Characteristics Associated With Antihypertensive Treatment and Blood Pressure Control

A Population-Based Follow-Up Study in Peru

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ABSTRACT

Background: Over one-quarter of the world's adult population has hypertension, yet achieving adequate treatment or control targets remains a challenge.

Objective: This study sought to identify, longitudinally, characteristics associated with antihypertensive treatment and blood pressure (BP) control among individuals with hypertension.

Methods: Data from individuals enrolled in the population-based CRONICAS Cohort Study (adults ≥35 years, living in 4 different rural/urban and coastal/high-altitude Peruvian settings) with hypertension at baseline were used. Antihypertensive treatment and BP control were assessed at baseline and at 15 months. Multinomial logistic regressions were used to estimate relative risk ratios (RRR) and 95% confidence intervals (95% CI) of factors associated with antihypertensive treatment and BP control at follow-up.

Results: At baseline, among 717 individuals with hypertension (53% women, mean age 61.5 ± 12.4 years), 28% were unaware of their hypertension status, 30% were aware but untreated, 16% were treated but uncontrolled, and 26% were treated and controlled. At follow-up, 89% of unaware and 82% of untreated individuals persisted untreated, and only 58% of controlled individuals remained controlled. Positive predictors of receiving treatment and being controlled at follow-up included age (RRR: 0.81; 95% CI: 0.73 to 0.91 for every 5 years) and family history of a chronic disease (RRR: 0.53; 95% CI: 0.31 to 0.92 vs. no history); whereas Puno rural site (RRR: 16.51; 95% CI: 1.90 to 143.56 vs. Lima) and male sex (RRR: 2.59; 95% CI: 1.54 to 4.36) were risk factors. Systolic BP at baseline (RRR: 1.27; 95% CI: 1.16 to 1.39 for every 5 mm Hg) and male sex (RRR: 1.75, 95% CI: 1.02 to 2.98) were risk factors for being treated but uncontrolled at follow-up.

Conclusions: Large gaps in treatment of hypertension were observed. Targeting specific populations such as men, younger individuals, or those without family history of disease may increase coverage of antihypertensive treatment. Also, targeting male individuals or those with higher systolic BP could yield better rates of BP control in the short term.

Worldwide, over one-quarter of the adult population has hypertension, and there is a disproportionate burden on developing countries [1,2]. Despite hypertension-related mortality decreasing around the world [3,4], hypertension still remains a leading cause of global mortality [5].

Achieving optimal blood pressure (BP) control is an important goal of hypertension management. It has been estimated that only 50% to 75% of hypertensive individuals are aware of their diagnosis, and 12% to 41% of those diagnosed receive treatment or achieve control targets [6–9]. In Peru, the prevalence of hypertension varies from 11% in rural areas to 29% in urban populations [10]. However, it has been estimated that only 6% of individuals with hypertension receive treatment and are adequately controlled with BP levels <140/90 mm Hg [11].

Hypertension management is a long-term process that is commonly challenging for patients and health care providers. A combination of lifestyle modification and pharmacologic treatment with antihypertensive medication is essential to achieving adequate BP control [12–14], yet nearly one-half of patients discontinue their antihypertensive regimens within the first year [15]. Poor BP control may be explained by unawareness of hypertension diagnosis, lack of knowledge of target BP goals, nonadherence to pharmacologic treatment [16], and unhealthy lifestyles [17]. Information from prospective

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studies from low- and middle-income country settings revealing the characteristics of individuals at risk of not taking medication or achieving BP control is scarce.

Identifying predictors of BP treatment and control is needed to adequately design and implement interventions to improve treatment and BP control rates. In this study, we aimed to characterize factors associated with the use of antihypertensive medication and BP control in the short term, according to previous awareness, treatment, and BP control status.

METHODS

Study design and setting

This study is an analysis in a sample of participants of the CRONICAS Cohort Study, a longitudinal, population-based study designed to determine progression toward cardiovascular and chronic pulmonary diseases in Peru. The original study design has been described elsewhere [18]. Briefly, a random age- and sex-stratified sample of individuals aged 35 years and older was selected from 4 different sites, spanning 3 regions that differ by degree of urbanization and elevation. These regions include: 1) Pampas de San Juan de Miraflores, a highly urbanized periurban community on the coast of Lima; 2) Puno, located in the Andes at 3,825 m above sea level, which contributed with both urban and rural sites; and 3) Tumbes, a semiurban group of villages on the northern coast of Peru. Health indicators in Puno were worse than those in Tumbes and Lima. According to Peru's national 2007 census, only 27% of Puno's population has health insurance, followed by 37% in San Juan de Miraflores and 48% in Tumbes [19]. In 2010, there were 1,412 inhabitants per physician in Puno, 1,184 in Tumbes, and 355 in Lima [20].

Study participants

For this study, we restrict our analysis to those participants who were classified as hypertensive at baseline and in whom complete data on BP, antihypertensive medication, and cardiometabolic risk factors evaluation were available. Hypertension was defined as follows: 1) measured systolic blood pressure (SBP) $\geq$140 mm Hg or diastolic blood pressure (DBP) $\geq$90 mm Hg; 2) self-reported diagnosis of hypertension (performed by a physician); or 3) current use of antihypertensive medication. All subjects were informed of their BP levels, and those with elevated BP readings were recommended to seek medical care at their nearest health facilities.

Procedures

Evaluation of participants was completed by trained and standardized research staff. At baseline, the protocol included a questionnaire to collect information about sociodemographic characteristics, cardiometabolic and behavioral risk factors, and antihypertensive treatment, as well as personal and family medical history of cardiovascular disease and other chronic diseases. BP was measured in triplicate after a 5-min period of rest using an automatic BP device (OMRON HEM-780, Omron Healthcare, Hoffman Estates, IL, USA). For the analysis, the mean value of the second and third measurements was used [21]. Anthropometric measures and laboratory analyses were conducted following standard procedures [18]. The protocol at 15-month follow-up was similar to the one used at baseline.

Exposure variables at baseline

Sociodemographic variables included sex, age (years), study site (Lima, urban Puno, rural Puno, and Tumbes), and education level (primary or less [<6 years], secondary [6 to 12 years], and superior [$\geq$12 years]). Socioeconomic status was divided into 3 categories corresponding to tertiles of the assets and household facilities dimensions of the composite wealth index score [22].

For analytic purposes, variables of interest were categorized using commonly reported cutoffs, when available. Three cardiometabolic and 1 behavioral factor were dichotomized according to the recommendations of the American Heart Association's ideal cardiovascular health metrics [23]. Body mass index was divided into healthy (18.5 to 24.9 kg/m^2) and excess of weight ($\geq$25.0 kg/m^2), total serum cholesterol into healthy (<200 mg/dl without cholesterol-lowering medication) and unhealthy ($\geq$200 mg/dl or cholesterol-lowering medication use), fasting blood glucose was divided into healthy (<100 mg/dl without glucose-lowering medication use) and unhealthy ($\geq$100 mg/dl or glucose-lowering medication use), and tobacco use into never/former smoker (not smoking even 1 cigarette for the last year or more) and current smoker (self-report of currently smoking). Physical activity, assessed using the leisure time domain of the International Physical Activity Questionnaire, was used to classify participants as active ($\geq$75 min/week vigorous intensity or $\geq$150 min/week moderate and vigorous intensity activity) or inactive (less than that amount), self-report of fruit and vegetable intake was used to classify participants as having a healthy ($\geq$4.5 cups of fruits and vegetables/day) or unhealthy (<4.5 cups of fruits and vegetables/day) diet, and alcohol consumption, which was assessed using the Alcohol Use Disorders Identification Test (AUDIT), was used to divide drinking patterns into not-hazardous (AUDIT score $\leq$7) and hazardous (AUDIT score $\geq$8) [24,25]. Personal history of disease included a diagnosis of heart disease or stroke by a physician. Family history of disease was based on self-report of a relative with a cardiometabolic disease such as high BP, heart disease, high serum cholesterol, diabetes, stroke, or other chronic disease such as tuberculosis, asthma, chronic bronchitis, chronic obstructive pulmonary disease, or lung cancer.

To incorporate hypertension awareness, antihypertensive treatment, and BP control (A-T-C) into a single analysis, a composite measure was created that yielded the following categories: 1) the unaware group (participants with SBP $\geq$140 mm Hg or DBP $\geq$90 mm Hg, without

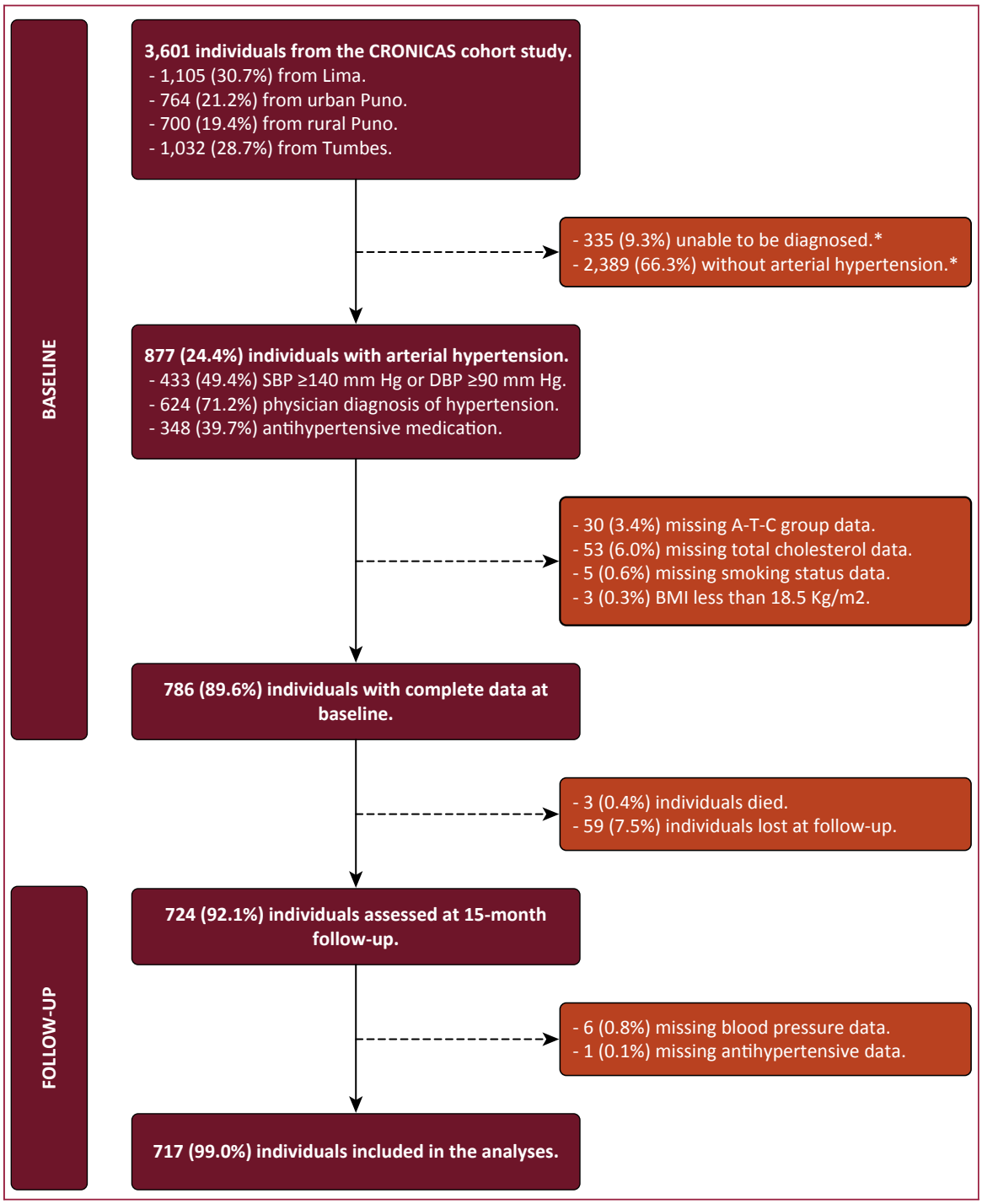

FIGURE 1. Inclusion of participants in the study. *Diagnosis of arterial hypertension was based on blood pressure measurement, physician diagnosis, and antihypertensive medication use. A-T-C, hypertension awareness, antihypertensive treatment, and blood pressure control; BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure.

TABLE 1. Characteristics of population with hypertension at baseline

	Unaware (n = 204)	Aware but Untreated (n = 215)	Treated but Uncontrolled (n= 115)	Treated and Controlled (n = 183)	p Value
Sociodemographic factors					
Age, yrs*	62.4 ± 12.9	56.7 ± 11.6	67.9 ± 10.2	62.0 ± 11.8	<0.001
Sex					<0.001
Female	61 (30)	125 (58)	73 (63)	124 (68)	
Male	143 (70)	90 (42)	42 (37)	59 (32)	
Site					<0.001
Lima	64 (31)	96 (45)	39 (34)	62 (34)	
Urban Puno	14 (7)	46 (21)	6 (5)	18 (10)	
Rural Puno	43 (21)	18 (8)	2 (2)	6 (3)	
Tumbes	83 (41)	55 (26)	68 (59)	97 (53)	
Socioeconomic status					0.757
Lowest	80 (39)	68 (32)	41 (36)	62 (34)	
Middle	60 (29)	70 (33)	34 (30)	53 (29)	
Highest	64 (31)	77 (36)	40 (35)	68 (37)	
Cardiometabolic factors					
Blood pressure					
SBP, mm Hg	148.9 ± 16.5	121.9 ± 19.3	156.9 ± 15.9	121.1 ± 11.6	<0.001
DBP, mm Hg	90.1 ± 12.0	75.9 ± 12.8	88.7 ± 10.3	73.1 ± 8.2	<0.001
Body mass index					0.002
Healthy	60 (29)	34 (16)	22 (19)	31 (17)	
Excess of weight	144 (71)	181 (84)	93 (81)	152 (83)	
Total serum cholesterol					0.014
Healthy	102 (50)	92 (43)	38 (33)	69 (38)	
Unhealthy	102 (50)	123 (57)	77 (67)	114 (62)	
Fasting plasma glucose					0.001
Healthy	131 (64)	151 (70)	57 (50)	103 (56)	
Unhealthy	73 (36)	64 (30)	58 (50)	80 (44)	
Behavioral factors					
Alcohol, AUDIT score					<0.001
Not-hazardous drinking	166 (81)	190 (88)	110 (96)	174 (95)	
Hazardous drinking	38 (19)	25 (12)	5 (4)	9 (5)	
Smoking status					0.057
Never/former smoker	172 (84)	189 (88)	104 (90)	170 (93)	
Current smoker	32 (16)	26 (12)	11 (10)	13 (7)	
Fruit and vegetables consumption					0.003
Healthy	5 (2)	24 (11)	5 (4)	13 (7)	
Unhealthy	199 (98)	191 (89)	110 (96)	170 (93)	
Leisure time physical activity					0.384
Active	9 (4)	10 (5)	2 (2)	11 (6)	
Inactive	195 (96)	205 (95)	113 (98)	172 (94)	
History of disease					
Personal history of heart disease					<0.001
No previous history	197 (97)	194 (90)	10 (9)	147 (80)	
Heart disease diagnosed by physician	7 (3)	21 (10)	13 (11)	36 (20)	
Personal history of stroke					0.019
No previous history	204 (100)	214 (100)	113 (98)	177 (97)	
Stroke diagnosed by physician	0 (0)	1 (0)	2 (2)	6 (3)	
Family history of cardiometabolic disease*					<0.001
No previous history	125 (61)	99 (46)	33 (29)	56 (31)	
At least 1 cardiometabolic disease	79 (39)	116 (54)	82 (71)	127 (69)	

(continued)

TABLE 1–*continued*. Characteristics of population with hypertension at baseline

	Unaware (n = 204)	Aware but Untreated (n = 215)	Treated but Uncontrolled (n= 115)	Treated and Controlled (n = 183)	p Value
Family history of a chronic disease[†]					<0.001
No family history	116 (57)	82 (38)	30 (26)	50 (27)	
At least 1 relative with any disease	88 (43)	133 (62)	85 (74)	133 (73)	

Values are mean ± SD or n (%). DBP, diastolic blood pressure; SBP, systolic blood pressure.

*Includes hypertension, heart disease, high cholesterol, diabetes, and stroke.

[†]Includes cardiometabolic diseases, as above, tuberculosis, asthma, chronic bronchitis, chronic obstructive pulmonary disease, or lung cancer.

a physician diagnosis of hypertension and without antihypertensive treatment); 2) the aware but untreated group (participants with a diagnosis of hypertension by a physician, without antihypertensive treatment); 3) the treated but uncontrolled group (participants taking antihypertensive treatment with SBP ≥140 mm Hg or DBP ≥90 mm Hg); and 4) the treated and controlled group (participants taking antihypertensive treatment with SBP <140 mm Hg and DBP <90 mm Hg).

Study outcome

At 15-month follow-up, antihypertensive treatment and BP control status were assessed and incorporated into a single 3-categories outcome (untreated, treated but uncontrolled, and treated and controlled). A participant was included in the untreated category if he/she did not take at least 1 antihypertensive medication, once per week, during the last month. The treated but uncontrolled BP was defined as SBP ≥140 mm Hg or DBP ≥90 mm Hg among participants taking antihypertensive medication. The treated and controlled BP was defined as SBP <140 mm Hg and DBP <90 mm Hg among participants taking antihypertensive medication. Awareness was not considered at follow-up because all participants included in the analysis had to satisfy the definition of hypertension at baseline and were informed of their hypertension diagnosis.

Statistical power

Using a 2-tailed alpha level of 0.05, with 717 participants, the study had 80% of power to detect risk ratios of treatment and BP control of 1.55 or higher, or 0.64 or lower. Statistical power was calculated using Power Analysis and Sample Size PASS software (version 11, NCSS, Kaysville, UT, USA).

Statistical analysis

A description of sociodemographic, cardiometabolic, and behavioral characteristics was performed for each of the 4 baseline A-T-C groups. Continuous variables are presented as mean ± SD and categorical variables are presented as proportions. Associations between baseline characteristics and treatment and BP control at follow-up were assessed using chi-squared for categorical variables and Student *t* or analysis of variance tests for continuous variables. Those characteristics statistically associated with the outcome of interest were included in a nested multinomial logistic regression model [26] to identify potential baseline risk factors associated with treatment and BP control at follow-up. The Akaike information criterion was used to select the variables with the better fitting model. Unadjusted and adjusted relative risk ratios (RRR), with 95% confidence intervals (95% CI), of being untreated, uncontrolled, and controlled at follow-up were estimated. Because BP measurements were only conducted during 1 visit, a sensitivity analysis was performed using higher thresholds for SBP (145 mm Hg and 150 mm Hg) to define unawareness status. This was done to minimize the possibility of including individuals without hypertension in the study. All analyses considered a 2-tailed p value <0.05 to be statistically significant. Stata 12.1 (Stata Corporation, College Station, TX, USA) was used for data analyses.

Ethical considerations

All participants of the CRONICAS Cohort Study provided verbal informed consent. Verbal consent was chosen over

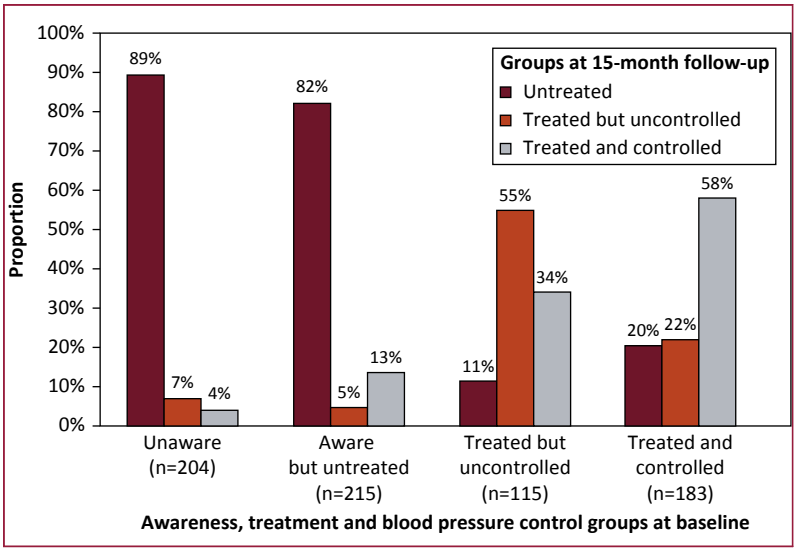

FIGURE 2. Antihypertensive treatment and blood pressure control at follow-up according to baseline status (N = 717).

TABLE 2. Baseline characteristics associated with antihypertensive treatment and BP control at follow-up

	n	Untreated (n = 408)	Treated but Uncontrolled (n = 127)	Treated and Controlled (n = 182)	p Value
Sociodemographic factors					
Age, yrs	717	58.9 ± 12.4.	66.7 ± 12.2	63.6 ± 10.8	<0.001
Sex					<0.001
Female	383	178 (46)	72 (19)	133 (35)	
Male	334	230 (69)	55 (16)	49 (15)	
Site					<0.001
Lima	261	149 (57)	38 (15)	74 (28)	
Urban Puno	84	62 (74)	6 (7)	16 (19)	
Rural Puno	69	65 (94)	3 (4)	1 (1)	
Tumbes	303	132 (44)	80 (26)	91 (30)	
Socioeconomic status					0.643
Lowest	251	140 (56)	47 (19)	64 (25)	
Middle	217	130 (60)	39 (18)	48 (22)	
Highest	249	138 (55)	41 (16)	70 (28)	
Cardiometabolic factors					
Blood pressure					
SBP, mm Hg	717	132.7 ± 21.7	150.5 ± 22.4	129.3 ± 18.4	<0.001
DBP, mm Hg	717	81.8 ± 13.7	85.4 ± 11.8	77.3 ± 12.8	<0.001
Body mass index					0.084
Healthy	147	93 (63)	27 (18)	27 (18)	
Excess of weight	570	315 (55)	100 (18)	155 (27%)	
Total serum cholesterol					<0.001
Healthy	301	199 (66)	40 (13)	62 (21)	
Unhealthy	416	209 (50)	87 (21)	120 (29)	
Fasting plasma glucose					0.001
Healthy	442	272 (62)	61 (14)	109 (25)	
Unhealthy	275	136 (49)	66 (24)	73 (27)	
Behavioral factors					
Alcohol, AUDIT score					<0.001
Not-hazardous drinking	640	346 (54)	117 (18)	177 (28)	
Hazardous drinking	77	62 (81)	10 (13)	5 (6)	
Smoking status					0.011
Never/former	635	351 (55)	112 (18)	172 (27)	
Current smoker	82	57 (70)	15 (18)	10 (12)	
Fruit and vegetables consumption					0.209
Healthy	47	31 (66)	4 (9)	12 (26)	
Unhealthy	670	377 (56)	123 (18)	170 (25)	
Leisure time physical activity					0.705
Active	32	20 (63)	4 (13)	8 (25)	
Inactive	685	388 (57)	123 (18)	174 (25)	
History of disease					
Personal history of heart disease					<0.001
No previous history	640	379 (59)	112 (18)	149 (23)	
Heart disease diagnosed by physician	77	29 (38)	15 (19)	33 (43)	
Personal history of stroke					<0.001
No previous history	708	408 (58)	125 (18)	175 (25)	
Stroke diagnosed by physician	9	0 (0)	2 (22)	7 (78)	
Family history of cardiometabolic disease*					<0.001
No previous history	313	220 (70)	44 (14)	49 (16)	
At least 1 cardiometabolic disease	404	188 (47)	83 (21)	133 (33)	

(continued)

TABLE 2–*continued*. Baseline characteristics associated with antihypertensive treatment and BP control at follow-up

	n	Untreated (n = 408)	Treated but Uncontrolled (n = 127)	Treated and Controlled (n = 182)	p Value
Family history of a chronic disease†					<0.001
No family history	278	196 (71)	41 (15)	41 (15)	
At least 1 relative with any disease	439	212 (48)	86 (20)	141 (32)	

Values are mean ± SD or n (%) unless otherwise indicated. BP, blood pressure; other abbreviations as in Table 1.

*Includes hypertension, heart disease, high cholesterol, diabetes, and stroke.

†Includes cardiometabolic diseases, as above, tuberculosis, asthma, chronic bronchitis, chronic obstructive pulmonary disease, or lung cancer.

written consent due to high rates of illiteracy especially in rural areas. The CRONICAS Cohort Study was approved by the institutional review boards at Universidad Peruana Cayetano Heredia and A.B. PRISMA, in Lima, Peru, and at the Bloomberg School of Public Health, Johns Hopkins University, in Baltimore, MD, USA.

RESULTS

Participants

A total of 3,601 individuals were enrolled into the study. At baseline, 877 individuals (24.4%) with hypertension were identified. However, 88 individuals were excluded because they did not have complete data, and 3 because their body mass index was lower than 18.5 kg/m^2. Of the 786 eligible participants at follow-up, 3 individuals (0.4%) were dead, 59 were lost to follow-up, and 7 had no data of BP or antihypertensive treatment. Therefore, 717 individuals (82% response rate, 53.4% female, mean age 61.5 ± 12.4 years) were included in the analyses (Figure 1).

Characteristics of study participants at baseline

At baseline, 362 individuals (50.5%) had high levels of SBP and/or DBP, 505 (70.4%) had a diagnosis by a physician, and 298 (41.6%) were taking antihypertensive medication.

TABLE 3. RRR of taking antihypertensive treatment and having BP control at follow-up

	n	Untreated Versus Treated and Controlled		Treated But Uncontrolled Versus Treated and Controlled	
		Unadjusted RRR (95% CI)	Adjusted RRR* (95% CI)	Unadjusted RRR (95% CI)	Adjusted RRR* (95% CI)
Groups at baseline					
Treated and controlled	183	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Treated but uncontrolled	115	0.95 (0.46–1.98)	2.17 (0.85–5.50)	4.28 (2.49–7.35)†	0.95 (0.43–2.08)
Aware but untreated	215	17.39 (10.11–29.91)†	16.03 (8.83–29.10)†	0.91 (0.41–2.04)	0.50 (0.20–1.25)
Unaware	204	65.18 (29.26–145.17)†	81.78 (30.74–217.54)†	4.64 (1.81–11.89)†	0.65 (0.20–2.12)
Systolic blood pressure, 5 mm Hg	717	1.04 (1.00–1.09)	0.92 (0.85–1.00)	1.25 (1.18–1.33)†	1.27 (1.16–1.39)†
Site					
Lima	261	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Urban Puno	84	1.92 (1.04–3.56)†	2.13 (0.97–4.70)	0.73 (0.26–2.02)	0.88 (0.28–2.72)
Rural Puno	69	32.28 (4.39–237.24)†	16.51 (1.90–143.56)†	5.84 (0.59–58.08)	6.54 (0.61–70.41)
Tumbes	303	0.72 (0.49–1.06)	0.93 (0.55–1.58)	1.71 (1.05–2.80)†	1.64 (0.95–2.83)
Sex					
Female	383	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Male	334	3.51 (2.39–5.14)†	2.59 (1.54–4.36)†	2.07 (1.28–3.35)†	1.75 (1.02–2.98)†
Age, 5 yrs	717	0.85 (0.79–0.92)†	0.81 (0.73–0.91)†	1.12 (1.02–1.23)†	0.97 (0.86–1.09)
Serum cholesterol					
Unhealthy	416	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Healthy	301	1.84 (1.28–2.65)†	1.64 (0.99–2.71)	0.89 (0.55–1.44)	0.69 (0.40–1.19)
Family history of a chronic disease‡					
No family history	278	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
At least 1 relative with any disease	439	0.31 (0.21–0.47)†	0.53 (0.31–0.92)†	0.61 (0.37–1.01)	0.58 (0.32–1.05)

BP, blood pressure; CI, confidence interval(s); RRR, relative risk ratio.

*Model adjusted for all other factors simultaneously.

†p value < 0.05.

‡Includes hypertension, heart disease, high cholesterol, diabetes, stroke, tuberculosis, asthma, chronic bronchitis, chronic obstructive pulmonary disease, or lung cancer.

Moreover, 204 (28.4%) individuals (50.5%) were unaware of their hypertension status, 215 (30%) were untreated, 115 (16%) were uncontrolled, and only 183 (25.5%) were controlled.

Sociodemographic, cardiometabolic, and behavioral characteristics according to A-T-C groups at baseline are presented in Table 1. The highest proportion of male individuals was in the unaware group (70%); it decreases in the untreated group and becomes the lowest in the controlled group (32%). Age varied across groups without a clear trend. Socioeconomic status was similar among A-T-C groups. The predominant educational level was primary or less (58%). The untreated group had the highest proportions of secondary (29%) and superior (23%) education levels. Only 10.5% of individuals met 4 to 6 of the ideal cardiovascular health metrics. Personal history of heart disease and stroke were infrequent (10.7% and 1.3%, respectively). Family history of disease was more frequent and increased with awareness, treatment, and BP control.

Factors associated with treatment and control of hypertension at follow-up

Individuals were followed on average for 15.5 ± 3.5 months. At follow-up, 408 individuals (56.9%) were untreated, 127 (17.7%) were uncontrolled, and 182 (25.4%) were controlled.

One-quarter of all individuals (n = 190, 26.5%) moved from their baseline A-T-C groups to other groups at follow-up. From the unaware group at baseline, 22 individuals (10.8%) became treated at follow-up, but only 8 (3.9%) had their BP controlled. From the untreated group at baseline, 39 individuals (18.1%) became treated at follow-up, and 29 (13.5%) had their BP controlled.

On the other hand, 39 individuals (33.9%) from the uncontrolled group at baseline became controlled at follow-up, but another 13 (11.3%) became untreated. From the controlled group at baseline, only 106 (57.9%) remained controlled, and 37 (20.2%) became untreated (Figure 2).

Factors associated with treatment and BP control are presented in Table 2. Being female, having unhealthy cardiometabolic factors, and personal and family history of disease were associated with taking treatment and achieving BP control at follow-up. Smoking and hazardous alcohol drinking at baseline were associated with being untreated at follow-up. Even, if individuals were treated at follow-up, they were more likely to have their BP uncontrolled.

Multinomial regression analyses

Results from the nested regression model are presented in Table 3. All models used the treated and controlled group at follow-up as the reference category.

Risk factors for being untreated at follow-up were A-T-C status at baseline, living in rural Puno, and male sex. Increasing age and family history of chronic disease were found to be protective factors.

Among those receiving treatment at follow-up, SBP levels at baseline (for each 5 mm Hg increase) and male sex were predictors of not meeting BP control targets.

Sensitivity analysis

Using an SBP cutoff of 145 mm Hg to diagnose unawareness, the distribution and the predictors of treatment and BP control at follow-up remained unchanged.

Using an SBP cutoff of 150 mm Hg, the proportion of individuals untreated at follow-up increased only 1% at the expense of the controlled ones. Additionally, having healthy total serum cholesterol at baseline gained marginal statistical significance as a predictor of being untreated at follow-up (RRR: 1.71; 95% CI: 1.01 to 2.87).

DISCUSSION

Main findings

The proportion of controlled individuals who became uncontrolled or untreated at follow-up was much higher than the proportion of unaware and untreated individuals who became treated or who achieved BP control. Becoming untreated was more frequently observed among previously controlled individuals. Predictors of taking antihypertensive treatment or achieving BP control in the short term were not the same. A-T-C status, younger age, living in Puno, and lack of family history of a chronic disease at baseline were risk factors for being untreated 15 months later, whereas higher SBP at baseline was a risk factor of being uncontrolled in the short term. Male sex was the only predictor of both not taking treatment and being uncontrolled 15 months later.

Comparison with other studies

In newly diagnosed hypertensive patients from developed countries, incidence of antihypertensive treatment initiation varies widely from 80% in 3 months to 40% in 4 years [27–30]. This range is much higher than the 10.8% found in our study. In addition, persistence of treatment within 1 year after diagnosis has been reported around 50% [31–33].

Our study shows a low rate of BP control at follow-up, even in patients with previously controlled BP. In contrast, studies from Japan and Turkey have reported BP control rates from 16% to 48% in previously uncontrolled, and from 35% to 72% in previously controlled individuals [34,35]. However, their BP goals for patients with diabetes or older age were lower than ours.

This study shows that female sex and older age were associated with taking treatment, which has been reported in other cross-sectional studies [36–38]. The protective role of healthier lifestyles including practicing leisure time physical activity and absence of smoking, as reported in other studies [38,39], was not reproduced in our study.

Cross-sectional studies have shown the role of weight [39,40] and lifestyle modification [41] on BP control. One

recent study showed that weight gain, elevated baseline low-density lipoprotein cholesterol, and no reduction in fasting glucose were predictors for failing to maintain BP goals [42]. However, in our study, no cardiometabolic or behavioral factors were associated with BP control. In addition, male sex was the only sociodemographic characteristic associated with uncontrolled BP in our study [36,40,41].

Findings interpretation

The group with unaware status at baseline may have incorporated individuals without established clinical hypertension, such as white-coat hypertension, elevated BP values in the presence of a health care worker but not in the home environment [43–45], or, regression to the mean phenomena, that is initial elevated BP values that later turn into lower BP values without any intervention [46,47]. These 2 particularities would partially explain the lack of treatment initiation at follow-up. Yet, only when SBP was set as the 150 mm Hg cutoff, minimal changes were observed, showing the robustness of our results. In addition, the aware but untreated group had a similar behavior at follow-up, suggesting that other reasons could explain this lack of treatment initiation. A qualitative study may help to elucidate whether the low treatment initiation rate is because the disease is asymptomatic, the nonacceptance of having a chronic disease, the rejection to start medication [48–50], or preference to behavioral changes rather than medication [51], or if the driving of nonadherence is poor execution or nonpersistence once treatment has been initiated [15]. Treatment discontinuation is a big problem because it is usually an intentional decision, and restarting treatment on these individuals is more difficult [52].

Living in rural Puno was associated with not taking treatment, which could be explained by its low-income level [38], the rural setting [39], or the low education level [53]. However, noncommunicable diseases are so related with low socioeconomic status that other potential explanations need to be further explored [54]. For example, barriers for access to health care and treatment in Lima include difficulties getting a medical appointment, low affordability of medication, reduced treatment adherence, and low access to self-monitoring equipment [55]. It is expected to find low treatment rates in Puno, where 73% of the population do not have a health insurance [19] and the number of inhabitants per physician is 4 times that of Lima [20]. Individuals with personal history of cardiovascular diseases or with family history of other chronic diseases were more likely to be treated and controlled. It suggests that having other diseases and/or other health-related experiences could influence acceptance of disease, decision to take treatment, and treatment compliance [50,51]. Despite this observation, a warning signal comes from other longitudinal studies that have shown that hypertensive populations without other medical comorbidities are less likely to achieve BP control targets [35,56].

Limitation and strengths

The following limitations merit consideration. Selection bias, due to individuals excluded because incomplete data, cannot be ruled out. Nevertheless, our findings about awareness, treatment, and BP control prevalence are similar to other community-based studies in Latin American populations, supporting the validity of our results [7,57]. In line with previous studies, the definition of hypertension was based on BP measurements taken on a single visit [8,37,39,40,57], which could misclassify healthy individuals as unaware of their hypertension condition. It is recommended that [21] BP measurements should be taken at 2 or more visits to avoid potential overestimation of hypertension status. Duration of disease and adherence to treatment were not ascertained with precision, but on the contrary, our study benefited from a large population-based study unraveling major proportions of unawareness of hypertension status and initiation of treatment in the short term.

Also, the prospective design of our study allowed the identification of protective factors as well as risk factors for well-defined profiles of treatment and control over time. These factors, albeit not modifiable, are easy to be recognized and could inform and frame resource allocation of future public health interventions targeting groups at risk. This study emphasizes the importance of identifying and distinguishing among risk factors that help to predict antihypertensive treatment from those that help to predict adequate BP control after 15 months. These characteristics should be taken in account in order to detect which patients would need more or strongest interventions to achieve goals of treatment or BP control.

CONCLUSIONS

Large treatment gaps were observed on a short-term 15-month evaluation of Peruvian adults with hypertension. Many missed opportunities for advancing BP treatment and control were identified including the following: 1) getting patients on pharmacological treatment, for example, more than 80% of patients potentially aware of their hypertension status were not receiving treatment; 2) improving the proportion of patients on treatment that achieve control, for example, nearly 60% of those treated at baseline remain uncontrolled; and 3) protecting the gains of those controlled, for example, nearly 40% of those controlled at baseline discontinued treatment or were not controlled at follow-up. Targeting specific populations such as men, younger individuals, or those without family history of disease may increase coverage of antihypertensive treatment. Also, targeting male individuals or those with higher systolic BP could yield better rates of BP control in the short term. Better strategies, including implementation designs tailored to each of the groups studied given their risk profile paired with patient's challenges and needs, are required to ensure better treatment coverage and control rates.

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REFERENCES

1. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. Lancet 2005;365:217–23.
2. Kearney PM, Whelton M, Reynolds K, Whelton PK, He J. Worldwide prevalence of hypertension: a systematic review. J Hypertens 2004; 22:11–9.
3. GBD 2013 Mortality and Causes of Death Collaborators. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990—2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 2015;385:117–71.
4. Tao L, Pu C, Shen S, et al. Tendency for age-specific mortality with hypertension in the European Union from 1980 to 2011. Int J Clin Exp Med 2015;8:1611–23.
5. Mendis S, Puska P, Norrving B, World Health Organization, World Heart Federation, World Stroke Organization. Global atlas on cardiovascular disease prevention and control. Geneva, Switzerland: World Health Organization; 2011.
6. Ma WJ, Tang JL, Zhang YH, et al. Hypertension prevalence, awareness, treatment, control, and associated factors in adults in southern China. Am J Hypertens 2012;25:590–6.
7. Hernandez-Hernandez R, Silva H, Velasco M, et al. Hypertension in seven Latin American cities: the Cardiovascular Risk Factor Multiple Evaluation in Latin America (CARMELA) study. J Hypertens 2010;28:24–34.
8. Chow CK, Teo KK, Rangarajan S, et al. for the PURE Study Investigators. Prevalence, awareness, treatment, and control of hypertension in rural and urban communities in high-, middle-, and low-income countries. JAMA 2013;310:959–68.
9. Bersamin A, Stafford RS, Winkleby MA. Predictors of hypertension awareness, treatment, and control among Mexican American women and men. J Gen Intern Med 2009;24(Suppl 3):521–7.
10. Miranda JJ, Gilman RH, Smeeth L. Differences in cardiovascular risk factors in rural, urban and rural-to-urban migrants in Peru. Heart 2011;97:787–96.
11. Lerner AG, Bernabe-Ortiz A, Gilman RH, Smeeth L, Miranda JJ. The "rule of halves" does not apply in Peru: awareness, treatment, and control of hypertension and diabetes in rural, urban, and rural-to-urban migrants. Crit Pathw Cardiol 2013;12:53–8.
12. Glynn LG, Murphy AW, Smith SM, Schroeder K, Fahey T. Interventions used to improve control of blood pressure in patients with hypertension. Cochrane Database Syst Rev 2010;3:CD005182.
13. Rees K, Dyakova M, Wilson N, Ward K, Thorogood M, Brunner E. Dietary advice for reducing cardiovascular risk. Cochrane Database Syst Rev 2013;12:CD002128.
14. Saito I, Suzuki H, Kageyama S, Saruta T. Effect of antihypertensive treatment on cardiovascular events in elderly hypertensive patients: Japan's Benidipine Research on Antihypertensive Effects in the Elderly (J-BRAVE). Clin Exp Hypertens 2011;33:133–40.
15. Vrijens B, Vincze G, Kristanto P, Urquhart J, Burnier M. Adherence to prescribed antihypertensive drug treatments: longitudinal study of electronically compiled dosing histories. BMJ 2008;336:1114–7.
16. Prugger C, Keil U, Wellmann J, et al. for the EUROASPIRE III Study Group. Blood pressure control and knowledge of target blood pressure in coronary patients across Europe: results from the EUROASPIRE III survey. J Hypertens 2011;29:1641–8.
17. Wu Y, Tai ES, Heng D, Tan CE, Low LP, Lee J. Risk factors associated with hypertension awareness, treatment, and control in a multiethnic Asian population. J Hypertens 2009;27:190–7.
18. Miranda JJ, Bernabe-Ortiz A, Smeeth L, et al. for the CRONICAS Cohort Study Group. Addressing geographical variation in the progression of non-communicable diseases in Peru: the CRONICAS cohort study protocol. BMJ Open 2012;2:e000610.
19. Instituto Nacional de Estadistica e Informatica. Censos Nacionales 2007: XI de Población y VI de Vivienda. Lima, Perú: INEI. Available at: http://censos.inei.gob.pe/Censos2007/IDSE/; 2007. Accessed July 28, 2015.
20. Instituto Nacional de Estadística e Informática. Número de habitantes por cada médico, según departamento. Available at: http://www.inei.gob.pe/estadisticas/indice-tematico/sociales/. Accessed July 28, 2015.
21. Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension 2003;42:1206–52.
22. Howe LD, Galobardes B, Matijasevich A, et al. Measuring socioeconomic position for epidemiological studies in low- and middle-income countries: a methods of measurement in epidemiology paper. Int J Epidemiol 2012;41:871–86.
23. Lloyd-Jones DM, Hong Y, Labarthe D, et al. for the American Heart Association Strategic Planning Task Force and Statistics Committee. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic Impact Goal through 2020 and beyond. Circulation 2010; 121:586–613.
24. Babor TF, Higgins-Biddle JC, Saunders JB, Monteiro MG, World Health Organization, Department of Mental Health and Substance Dependence. AUDIT: The Alcohol Use Disorders Identification Test: Guidelines for Use in Primary Health Care. 2nd edition. Geneva, Switzerland: World Health Organization; 2001.
25. De Silva P, Jayawardana P, Pathmeswaran A. Concurrent validity of the alcohol use disorders identification test (AUDIT). Alcohol Alcohol 2008;43:49–50.
26. Hausman J, McFadden D. Specification tests for the multinomial logit model. Econometrica 1984;52:1219–40.
27. Neutel CI, Campbell NR. Antihypertensive medication use by recently diagnosed hypertensive Canadians. Can J Cardiol 2007;23:561–5.
28. Mazzaglia G, Mantovani LG, Sturkenboom MC, et al. Patterns of persistence with antihypertensive medications in newly diagnosed hypertensive patients in Italy: a retrospective cohort study in primary care. J Hypertens 2005;23:2093–100.
29. Johnson HM, Thorpe CT, Bartels CM, et al. Antihypertensive medication initiation among young adults with regular primary care use. J Gen Intern Med 2014;29:723–31.
30. Baggarly SA, Kemp RJ, Wang X, Magoun AD. Factors associated with medication adherence and persistence of treatment for hypertension in a Medicaid population. Res Social Adm Pharm 2014;10: e99–112.
31. Lemstra M, Alsabbagh MW. Proportion and risk indicators of nonadherence to antihypertensive therapy: a meta-analysis. Patient Prefer Adherence 2014;8:211–8.
32. Corrao G, Soranna D, La Vecchia C, et al. Medication persistence and the use of generic and brand-name blood pressure-lowering agents. J Hypertens 2014;32:1146–53.
33. Hasford J, Mimran A, Simons WR. A population-based European cohort study of persistence in newly diagnosed hypertensive patients. J Hum Hypertens 2002;16:569–75.

34. Yokokawa H, Sanada H, Goto A, et al. Characteristics of antihypertensive medication and change of prescription over 1 year of follow up in Japan: Fukushima Research of Hypertension (FRESH). Am J Hypertens 2010;23:1299–305.

35. Aydogan U, Doganer YC, Atik A, et al. Blood pressure control in patients with hypertension: a retrospective cohort study. J Eval Clin Pract 2015;21:313–9.

36. Agyemang C, Bruijnzeels MA, Owusu-Dabo E. Factors associated with hypertension awareness, treatment, and control in Ghana, West Africa. J Hum Hypertens 2006;20:67–71.

37. Polonia J, Martins L, Pinto F, et al. for the PHYSA Study Investigators. Prevalence, awareness, treatment and control of hypertension and salt intake in Portugal: changes over a decade. The PHYSA study. J Hypertens 2014;32:1211–21.

38. Ferreira RA, Barreto SM, Giatti L. [Self-reported hypertension and non-adherence to continuous-use medication in Brazil: a population-based study]. Cad Saude Publica 2014;30:815–26 [in Portuguese].

39. Wang H, Zhang X, Zhang J, et al. Factors associated with prevalence, awareness, treatment and control of hypertension among adults in Southern China: a community-based, cross-sectional survey. PLoS One 2013;8:e62469.

40. Lloyd-Sherlock P, Beard J, Minicuci N, Ebrahim S, Chatterji S. Hypertension among older adults in low- and middle-income countries: prevalence, awareness and control. Int J Epidemiol 2014;43:116–28.

41. Balijepalli C, Bramlage P, Losch C, Zemmrich C, Humphries KH, Moebus S. Prevalence and control of high blood pressure in primary care: results from the German Metabolic and Cardiovascular Risk Study (GEMCAS). Hypertens Res 2014;37:580–4.

42. Suarez C, Galgo A, Mantilla T, Leal M, Escobar C. Variables associated with change in blood pressure control status after 1-year follow up in primary care: a retrospective analysis: the TAPAS study. Eur J Prev Cardiol 2014;21:12–20.

43. Kang YY, Li Y, Huang QF, et al. Accuracy of home versus ambulatory blood pressure monitoring in the diagnosis of white-coat and masked hypertension. J Hypertens 2015;33:1580–7.

44. Sipahioglu NT, Sipahioglu F. Closer look at white-coat hypertension. World J Methodol 2014;4:144–50.

45. Niiranen TJ, Jula AM, Kantola IM, Reunanen A. Prevalence and determinants of isolated clinic hypertension in the Finnish population: the Finn-HOME study. J Hypertens 2006;24:463–70.

46. Ambrosio GB, Dowd JE, Strasser T, Tuomilehto J. The dynamics of blood pressure in populations and hypertensive cohorts. Bull World Health Organ 1986;64:93–9.

47. Linden A. Assessing regression to the mean effects in health care initiatives. BMC Med Res Methodol 2013;13:119.

48. Morrell RW, Park DC, Kidder DP, Martin M. Adherence to antihypertensive medications across the life span. Gerontologist 1997;37:609–19.

49. Yiannakopoulou E, Papadopulos JS, Cokkinos DV, Mountokalakis TD. Adherence to antihypertensive treatment: a critical factor for blood pressure control. Eur J Cardiovasc Prev Rehabil 2005;12:243–9.

50. Chapman RH, Benner JS, Petrilla AA, et al. Predictors of adherence with antihypertensive and lipid-lowering therapy. Arch Intern Med 2005;165:1147–52.

51. Pound P, Britten N, Morgan M, et al. Resisting medicines: a synthesis of qualitative studies of medicine taking. Soc Sci Med 2005;61:133–55.

52. Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J 2013;34:2159–219.

53. Wang W, Lau Y, Loo A, Chow A, Thompson DR. Medication adherence and its associated factors among Chinese community-dwelling older adults with hypertension. Heart Lung 2014;43:278–83.

54. Diaz-Perera G, Bacallao J, Alemany E. [Subpopulations with particular epidemiologic profiles and risks in Havana, Cuba: diabetes, hypertension, and tobacco-related illnesses]. Rev Panam Salud Publica 2012;32:9–14.

55. Cardenas M, Moran D, Beran D, Miranda J. Identifying the Barriers for Access to Care and Treatment for Arterial Hypertension and Diabetes in Lima, Peru: Executive Summary. Lima, Peru: CRONICAS Center of Excellence in Chronic Diseases, Universidad Peruana Cayetano Heredia; 2014.

56. Yokokawa H, Goto A, Sanada H, et al. Association between control to target blood pressures and healthy lifestyle factors among Japanese hypertensive patients: longitudinal data analysis from Fukushima Research of Hypertension (FRESH). Obes Res Clin Pract 2014;8:e364–73.

57. Sorlie PD, Allison MA, Aviles-Santa ML, et al. Prevalence of hypertension, awareness, treatment, and control in the Hispanic Community Health Study/Study of Latinos. Am J Hypertens 2014;27:793–800.