



## Original article

# Blood pressure reference curves by age and residential altitude in Peruvian adults

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## ABSTRACT

**Objectives.** To develop age-specific percentile curves for mean arterial pressure (MAP), diastolic blood pressure (DBP), and systolic blood pressure (SBP) in Peruvian adults aged 20-59 years, stratified by altitude of residence. **Materials and methods.** An analytical cross-sectional study was conducted using data from the 2014-2024 Demographic and Family Health Survey (ENDES). Adults aged 20-59 years with two valid blood pressure measurements and no prior diagnosis of hypertension were included. Altitude of residence was classified as <2500, 2500-3499, and ≥3500 meters above sea level (masl). Percentile curves (P5-P95) for MAP, DBP, and SBP were estimated using Generalized Additive Models for Location, Scale, and Shape (GAMLSS) with the Box-Cox Cole and Green (BCCG) distribution. **Results.** A total of 227,093 adults were analyzed (mean age: 35.7 years; 56.2% women). Across all altitude strata, MAP, DBP, and SBP increased progressively from ages 20 to 50, although the magnitude of increase was attenuated at higher altitudes. MAP and DBP showed relative stability after age 50, whereas SBP continued to rise more steadily. At ages 50 and 59, SBP values were consistently lower at ≥3500 compared with <2500 masl. **Conclusions.** Blood pressure distribution varies according to altitude of residence, with less pronounced age-related increases at higher elevations. The percentile reference curves generated here may support context-specific interpretation of blood pressure in high-altitude populations and strengthen epidemiological surveillance.

**Keywords:** Arterial pressure; Altitude; Age factors; Adult; Peru (Source: MeSH-NLM).

## RESUMEN

## Curvas de referencia de presión arterial según edad y altitud de residencia en adultos peruanos

**Objetivos.** Desarrollar curvas percentilares por edad para la presión arterial media (PAM), diastólica (PAD) y sistólica (PAS) en adultos peruanos de 20-59 años, estratificadas por altitud de residencia. **Materiales y métodos.** Se realizó un estudio transversal analítico con la Encuesta Demográfica y de Salud Familiar (ENDES) 2014-2024. Se incluyeron adultos de 20-59 años con dos mediciones válidas de presión arterial y sin diagnóstico previo de hipertensión. La altitud de residencia se clasificó en <2500, 2500-3499 y ≥3500 metros sobre el nivel del mar (m s.n.m.). Los percentiles (P5-P95) de la PAM, PAD y PAS se estimaron empleando modelos aditivos generalizados para localización, escala y forma (GAMLSS) con distribución Box-Cox Cole and Green (BCCG). **Resultados.** Se analizaron 227 093 adultos (edad media: 35,7 años; 56,2% mujeres). En todos los estratos de altitud, la PAM, PAD y PAS mostraron incrementos graduales entre los 20 y 50 años, aunque la magnitud del incremento se atenuó a mayor altitud. La PAD y la PAM mostraron relativa estabilidad después de los 50 años, mientras que la PAS continuó aumentando de forma más progresiva. A los 50 y 59 años, los valores de PAS fueron sistemáticamente más bajos en altitudes ≥3500 que en <2500 m s.n.m. **Conclusiones.** La distribución de la presión arterial varía según la altitud de residencia, con incrementos por edad menos marcados en zonas de mayor altitud. Las curvas de referencia percentilares generadas pueden aportar a la interpretación contextualizada de la presión arterial en poblaciones de alta altitud y fortalecer la vigilancia epidemiológica.

**Palabras clave:** Presión arterial; Altitud; Factores de Edad; Adultos; Perú (Fuente: DeCS-BIREME).

## Introduction

Blood pressure (BP) is an essential physiological parameter for maintaining tissue perfusion and haemodynamic balance <sup>(1)</sup>. Since the late 1940s, sustained elevation of BP has been recognised as a modifiable risk factor for cardiovascular, renal, and cerebrovascular disease <sup>(2)</sup>. BP values are not uniform, either within individuals or between individuals, and vary systematically according to age, sex, body composition, physical activity, environmental determinants, and other sociodemographic factors <sup>(2,3)</sup>, reflecting the complex biological and contextual regulation of this parameter.

Altitude of residence is a key environmental factor influencing BP through chronic exposure to hypobaric hypoxia, which induces cardiovascular adaptations such as changes in cardiac output, increased blood viscosity, and adjustments in peripheral vascular resistance <sup>(4)</sup>. These responses, necessary to maintain tissue oxygenation, may alter BP levels through both increases and decreases <sup>(5)</sup>, as well as its trajectory across the life course. This is particularly relevant in Andean countries such as Peru, where approximately one-quarter of the population resides above 2500 metres above sea level (m.a.s.l.), compared with around 1% of the global population exposed to such altitudes <sup>(6)</sup>. Although the increase in BP with age is well documented <sup>(2)</sup>, some native populations maintain stable BP values throughout adulthood <sup>(2)</sup>. Likewise, the geographical distribution of hypertension shows lower prevalence in the Peruvian highlands, characterised by higher altitudes <sup>(7)</sup>. Taken together, this suggests that BP trajectories across age may differ according to altitude of residence.

Population-level characterisation of BP requires assessment of its full distribution. Although changes in the population mean explain a substantial proportion of temporal and geographical variation in hypertension prevalence <sup>(8)</sup>, BP exhibits a right-skewed distribution that becomes more pronounced with age <sup>(9)</sup>, indicating that its behaviour may differ according to physiological and environmental determinants <sup>(5)</sup>. In this context, percentile curves allow the identification of patterns not evident from averages, provide an adequate description of the distribution tails, and facilitate comparisons across population subgroups with different exposures. This approach is particularly relevant when factors such as altitude and age may modify upper percentiles due to the influence of chronic hypoxia and ageing on the haemodynamic determinants of BP. Moreover, changes in upper percentiles may influence the proportion of individuals reaching clinically elevated BP levels.

Despite the epidemiological and clinical importance of these variations, there are currently no reference BP curves for adults living at different altitudes, which limits the contextualised interpretation of BP across adulthood in

populations residing in high-altitude regions. Therefore, the aim of this study was to develop age-specific percentile curves for mean arterial pressure (MAP), systolic blood pressure (SBP), and diastolic blood pressure (DBP) in Peruvian adults aged 20-59 years, stratified by altitude of residence.

## Materials and methods

### Study design and data source

An analytical cross-sectional study was conducted using secondary data from the Demographic and Family Health Survey (ENDES, in Spanish) 2014-2024 <sup>(10)</sup>, carried out annually by the National Institute of Statistics and Informatics of Peru (INEI, in Spanish) using a probabilistic, stratified, two-stage sampling design, with weighting that allows population-representative inferences at the national level <sup>(10)</sup>.

### Study sample

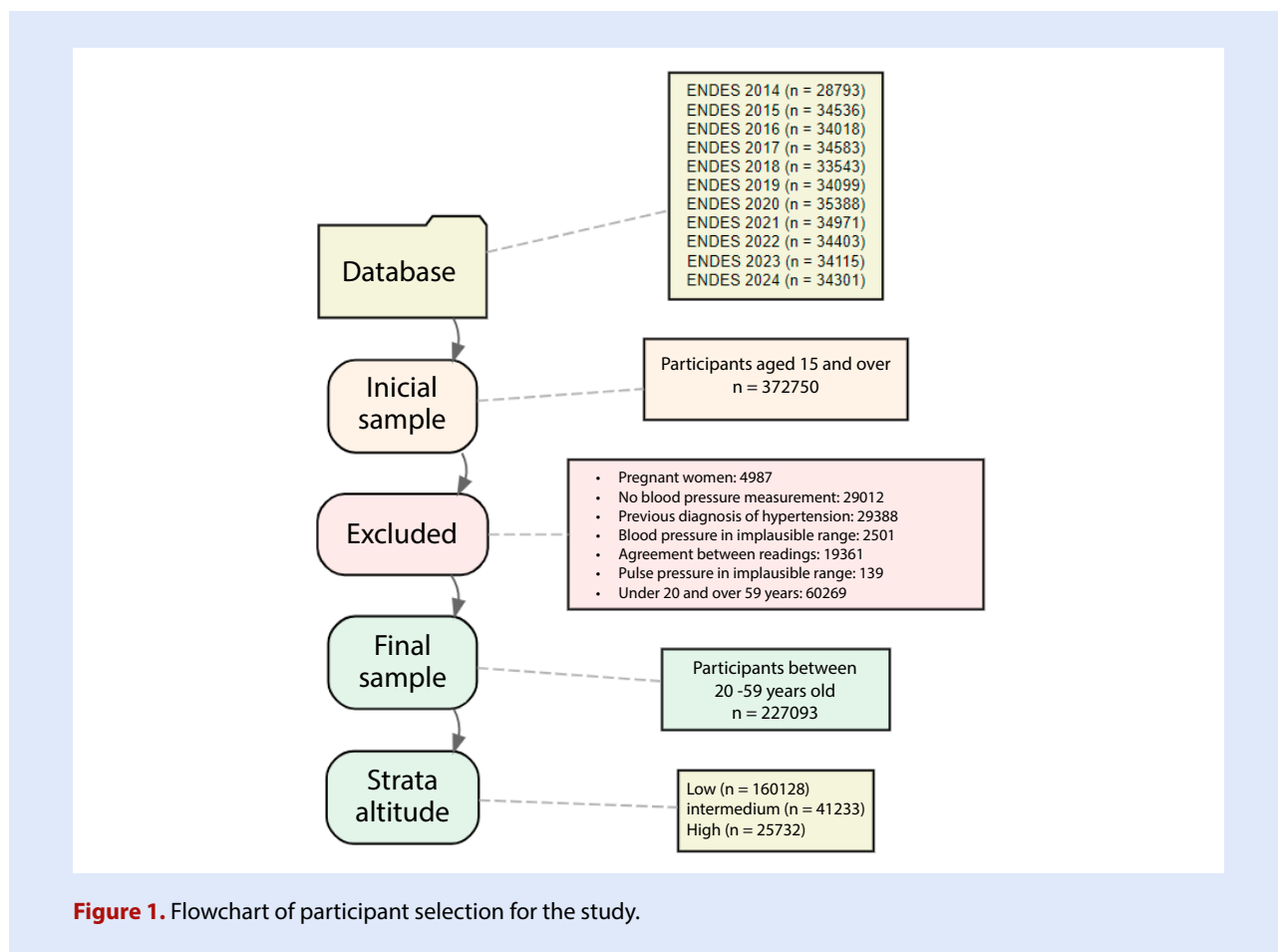
The study sample comprised adults aged 20-59 years who participated in ENDES between 2014 and 2024. This age group was selected to reduce physiological variability associated with ageing <sup>(9)</sup>, particularly due to increased arterial stiffness and greater dispersion of BP values in adolescents and older adults.

Participants aged 20-59 years with two measurements of SBP and DBP, and complete information on study variables, were included. Participants with physiologically implausible values, defined as SBP <70 mmHg or >270 mmHg and DBP <50 mmHg or >150 mmHg, as previously reported <sup>(11,12)</sup>, were excluded, as were those with differences between the averages of the two BP measurements (both systolic and diastolic) of  $\geq \pm 10$  mmHg <sup>(13)</sup>. Pregnant women and those with a prior diagnosis of hypertension were also excluded, as their inclusion could distort the estimation of population percentiles through overestimation or underestimation. The final sample comprised 227,093 participants (**Figure 1**).

### Study variables

The main study variables were MAP, DBP, and SBP, calculated from direct BP measurements obtained in ENDES. Each participant had two SBP and DBP measurements taken during the same visit, following the standardised protocol established by INEI. From these measurements, three variables were derived: mean SBP (average of the two SBP measurements), mean DBP (average of the two DBP measurements), and MAP, estimated using the formula  $DBP + (SBP - DBP)/3$ .

BP was measured according to the standardised ENDES protocol, detailed in the interviewer manual <sup>(14)</sup>. Since 2017, an automated OMRON HEM-7113 sphygmomanometer (range



0-299 mmHg; accuracy  $\pm 3$  mmHg) has been used, with cuff sizes adapted to the participant's arm circumference (standard 220-320 mm and large 320-420 mm)<sup>(15)</sup>. Measurements were taken after at least 5 minutes of rest in a seated position, with feet flat on the floor, the right arm uncovered and supported at heart level, and after avoiding tea, coffee, alcohol, or tobacco consumption in the preceding 30 minutes. Two consecutive measurements were obtained with a 2-minute interval; a third measurement was taken if the difference between the first two exceeded  $>20$  mmHg for SBP or  $>10$  mmHg for DBP, and only consistent measurements were recorded. Further details are available in the interviewer manual<sup>(14)</sup>.

Altitude of residence was used as a stratification variable, expressed in m.a.s.l. For analysis, it was categorised into three groups:  $<2500$  m.a.s.l., 2500-3499 m.a.s.l., and  $\geq 3500$  m.a.s.l. Additionally, an overall category was included to group all participants regardless of altitude. Given that BP variation patterns during adulthood are similar in both sexes, with only small differences in magnitude<sup>(16)</sup>, sex was not used as a stratification variable.

Sociodemographic variables included age (continuous, in completed years; **Figure 2**), sex (male or female), area

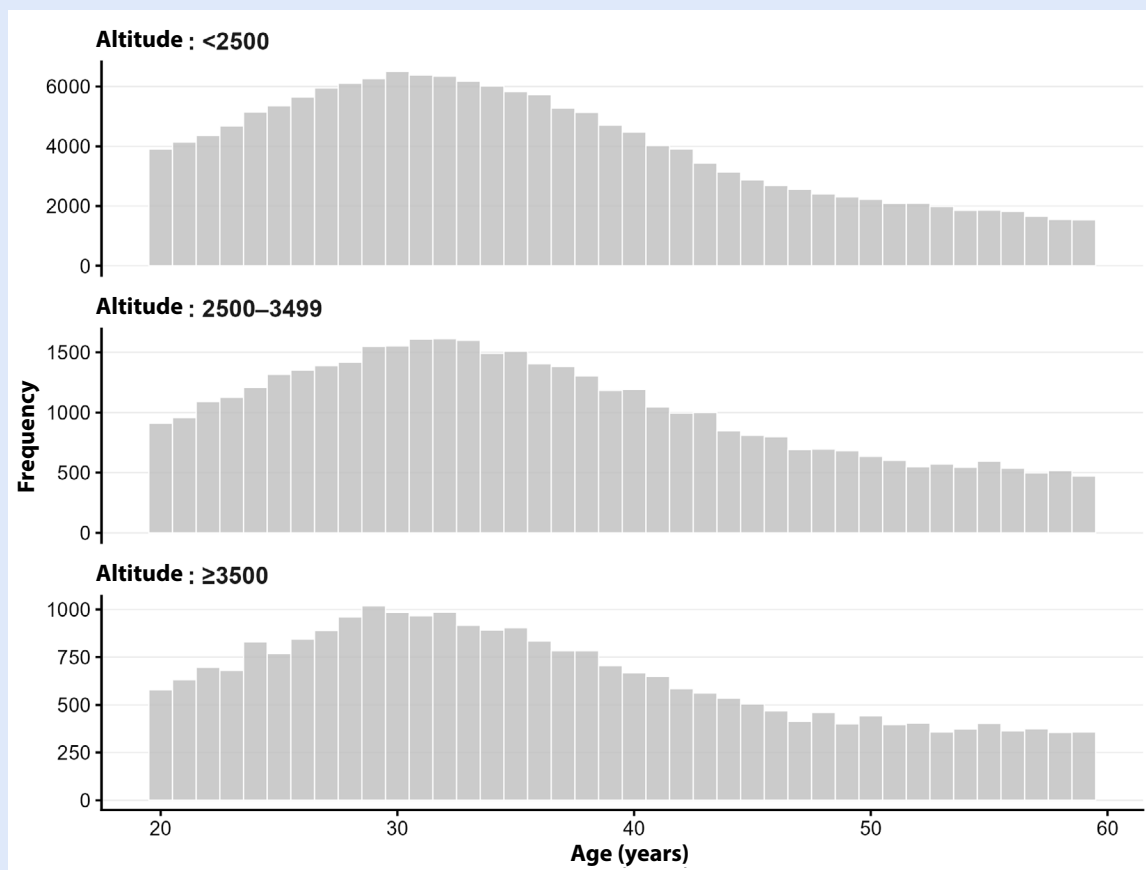
of residence (urban or rural), and region or department corresponding to the 25 political-administrative units of the country (24 departments and the Constitutional Province of Callao).

### Statistical analysis

A descriptive analysis was conducted for the overall sample and by altitude categories. Age was summarised using mean and standard deviation (SD), as well as median and interquartile range (IQR). Sex, area of residence, and department were described using absolute and relative frequencies.

Reference curves for MAP, DBP, and SBP were estimated as a function of age for both the total sample and each altitude stratum, describing BP patterns between 20 and 59 years according to altitude of residence. Generalised additive models for location, scale, and shape (GAMLSS) were used, a flexible regression approach that allows simultaneous modelling of the parameters of the conditional distribution of the response variable<sup>(17)</sup>.

Different continuous distribution families available in GAMLSS were evaluated, including Normal (NO), Box-Cox Cole and Green (BCCG), Box-Cox Power Exponential (BCPE),



**Figure 2.** Distribution of the sample according to age and altitude of residence.

and Box-Cox  $t$  (BCT). Model comparison was conducted using information criteria (AIC, BIC, and GAIC), with the BCCG distribution selected based on its overall goodness of fit according to GAIC. The BCCG distribution, recommended for constructing percentile curves and estimating percentiles in continuous physiological parameters with potential skewness, was used for modelling because it provides parameters directly interpretable on the original scale of the response variable<sup>(18,19)</sup>. Models were fitted using age (in years) as a continuous variable, applying penalised smoothing functions (p-splines) for location ( $\mu$ ) and scale ( $\sigma$ ) parameters. Model adequacy was assessed using GAMLSS-specific diagnostic plots, including worm plots, bucket plots, and Q-statistics for residual normality. From the final models, smoothed predictions of percentiles (P5, P10, P25, P50, P75, P90, and P95) were generated across the age range, and separate graphs were constructed for the overall sample and each altitude stratum.

All analyses were performed using R version 4.3.2 (R Foundation for Statistical Computing, Vienna, Austria), using the `gamlss` package for modelling (without incorporating sampling weights or survey design features due to package limitations) and `ggplot2` for figure generation.

### Ethical aspects

This study was based on secondary analysis of anonymised, publicly available datasets; therefore, ethics committee approval was not required.

## Results

A total of 227,093 adults aged 20-59 years were analysed. The mean age was 35.7 years (SD: 10.1), and 56.2% were women. The urban-rural distribution varied according to altitude of residence. At <2500 m.a.s.l., most participants resided in urban areas (76.5% vs. 23.5%). In contrast, at 2500-3499 m.a.s.l. and  $\geq 3500$  m.a.s.l., rural residence predominated (52.4% vs. 47.6% and 63.9% vs. 36.1%, respectively). The distribution of sociodemographic characteristics and political-administrative regions by altitude categories is shown in **Table 1**.

In the overall sample (**Figure 1A, Supplementary Table 1**), the median MAP showed an increasing pattern with age (from 82.2 mmHg at age 20 to 89.1 mmHg at age 46), with relative stabilisation by age 59 (89.8 mmHg). Lower percentiles (P5 and P10) increased between ages 20 and 49 and showed a slight

**Table 1.** Sociodemographic characteristics of participants according to altitude of residence.

Characteristic	Total (n = 227,093)	<2500 m.a.s.l. (n = 160,128)	2500–3499 m.a.s.l. (n = 41,233)	≥3500 m.a.s.l. (n = 25,732)
<b>Age (years)</b>				
Mean (SD)	35.7 (10.1)	35.5 (10.0)	36.2 (10.2)	36.4 (10.5)
Median (IQR)	34.0 (28.0-42.0)	34.0 (28.0-42.0)	35.0 (28.0-43.0)	35.0 (28.0-44.0)
<b>Sex</b>				
Male	99,371 (43.8)	71,087 (44.4)	17,521 (42.5)	10,763 (41.8)
Female	127,722 (56.2)	89,041 (55.6)	23,712 (57.5)	14,969 (58.2)
<b>Residence</b>				
Urban	151,333 (66.6)	122,418 (76.5)	19,615 (47.6)	9,300 (36.1)
Rural	75,760 (33.4)	37,710 (23.5)	21,618 (52.4)	16,432 (63.9)
<b>Department of residence</b>				
Amazonas	9,208 (4.1)	8,504 (5.3)	704 (1.7)	0 (0.0)
Ancash	8,202 (3.6)	3,880 (2.4)	3,847 (9.3)	475 (1.8)
Apurímac	8,123 (3.6)	992 (0.6)	5,235 (12.7)	1,896 (7.4)
Arequipa	8,236 (3.6)	5,894 (3.7)	1,913 (4.6)	429 (1.7)
Ayacucho	9,252 (4.1)	1,454 (0.9)	6,873 (16.7)	925 (3.6)
Cajamarca	8,253 (3.6)	3,912 (2.4)	4,054 (9.8)	287 (1.1)
Callao	7,946 (3.5)	7,946 (5.0)	0 (0.0)	0 (0.0)
Cusco	7,545 (3.3)	1,377 (0.9)	3,409 (8.3)	2,759 (10.7)
Huancavelica	7,688 (3.4)	320 (0.2)	2,889 (7.0)	4,479 (17.4)
Huánuco	9,033 (4.0)	5,381 (3.4)	2,260 (5.5)	1,392 (5.4)
Ica	8,717 (3.8)	8,633 (5.4)	35 (0.1)	49 (0.2)
Junín	8,520 (3.8)	2,697 (1.7)	4,796 (11.6)	1,027 (4.0)
La Libertad	8,325 (3.7)	6,244 (3.9)	1,768 (4.3)	313 (1.2)
Lambayeque	8,663 (3.8)	8,557 (5.3)	98 (0.2)	8 (0.0)
Lima	26,629 (11.7)	25,930 (16.2)	385 (0.9)	314 (1.2)
Loreto	7,657 (3.4)	7,657 (4.8)	0 (0.0)	0 (0.0)
Madre de Dios	8,240 (3.6)	8,240 (5.1)	0 (0.0)	0 (0.0)
Moquegua	7,747 (3.4)	6,583 (4.1)	811 (2.0)	353 (1.4)
Pasco	8,238 (3.6)	2,991 (1.9)	1,429 (3.5)	3,818 (14.8)
Piura	8,619 (3.8)	8,427 (5.3)	171 (0.4)	21 (0.1)
Puno	7,625 (3.4)	448 (0.3)	139 (0.3)	7,038 (27.4)
San Martín	8,858 (3.9)	8,858 (5.5)	0 (0.0)	0 (0.0)
Tacna	8,364 (3.7)	7,798 (4.9)	417 (1.0)	149 (0.6)
Tumbes	8,502 (3.7)	8,502 (5.3)	0 (0.0)	0 (0.0)
Ucayali	8,903 (3.9)	8,903 (5.6)	0 (0.0)	0 (0.0)

SD: standard deviation. IQR: interquartile range.

Percentages are presented in parentheses and correspond to column percentages unless otherwise specified.

decline by age 59. Higher percentiles (P90 and P95) exhibited a sustained increase across the entire age range, although with more modest increases after ages 49-50 (**Figure 1A, Supplementary Table 1**).

**Figures 1B to 1D** present MAP percentile curves according to altitude of residence. Among residents at <2500 m.a.s.l. (**Figure 1B, Supplementary Table 2**) and 2500-3499

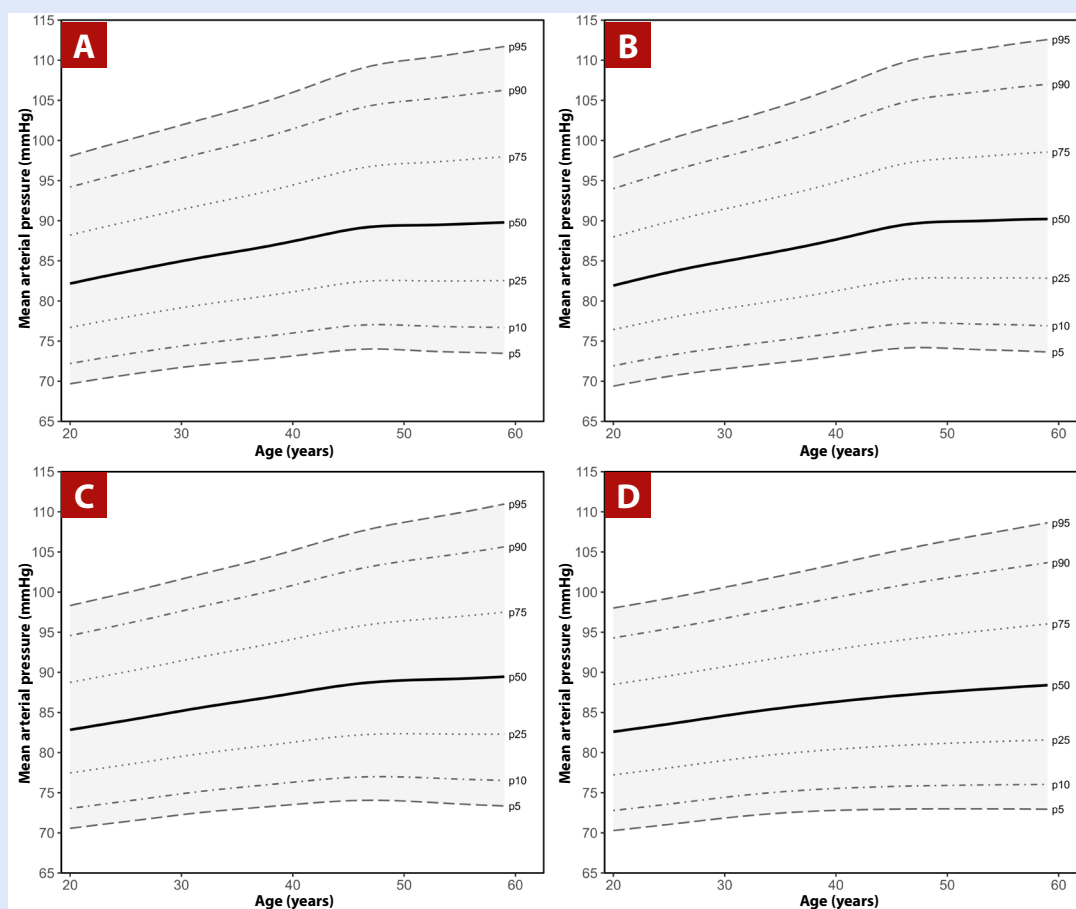
m.a.s.l. (**Figure 1C, Supplementary Table 3**), the median MAP increased progressively from age 20 to approximately 47-50 years, followed by relative stabilisation by age 59. Lower percentiles (P5 and P10) showed gradual increases from age 20 to around 47-50 years, followed by a slight decline in the subsequent decade, remaining near 73-77 mmHg by age 59. Higher percentiles (P90 and P95) showed sustained increases

across the age range, although less pronounced in the 2500-3499 m.a.s.l. group (P90/P95 at age 59: 107.0/112.6 mmHg and 105.6/111.0 mmHg, respectively). In contrast, residents at  $\geq 3500$  m.a.s.l. did not exhibit a clear plateau at older ages. The median MAP increased from 82.6 mmHg at age 20 to 88.4 mmHg at age 59, maintaining a continuous upward trend, although with smaller increases after age 50. Lower percentiles (P5 and P10) also showed sustained increases with minimal variation at older ages. Higher percentiles (P90 and P95) demonstrated more pronounced increases, with an upward trajectory throughout adulthood (**Figure 1D, Supplementary Table 4**).

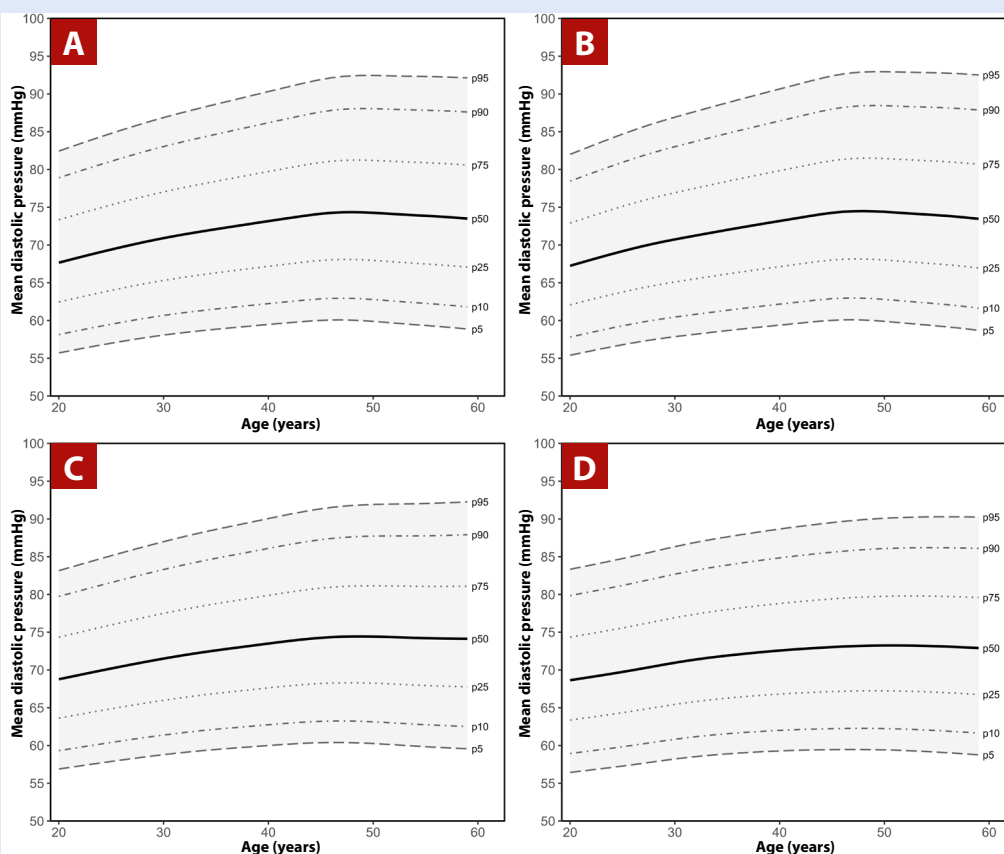
In the overall sample, the median DBP showed an age-related increase, from 67.7 mmHg at age 20 to 74.3 mmHg at age 50, followed by a slight decline by age 59 (73.5 mmHg). This pattern was also observed in lower percentiles (P5 and P10), which increased from age 20 to 49 and then declined by age 59. In higher percentiles (P90 and P95), DBP increased steadily until age 50, followed by stabilisation by age 59 (**Figure 2A, Supplementary Table 5**). However, DBP patterns by age were not uniform across altitude levels. Between ages

20 and 50, DBP increased across all percentiles at all altitudes, although the increase was more pronounced in residents at  $< 2500$  m.a.s.l. (**Figure 2B, Supplementary Table 6**) and progressively smaller in those at 2500-3499 m.a.s.l. (**Figure 2C, Supplementary Table 7**) and  $\geq 3500$  m.a.s.l. (**Figure 2D, Supplementary Table 8**). Between ages 50 and 59, the median and both lower and upper percentiles of DBP declined slightly among residents at  $< 2500$  m.a.s.l. In contrast, among residents at  $\geq 2500$  m.a.s.l., the median and upper percentiles showed relative stabilisation with minimal variation, while lower percentiles (P5 and P10) showed slight declines. Moreover, among residents at  $\geq 3500$  m.a.s.l., DBP values at age 20 were slightly higher than those at  $< 2500$  m.a.s.l. (median: 68.6 mmHg vs. 67.2 mmHg), a pattern also observed in the 2500-3499 m.a.s.l. group.

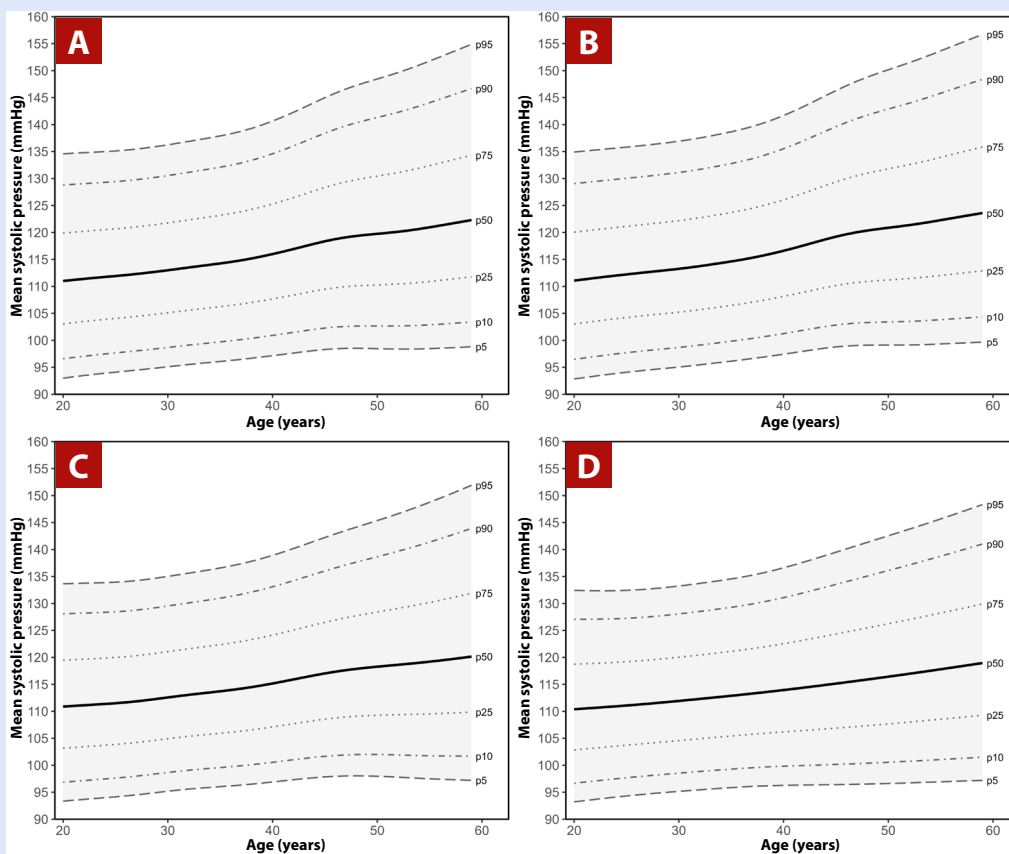
The median SBP in the overall sample (**Figure 3A, Supplementary Table 9**) showed a progressive increase from age 20 (111.0 mmHg) to age 50 (119.7 mmHg), followed by a more gradual increase by age 59 (122.3 mmHg). This pattern was also observed in both higher (P90-P95) and lower (P5-P10) percentiles, although increases in the latter were more gradual.



**Figure 3.** Percentile curves (P5, P10, P25, P50, P75, P90, P95) of mean arterial pressure according to age in Peruvian adults aged 20-59 years. **A)** Overall sample; **B)**  $< 2500$  m.a.s.l.; **C)** 2500-3499 m.a.s.l.; **D)**  $\geq 3500$  m.a.s.l.



**Figure 4.** Percentile curves (P5, P10, P25, P50, P75, P90, P95) of diastolic blood pressure according to age in Peruvian adults aged 20-59 years. **A)** Overall sample; **B)** <2500 m.a.s.l.; **C)** 2500-3499 m.a.s.l.; **D)** ≥3500 m.a.s.l.



**Figure 5.** Percentile curves (P5, P10, P25, P50, P75, P90, P95) of systolic blood pressure according to age in Peruvian adults aged 20-59 years. **A)** Overall sample; **B)** <2500 m.a.s.l.; **C)** 2500-3499 m.a.s.l.; **D)** ≥3500 m.a.s.l.

Analysis of SBP by altitude showed an increasing pattern across the age range, with differences in magnitude. Between ages 20 and 50, SBP increased progressively across all altitude levels and percentiles; however, the magnitude of increase diminished with higher altitude. The median SBP in this age range (20-50 years) increased from 111.1 mmHg to 120.9 mmHg among residents at <2500 m.a.s.l. (**Figure 3B, Supplementary Table 10**), from 110.9 mmHg to 118.3 mmHg at 2500-3499 m.a.s.l. (**Figure 3C, Supplementary Table 11**), and from 110.4 mmHg to 116.4 mmHg at  $\geq$ 3500 m.a.s.l. (**Figure 3D, Supplementary Table 12**). Between ages 50 and 59, SBP continued to increase across all altitude levels and percentiles, although the magnitude of increase remained attenuated at higher altitudes. Furthermore, SBP values at age 20 were similar for lower percentiles across all altitude levels, whereas the median and higher percentiles (P90 and P95) were slightly lower in the  $\geq$ 3500 m.a.s.l. group compared with <2500 and 2500-3499 m.a.s.l. groups. In contrast, SBP values at ages 50 and 59 were lower across all percentiles with increasing altitude (**Supplementary Tables 10-12**).

## Discussion

This study modelled age-specific reference curves for MAP, DBP, and SBP, stratified by altitude of residence. Across all altitude strata, MAP, DBP, and SBP increased progressively between ages 20 and approximately 50 years, although at  $\geq$ 2500 m.a.s.l. the magnitude of this increase was consistently smaller. Beyond age 50, BP trajectories were not uniform. MAP and DBP showed relative stabilisation across all altitude groups, with more marked attenuation in populations residing at  $\geq$ 2500 m.a.s.l., whereas SBP showed no clear evidence of stabilisation between ages 50 and 59 and increased steadily across the entire age range, with more gradual increments at older ages and more pronounced attenuation at higher altitudes. Additionally, between ages 50 and 59, SBP values were consistently lower across all percentiles among residents at  $\geq$ 2500 m.a.s.l. compared with those at <2500 m.a.s.l.

Altitude exposure is characterised by hypobaric hypoxia as the primary physiological stimulus, which modulates cardiovascular function. While acute exposure to hypoxia increases sympathetic activity, heart rate, and BP<sup>(4)</sup>, chronic high-altitude residence is characterised by haematological, vascular, and metabolic adaptations that modulate the pressor response<sup>(4)</sup>. However, the magnitude of these adaptations is not uniform across populations and depends, in part, on ethnic and genetic factors<sup>(20)</sup>.

The sustained increase in SBP, DBP, and MAP between ages 20 and 50 observed in all altitude strata is consistent with findings in populations not exposed to altitude<sup>(9,16,21)</sup> and aligns

with the physiology of vascular ageing, characterised by fatigue and fragmentation of elastin fibres in central arteries, increased aortic stiffness, altered pulse wave propagation<sup>(22,23)</sup>, and increased peripheral vascular resistance in small vessels<sup>(24,25)</sup>. In this context, DBP increases mainly due to higher peripheral vascular resistance, whereas SBP rises due to the combined effects of DBP and arterial stiffness<sup>(24,25)</sup>. After age 50, arterial stiffness progresses more rapidly, resulting in a more marked increase in SBP and, simultaneously, stabilisation or reduction of DBP<sup>(24)</sup>. Our findings show that the magnitude of these increases was consistently smaller at higher altitudes, which may reflect attenuation of the typical vascular ageing pattern in the context of high-altitude residence.

SBP showed a sustained increase across the entire age range in all altitude strata, consistent with arterial ageing physiology<sup>(23,24)</sup>. However, the increase was less pronounced at higher altitudes, which is compatible with heterogeneous responses in high-altitude populations. For example, a systematic review reported that among Tibetans, SBP increased by 17 mmHg for every additional 1000 m of elevation, whereas in non-Tibetan populations SBP tends to decrease or show no significant variation<sup>(5)</sup>. Similarly, in the Ladakh population (~3500 m.a.s.l.), steeper age-related increases have been described compared with sea-level populations<sup>(26)</sup>. In contrast, among adults residing at ~2850 m.a.s.l. in Ecuador, SBP increases with age but with a smaller magnitude than at sea level<sup>(27)</sup>, consistent with our findings. Likewise, in high-Andean populations in Peru residing at  $\geq$ 5000 m.a.s.l., the absence of substantial SBP increases has been reported<sup>(28)</sup>.

Additionally, our findings show that from age 50 onwards, SBP was lower among residents at  $\geq$ 3500 m.a.s.l. compared with those at <2500 m.a.s.l. In the latter group, higher percentiles (P90 and P95) exceeded 140 mmHg, whereas at  $\geq$ 3500 m.a.s.l., P90 remained below and P95 only slightly exceeded the hypertension threshold. Overall, our findings indicate that the magnitude of SBP increase with age does not follow a uniform pattern across populations residing at different altitudes. In high-Andean populations, positive selection has been described in genes related to vascular regulation (EDNRA), energy metabolism (PRKAA1), and the nitric oxide pathway (NOS2A)<sup>(29)</sup>, supporting the existence of differentiated adaptive pathways centred on modulation of nitric oxide signalling and cardiovascular regulation<sup>(4)</sup>.

DBP increased between ages 20 and 50 across all altitude strata, consistent with findings in non-altitude populations<sup>(9,16,21)</sup>, although with progressively smaller magnitude at higher altitudes. From age 50 onwards, DBP tended to stabilise, consistent with the physiological transition in which increasing aortic stiffness begins to reduce DBP<sup>(24)</sup>. In our study, this stabilisation was observed across all altitude levels; however, at  $\geq$ 3500 m.a.s.l., DBP

values approached the 90 mmHg threshold between ages 50 and 59, suggesting that chronic adaptation to hypoxia attenuates age-related increases but does not prevent clinically relevant BP levels at older ages. MAP followed a pattern similar to DBP, with progressive increases from ages 20 to 50 across all altitude strata. As MAP reflects the balance between SBP, DBP, and peripheral vascular resistance, its trajectory synthesises the haemodynamic changes associated with ageing<sup>(24)</sup>. After age 50, MAP tended to stabilise, consistent with the deceleration of systolic increase and diastolic plateau observed in this age range.

Taken together, these findings highlight that the relationship between altitude, age, and BP does not follow a uniform pattern across human populations. Traditional populations not exposed to hypoxia, such as the Tsimane, Yanomami, or Kuna, maintain low and relatively stable BP levels throughout adulthood<sup>(2)</sup>, supporting the notion that BP progression results from specific interactions between biology, environment, and lifestyle<sup>(2)</sup>. Moreover, part of the heterogeneity observed in high-altitude populations may be related to differences in measurement methods. For example, BP assessed using 24-hour ambulatory monitoring shows a distinct circadian variability at altitude, with greater increases at night than during the day<sup>(30)</sup>. This suggests that single-point measurements used in population surveys may not fully capture BP variability at altitude and underscores the need for future studies incorporating time-sensitive assessment methods.

The findings of this study show that the magnitude of SBP and DBP increases with age is smaller in high-Andean populations residing at higher altitudes. Although these patterns do not justify redefining diagnostic thresholds nor imply lower cardiovascular risk, they highlight the importance of contextualised BP interpretation. In a country such as Peru, where approximately one-quarter of the population lives at  $\geq 2500$  m.a.s.l.<sup>(6)</sup>, prevention and epidemiological surveillance could benefit from context-adapted approaches, recognising that population BP dynamics are not equivalent across regions and that the same absolute SBP value may represent very different epidemiological realities depending on altitude. For example, according to our findings, at age 50, an SBP of 150 mmHg places a resident at  $< 2500$  m.a.s.l. near the upper 5% of the distribution, whereas at  $\geq 3500$  m.a.s.l., this value clearly exceeds the local P95 (142.5 mmHg). Thus, an SBP of 150 mmHg, already elevated at lower altitudes, becomes exceptional at higher altitudes. Although this does not alter diagnostic thresholds or therapeutic targets, it provides useful interpretative context regarding deviation from local population patterns. Differences in upper percentiles also suggest that primary prevention efforts should consider the local BP distribution. Furthermore, given that distinct circadian variability has been documented in high-altitude populations<sup>(30)</sup>, future studies should evaluate whether

these patterns translate into differences in cardiovascular risk using 24-hour ambulatory measurements.

This study has several limitations that should be considered when interpreting the results. First, the cross-sectional design precludes distinguishing whether observed age-related and altitude-related patterns reflect physiological ageing processes or generational differences. Likewise, it cannot be determined whether the observed percentile distributions reflect long-term physiological adaptations or intrinsic characteristics of populations within each altitude stratum. Second, the exclusion of individuals with prior hypertension, although necessary to avoid distortion of the distribution by clearly pathological values, limits generalisability to the broader adult population (20-59 years) and may underestimate true BP levels by not excluding undiagnosed hypertension. Third, prior hypertension and pregnancy status were based on self-report, potentially introducing misclassification bias. Fourth, information on duration of residence at altitude or migration history was not available, despite their potential influence on BP values. Fifth, combining data from multiple years assumes temporal stability in BP patterns, which may not hold if cardiovascular risk factors changed during this period. Sixth, the use of secondary data collected across different periods and by different interviewers does not exclude variability in measurement technique and may introduce measurement bias. Seventh, altitude measurement based on cluster centroid rather than household location may misclassify altitude exposure. Eighth, the analysis did not incorporate sampling weights or complex survey design features of ENDES due to limitations of the *gamlss* package, which does not allow specification of strata, clusters, or expansion factors in parametric distribution modelling. This limitation may introduce bias through underestimation of standard errors and overrepresentation of urban and lower-altitude areas relative to their true population weights; therefore, results should not be interpreted as precise population estimates. Finally, smaller sample sizes at the extremes of the age range in higher altitude strata may affect the stability of extreme percentile estimates, and larger samples would be required for robust estimation.

In conclusion, BP in Peruvian adults aged 20-59 years showed less pronounced age-related increases in populations residing at higher altitudes. The generated percentile curves highlight these differences and may contribute to a more contextualised interpretation of BP in high-altitude settings, as well as to strengthening epidemiological surveillance in geographically heterogeneous environments. However, these findings should be interpreted from an exploratory perspective and not as parameters intended to redefine diagnostic thresholds or to infer lower cardiovascular risk in these populations.

### Author contributions

**AHV:** conceptualisation, data curation, formal analysis, investigation, methodology, resources, software, supervision, validation, visualisation, writing-original draft, writing-review and editing. **JGV:** conceptualisation, investigation,

methodology, validation, writing-original draft, writing-review and editing. **RVF:** conceptualisation, investigation, validation, writing-original draft, writing-review and editing. All authors have read and approved the published version of the manuscript.

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