or going alone were problems or barriers when seeking healthcare. (See Figure 7 for more on barriers to healthcare.)

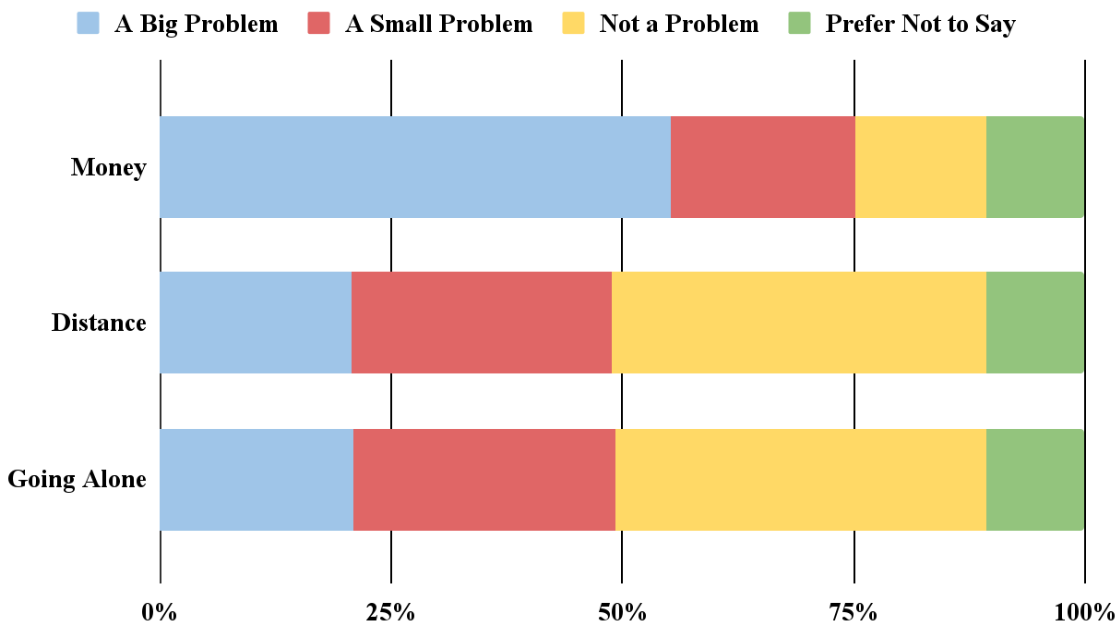

Figure 7: Stacked Graph Comparing Barriers to Healthcare

4. Discussion

This population, located in the Sava Region of Madagascar, was found to have unexpectedly high rates of hypertensive blood pressure. Depending on the standard hypertensive threshold used, 27.6% (WHO standard) or 56.9% (ACC/AHA standard) of participants had hypertensive blood pressure, representing a more-than-doubling of the prevalence of hypertension under the more stringent standard. These rates are comparably higher than those observed in other studies done in Madagascar or in other areas of the world. Implications and comparisons related to these prevalence findings are explored further below.

Salt intake and stress, hypothesized to be positive predictors of blood pressure, were not found to be significant predictors of blood pressure for this population in this study. Only age and BMI were found to have a significant influence on blood pressure. The various predictors explored in this study require further research, potentially using differing tools of measurement and larger samples, to establish if they are related to blood pressure.

4.1 Prevalence Comparisons

As expected, the prevalence of hypertensive blood pressure based on the ACC/AHA standard was more than that based on the WHO definition for hypertension, more than double to be precise. Almost 57% of participants had a hypertensive blood pressure reading according to the ACC/AHA standard, while less than 28% had hypertensive readings according to the WHO. In the United States, where the ACC/AHA standard is in practice [33], 47% of adults have hypertension [34]. The US estimate is ten percentage points lower than the study sample estimate. A study looking at hypertension in 44 LMICs found that 17.5% of adult residents had hypertension based on the WHO definition for hypertension [35]. Again, this study prevalence estimate (27.6%) was ten percentage points higher than the comparable prevalence in other LMICs [35]. Another study that investigated blood pressure in this same region found a prevalence of 49.1% for hypertensive blood pressure as defined by the ACC/AHA standard, 13.7% less than found in this study [3]. The prevalence of hypertension is expected to increase in this area as Madagascar's life expectancy increases and the 2.6% population increase occurs annually [36].

4.2 Predictors and Blood Pressure

Age and BMI affect blood pressure [21, 37] and in this study, both were found to be positive predictors of blood pressure. Outside studies also found links between BMI and blood pressure [21] including one done in this same region. The study had similar rates of BMI, but a smaller sample, and also found BMI to be a significant predictor of blood pressure [3]. Many studies have been done that connect age with hypertension [37], however some have argued that lifestyle factors correlated with aging and not age itself are better predictors for hypertension [38]. In all the statistical models in this study, gender was not found to be a significant predictor of blood pressure or hypertensive state.

Concerning lifestyle factors, the author investigated the hypothesis that increased salt intake increases blood pressure; however, no support was found for this hypothesis.

Salt intake was not found to be a significant predictor of SBP or DBP, or a predictor for hypertensive state as defined by the ACC/AHA and the WHO. This could be due to the limited sample size or types of measurement used to quantify salt usage (only one household salt intake measurement was taken over the course of a week). Other studies have shown that reducing salt in the diet decreases overall blood pressure, especially in people with hypertension [20], linking the influence of salt consumption to blood pressure. The recommended amount of salt per day per person over the age of 18 years is 5 grams according to the WHO [39]. The WHO also reports that the global average of salt intake is 9-12 grams per day per adult. This study's estimate was approximately 10 grams of salt per day per person, congruent with the predicted global average and yet higher than what is recommended. Much of this population reported that they think they eat "just the right amount" of salt.

The author also investigated the hypothesis that increased stress positively influences blood pressure. Using the PSS questionnaire, however, a significant association was not found between perceived stress and SBP or DBP, or with hypertensive state as defined by the WHO or ACC/AHA guideline. Stress has also been linked to blood pressure in other studies [40], and according to the systematic review by Lui et al. [22], stress increases blood pressure and the risk of hypertension. Their analyses found a positive association between prolonged psychological stress and rates of hypertension in adults.

4.3 Implications for Policy and Practice

Any change in practice, especially regarding blood pressure thresholds, should be considered carefully because it is unclear if Madagascar has a formal standard for diagnosis, practice, and care of hypertension [4]. The WHO estimates that only 19% of adult women and 13% of adult men in Madagascar are treated for hypertension [41] and if the estimates of this study reflect the prevalence of hypertension in Madagascar those estimates may be, in reality, lower than predicted. Policy changes, such as implementing a national hypertension standard, should be further researched and carefully explored as such a change may negatively impact the burden of care related to hypertension.

Nevertheless, considerable amounts of negative events or CVDs continue to occur between the 130mmHg and140mmHg SBP thresholds [42]. Whether standardization occurs, hypertension must continue receiving attention in all levels of healthcare and policy. Lifestyle factors, such as salt intake and stress, should also be considered in practice when treating hypertension, given that these factors have been shown to influence blood pressure in other studies [19-20, 22, 43].

4.4 Implications for Further Research

It is difficult to quantify salt intake or dietary habits, but further research could be done using a variety of methods and measurement tools such as a 24-hour urine specimen collection [44]. It would be beneficial to do more in-depth analyses of diet and its influence on heart health, especially in populations where factors such as stress and gender are not found to be predictors. As this particular area of Madagascar continues to develop, changes in lifestyle, food sources, and diet will inevitably follow. It is important to understand the extent of influence diet has on blood pressure in this population. These developments and changes may additionally bring new sources of stress, whether physical, mental, or emotional. In this study, stress was only measured on a standardized stress scale; it may be beneficial to use other indicators or measurements of stress to determine the true relationship between stress and blood pressure in this population. It would also be beneficial to conduct a more longitudinal study to determine more concretely the prevalence of hypertension and treatment in this population. Further information and study are recommended for improved hypertension control and treatment in Madagascar.

4.5 Study Limitations

This study had several limitations, including the sampling method, generalizability of results, and the study design. Snowball sampling was done for the purpose of a larger study that was designed to look at network connectivity. However, with a large group sample there was adequate distribution between subgroups, with the exception that BMI exhibited less variance than seen in high-income countries, with the majority of participants falling in the “normal” category. A potentially better sampling approach would include random sampling as far as circumstances would permit.

This study was conducted only in the Sava Region of Madagascar and may be limited in its representation of Madagascar as a whole. There is minimal information on hypertension rates and healthcare infrastructure in Madagascar [4], restricting comparisons within the country or relative to other countries. Because there are only a few studies of hypertension conducted in Madagascar, this study reporting prevalence on both standards helps increase the information available regarding hypertensive blood pressure in Madagascar. However, it is important to note that this study was looking at individual rates and predictors of hypertension, and not at the predictors of hypertension changes at a population level in Madagascar. Furthermore, BMI and PSS categories were based on western standards and may not adequately represent this population.

A cross-sectional design was used due to time and funding constraints, and because data were also collected for the purpose of an additional study. Prevalence estimates were used in analyses to calculate the correlations between outcomes of blood pressure and predictors of blood pressure and may limit precision of results. Measurement error was low in terms of the actual blood pressure measurements. Three blood pressure measurements were taken on each participant using best practices [26]. More longitudinal studies are recommended to better determine predictors and rates of hypertension.

5. Conclusion

Although findings regarding lifestyle factors as individual drivers of blood pressure were inconclusive in this study, age and BMI were found to be positive predictors of blood pressure. Salt intake and stress, both extensively studied predictors of blood pressure [20, 22], are subject to change as Madagascar's agricultural economy and dynamics shift. Lifestyle factors and their influence on cardiovascular health should be studied longitudinally, especially in this unique population. In this study, the prevalence of hypertensive blood pressure readings doubled between the standard hypertensive blood pressure cutoffs of 140/90mmHg and 130/80mmHg. Establishing a hypertension threshold at 130/80mmHg potentially doubles the burden of disease and care and would impact an already strained healthcare infrastructure. The standard of care should be carefully considered, and more research should be done to determine the impact of any implementation of a standard of care for hypertension in Madagascar.

Appendix A

Table 3: Sample Characteristics

Characteristic:		**Sample: n=3784 (100%)**
Age:	mean (SD)	36.7 years (15.5 years)
Gender:		
Female	n (%)	1761 (45.7%)
Male	n (%)	2094 (54.3%)
BMI (continuous):	mean (SD)	21.5kg/m2 (3.0kg/m2)
Height:	mean (SD)	1.60m (0.08m)
Weight:	mean (SD)	54.8kg (8.2kg)
BMI (categorical):		
Underweight	n (%)	486 (12.6%)
Normal	n (%)	2847 (73.9%)
Overweight	n (%)	414 (10.7%)
Obese	n (%)	42 (1.1%)
Village:		
Mandena	n (%)	789 (20.5%)
Sarahandrano	n (%)	1272 (33.0%)
Andatsakala	n (%)	1383 (35.9%)
Ampandrana	n (%)	411 (10.6%)
Systolic Blood Pressure:	mean (SD)	127.1mmHg (20.5mmHg)
Diastolic Blood Pressure:	mean (SD)	82.5mmHg (12.2mmHg)

Table 4: Healthcare Utilization

Type of Treatment (Participants selected all that applied)	**"Yes" n(%)**	**"Preferred not to say" n(%)**	**"No" n(%)**
Government Hospital	818 (63.7%)	5 (0.4%)	462 (35.9%)
Private Hospital	364 (28.3%)	8 (0.6%)	913 (71.1%)
Traveling Doctor/Nurse	170 (13.2%)	6 (0.5%)	1109 (86.3%)
Pharmacy	413 (32.1%)	7 (0.5%)	865 (67.4%)
Traditional Practitioner	587 (45.7%)	8 (0.6%)	690 (53.7%)
Market	50 (3.9%)	8 (0.6%)	1227 (95.5%)
Traveling Drug Seller	100 (7.8%)	9 (0.7%)	1176 (91.5%)
Private Doctor	255 (19.8%)	9 (0.7%)	1021 (79.5%)
Other*	115 (8.9%)	0 (0.0%)	1170 (91.1%)
*Other includes: massage (62), buying medicine at a local store (48), go to soccer field (1), wait at home (1), medicinal plants (3)			

Table 5: Prevalence and Differences Between WHO and ACC/AHA In All Groups

	Normal WHO n(%)	Normal ACC/AHA n(%)	Hypertensive WHO n(%)	Hypertensive ACC/AHA n(%)	Prevalence Difference n(%)
Total: 1272 (100%)	923 (72.6%)	550 (43.2%)	349 (27.4%)	722 (56.8%)	373 (29.3%)
Age (continuous): Median (IQR)*	30 (19)	28 (19)	47 (26)	37 (24)	31 (18)
Age (categorical): 1269 (100%)*					
18-23 years: 300 (23.6%)	277 (92.3%)	185 (61.7%)	23 (7.7%)	115 (38.3%)	92 (30.7%)
24-32 years: 329 (25.9%)	258 (78.4%)	156 (47.4%)	71 (21.6%)	173 (52.6%)	102 (31.0%)
33-46 years: 308 (24.3%)	232 (75.3%)	126 (40.9%)	76 (24.7%)	182 (59.1%)	106 (34.4%)
47 years above: 332 (26.2%)	154 (46.4%)	81 (24.4%)	178 (53.6%)	251 (75.6%)	73 (22.0%)
Gender: 1272 (100%)					
Female: 581 (45.7%)	415 (71.4%)	239 (41.1%)	166 (28.6%)	342 (58.9%)	176 (30.3%)
Male: 691 (54.3%)	508 (73.5%)	311 (45.0%)	183 (26.5%)	380 (55.0%)	197 (28.5%)
BMI: 1259 (100%)^					
Less than 18 kg/m2: 160 (12.7%)	111 (69.4%)	66 (41.3%)	49 (30.6%)	94 (58.5%)	45 (28.1%)
18-25 kg/m2: 948 (75.3%)	707 (74.6%)	428 (45.1%)	241 (25.4%)	520 (54.9%)	279 (29.4%)
25-30 kg/m2: 137 (10.9%)	86 (62.8%)	48 (35.0%)	51 (37.2%)	89 (65.0%)	38 (27.7%)
More than 30 kg/m2: 14 (1.1%)	11 (78.6%)	4 (28.6%)	3 (21.4%)	10 (71.4%)	7 (50.0%)

Village: 1272 (100%)					
Mandena: 259 (20.3%)	190 (73.4%)	122 (47.1%)	69 (26.6%)	137 (52.9%)	68 (26.3%)
Sarahandrano: 421 (33.1%)	297 (70.5%)	166 (39.4%)	124 (29.5%)	255 (60.6%)	131 (31.1%)
Andatsakala: 456 (35.8%)	339 (74.3%)	212 (46.5%)	117 (25.7%)	244 (53.5%)	127 (27.9%)
Ampandrana: 136 (10.7%)	97 (71.3%)	50 (36.8%)	39 (28.7%)	86 (63.2%)	47 (34.6%)
*3 missing due to no age reported					
^13 missing due to no height or weight reported					

Table 6: Salt Survey Questions and Results

Questions:	Possible Responses:	Total number of participants who answered n=191 (100%)	Hypertensive (WHO) n=61 (100%)	Hypertensive (AHA) n=124 (100%)
1.How often do you add salt or salty sauce to your food when cooking?	Always	125 (65.4%)	33 (54.1%)	79 (63.7%)
	Often	33 (17.3%)	14 (23.0%)	22 (17.7%)
	Sometimes	15 (7.9%)	10 (16.4%)	12 (9.7%)
	Never	17 (8.9%)	4 (6.6%)	11 (8.9%)
	NA*	1 (0.5%)	0 (0%)	0 (0%)
2. How often do you add salt or salty sauce to your food when eating?	Always	43 (22.5%)	8 (13.1%)	26 (21.0%)
	Often	36 (18.8%)	11 (18.0%)	19 (15.3%)
	Sometimes	19 (9.9%)	5 (8.2%)	15 (12.1%)
	Rarely	3 (1.6%)	3 (4.9%)	3 (2.4%)
	Never	90 (47.1%)	34 (55.7%)	61 (49.2%)
3. How much salt or salty sauce do you think you consume?	Far too much	19 (9.9%)	4 (6.6%)	10 (8.1%)
	Too much	61 (31.9%)	16 (26.2%)	44 (35.5%)
	Just the right amount	73 (38.2%)	23 (37.7%)	45 (36.3%)
	Too little	36 (18.8%)	17 (27.9%)	24 (19.4%)
	Far too little	2 (1.0%)	1 (1.6%)	1 (0.8%)
4. In the past week, how often have you consumed packaged	Always	50 (26.5%)	14 (23.0%)	34 (27.4%)
	Often	47 (24.9%)	18 (29.5%)	28 (22.6%)
	Sometimes	14 (7.4%)	4 (6.6%)	7 (5.6%)
	Rarely	20 (10.6%)	3 (4.9%)	15 (12.1%)

foods? Examples include crackers, chips, and cookies.	Never	58 (30.7%)	22 (36.1%)	40 (32.3%)
5. To what degree do you like salty food? Rate yourself on a scale of 1 to 10, with 10 being very strong preference for salty food^	2	1 (0.5%)	0 (0%)	0 (0%)
	3	10 (5.2%)	5 (8.2%)	7 (5.6%)
	4	26 (13.6%)	10 (16.4%)	16 (12.9%)
	5	66 (34.6%)	23 (37.7%)	40 (32.3%)
	6	24 (12.6%)	8 (13.1%)	18 (14.5%)
	7	33 (17.3%)	10 (16.4%)	26 (21.0%)
	8	27 (14.1%)	5 (8.2%)	16 (12.9%)
	9	4 (2.1%)	0 (0%)	1 (0.8%)

Notes: *Only one person in the sample answered "Not Applicable"
^No participant in the sample answered a 1 or a 10 for this question

Appendix B

<u>Questions Regarding Healthcare Utilization and Healthcare Barriers:</u>

1. If you were very sick and needed treatment, where would you go? (Select all that apply)
    a. Government hospital
    b. Private hospital
    c. Traveling doctor/nurse
    d. Pharmacy
    e. Traditional practitioner
    f. Market
    g. Traveling drug seller
    h. Private doctor
    i. Other
2. When you are sick and want to get medical advice or treatment, how big a problem is each of the following? (A big problem, A small problem, Not a problem, Prefer not to say)
    a. Getting money needed for advice or treatment
    b. The distance to the healthy facility
    c. Not wanting to go alone

<u>PSS Questionnaire:</u>

1. l. In the last month, how often have you been upset because of something that happened unexpectedly?
2. In the last month, how often have you felt that you were unable to control the important things in your life?
3. In the last month, how often have you felt nervous and stressed?
4. In the last month, how often have you felt confident about your ability to handle your personal problems?
5. In the last month, how often have you felt that things were going your way?
6. In the last month, how often have you found that you could not cope with all the things that you had to do?
7. In the last month, how often have you been able to control irritations in your life?
8. In the last month, how often have you felt that you were on top of things?
9. In the last month, how often have you been angered because of things that happened that were outside of your control?
10. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?

For each question choose from the following alternatives:

0 - never 1 - almost never 2 - sometimes 3 - fairly often 4 - very often

Appendix C

Table 7: Model Averaging Estimates and Confidence Intervals (95% CI)

Model 1 n=3,784	Systolic	Diastolic	WHO	ACC/AHA
Age	0.149 (0.133, 0.166)	0.119 (0.103, 0.135)	5.887 (4.880, 6.894)	4.158 (3.362, 4.955)
Gender	0.023 (0.001, 0.045)	-0.005 (-0.024, 0.013)	0.061 (-0.367, 0.490)	-0.040 (-0.349, 0.270)
BMI	0.117 (0.061, 0.173)	0.110 (0.055, 0.165)	2.534 (-0.744, 5.811)	4.265 (2.300, 6.230)
Model 2 n=404	Systolic	Diastolic	WHO	ACC/AHA
Age	0.212 (0.146, 0.278)	0.142 (0.083, 0.201)	5.912 (2.733, 9.091)	5.195 (2.664, 7.725)
Gender	0.000 (-0.008, 0.008)	-0.001 (-0.012, 0.010)	-0.100 (-1.139, 0.938)	0.167 (-0.854, 1.188)
BMI	0.188 (-0.082, 0.457)	0.101 (-0.123, 0.326)	7.894 (-0.353, 16.140)	7.099 (-0.271, 14.469)
Salt Intake	0.000 (-0.005, 0.005)	0.000 (-0.007, 0.008)	0.177 (-0.753, 1.107)	0.072 (-0.623, 0.767)
Model 3 n=143	Systolic	Diastolic	WHO	ACC/AHA
Age	0.247 (0.136, 0.358)	0.145 (0.012, 0.278)	6.638 (-0.285, 13.560)	3.623 (1.027, 6.219)
Gender	0.001 (-0.019, 0.020)	0.000 (-0.015, 0.015)	0.197 (-1.666, 2.061)	0.007 (-0.815, 0.829)
BMI	0.009 (-0.113, 0.130)	0.008 (-0.098, 0.114)	0.193 (-5.585, 5.971)	0.419 (-2.977, 3.815)
PSS	-0.001 (-0.001, 0.001)	-0.001 (-0.001, 0.001)	-0.007 (-0.216, 0.202)	-0.038 (-0.193, 0.117)
Model 4 n=116	Systolic	Diastolic	WHO	ACC/AHA
Age	0.273 (0.129, 0.417)	0.133 (-0.045, 0.311)	6.816 (-0.495, 14.128)	3.369 (-0.195, 6.933)
Gender	-0.001 (-0.022, 0.021)	-0.001 (-0.023, 0.021)	-0.357 (-2.589, 1.874)	-0.110 (-1.177, 0.956)

BMI	-0.002 (-0.124, 0.119)	-0.006 (-0.117, 0.104)	-1.666 (-9.847, 6.515)	0.245 (-3.527, 4.017)
Salt Intake	0.000 (-0.019, 0.019)	0.001 (-0.017, 0.018)	2.003 (-2.550, 6.556)	0.113 (-0.855, 1.081)
PSS	-0.001 (-0.001, 0.001)	-0.001 (-0.001, 0.001)	-0.012 (-0.240, 0.216)	-0.040 (-0.225, 0.144)

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