Hypertension
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

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Hypertension. published online May 21, 2012;
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0194-911X. Online ISSN: 1524-4563

Does Blood Pressure Inevitably Rise With Age?

Longitudinal Evidence Among Forager-Horticulturalists

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***Abstract*—**The rise in blood pressure with age is a major risk factor for cardiovascular and renal disease, stroke, and type 2 diabetes mellitus. Age-related increases in blood pressure have been observed in almost every population, except among hunter-gatherers, farmers, and pastoralists. Here we tested for age-related increases in blood pressure among Tsimane forager-farmers. We also test whether lifestyle changes associated with modernization lead to higher blood pressure and a greater rate of age-related increase in blood pressure. We measured blood pressure longitudinally on 2248 adults age ≥20 years (n=6468 observations over 8 years). Prevalence of hypertension was 3.9% for women and 5.2% for men, although diagnosis of persistent hypertension based on multiple observations reduced prevalence to 2.9% for both sexes. Mixed-effects models revealed systolic, diastolic, and pulse blood pressure increases of 2.86 ($P<0.001$), 0.95 ($P<0.001$), and 1.95 mm Hg ($P<0.001$) per decade for women and 0.91 ($P<0.001$), 0.93 ($P<0.001$), and −0.02 mm Hg ($P=0.93$) for men, substantially lower than rates found elsewhere. Lifestyle factors, such as smoking and Spanish fluency, had minimal effect on mean blood pressure and no effect on age-related increases in blood pressure. Greater town proximity was associated with a lower age-related increase in pulse pressure. Effects of modernization were, therefore, deemed minimal among Tsimane, in light of their lean physique, active lifestyle, and protective diet. **(*Hypertension*. 2012;60:00.)** • **Online Data Supplement**

Key Words: hypertension ■ Tsimane ■ blood pressure ■ modernization

An age-related increase in blood pressure (BP) is viewed as a universal feature of human aging.[1–3] Among Westerners over age 40 years, systolic BP (SBP) increases by ≈7 mm Hg per decade.[4] Epidemiological surveys show a progressive increase in SBP with age, reaching an average of ≈140 mm Hg by the eighth decade.[5] Diastolic BP (DBP) also increases with age but at a lower rate than SBP; DBP may even fall at late ages.[6] Women show lower SBP and DBP than men up until the age of menopause, when women's SBP surpasses that of men.[7] By age 70 years, more than three quarters of US adults have hypertension.

Understanding the conditions affecting age-related BP increase is of obvious clinical importance. Higher BP is associated with cardiovascular and renal disease across diverse populations, even controlling for other factors.[5] Hypertension is the leading cause of cardiovascular mortality, and age-related BP increase is a high-priority target for intervention.[8]

The only reported cases of no age-related BP increase come from studies of subsistence-level populations.[9–11] These studies, however, are problematic: they are cross-sectional; use small, sometimes biased samples; and often do not specify explicit measurement methods. Age estimates of older adults are also poor.[12] Because of epidemiological and economic transitions, cohort effects may also have muted age effects; younger adults may have higher BP than older adults did when they were younger.

Nonetheless, results from many studies suggest that "modernization" results in changes in diet, adiposity, activity, and psychosocial stress, leading to higher BP and greater age-related increases in BP.[13–15] Although available evidence shows that hypertension is more common among those with modern lifestyles, it is unclear whether these changes impact the rate of increase in BP. It is also unclear whether these changes impact everyone equally or just high risk subpopulations. Heterogeneity in susceptibility and modernization could reveal further variability in longitudinal age trajectories of BP.

Here we assess the extent to which BP increases with age using longitudinal and cross-sectional data collected among Tsimane of the Bolivian Amazon. Tsimane are lowland forager-horticulturalists (population, ≈11 000) subsisting on plantains, rice, corn and manioc, fish, and hunted game. Tsimane are currently undergoing epidemiological and tech-

Received December 4, 2011; first decision December 29, 2011; revision accepted April 12, 2012.

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The online-only Data Supplement is available with this article at http://hyper.ahajournals.org/lookup/suppl/doi:10.1161/HYPERTENSIONAHA.111.189100/-/DC1.

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nological transitions,[16] although there was no electricity, running water, or waste management at the time of study. Villages vary in their degree of healthcare access. Modernization takes several forms, including visits to the town of San Borja (population, ≈24 000), wage labor with loggers or colonists, debt peonage with itinerant river merchants, and schooling. Schools now exist in >75% of villages, but many older adults have little or no schooling.

We first assessed hypertension prevalence and examined age-related changes in SBP, DBP, and pulse pressure (PP) to test the general hypothesis that BP increase is a robust feature of human aging. We then tested whether both BP and age-related increase in BP increased with modernization, operationalized by Spanish fluency, distance to town, smoking frequency, and body mass index (BMI). We also assessed whether an increase in BP with age occurred uniformly or was instead concentrated among a high-risk subpopulation.

Methods

Study Population

A total of 2248 adults aged 20 to 90 years (n=82 villages) participated in the Tsimane Health and Life History Project from July 2002 to December 2010. Adults were sampled anywhere from 1 to 9 times during medical rounds, yielding a sample of 6468 person-observations; 61% of adults were sampled at least twice and 36% ≥4 times (Table S1, available in the online-only Data Supplement). Sample size varied from 268 to 1186 individuals across 9 medical rounds (Table S2).

BP and Controls

SBP and DBP were measured on the right arm by trained Bolivian physicians with a Welch Allyn Tycos Aneroid 5090 sphygmomanometer and Littman stethoscope. Patients were seated or supine for ≥20 minutes before measurements. After 2008, all of the hypertensive readings were repeated after ≥30 minutes to confirm preliminary diagnoses. No Tsimane has ever taken medication to control hypertension. We use the Joint National Committee on Prevention, Detection, and Treatment of High Blood Pressure classification scheme to define BP categories as hypertensive (SBP ≥140 mm Hg or DBP ≥90 mm Hg), prehypertensive (120–139 mm Hg SBP or 80–89 mm Hg DBP), and normotensive (SBP <120 mm Hg and DBP <80 mm Hg).

Height (in centimeters) was measured by trained Tsimane research assistants with a portable Seca stadiometer. Weight (in kilograms) and body fat percentage were measured using a Tanita BF-572 weigh scale.

Modernization

Village-level variance in distance to San Borja is substantial (mean±SD, 41±23 km; minimum, 6; maximum, 82). Highest level of schooling and Spanish fluency were assessed during census updates and demographic interviews. Cumulative smoking was measured in cigarette pack-years based on interviews of number of cigarettes smoked per week and age at which the interviewee started smoking. One pack-year is equal to a pack of cigarettes smoked per day for 1 year. Given potential problems with recall bias, cumulative smoking experience was categorized into tertiles, including first (0.003–0.070 pack-years), second (0.07–0.30 pack-years), or third (>0.30 pack-years).

Statistical Analysis

Cross-Sectional Analyses

We used mixed- and fixed-effect models with linear and nonlinear age parameters. Linear models were fit with the *lm* and *lme* procedures in R 2.13.1. Nonlinear models used generalized additive models.[17,18] Generalized additive models use a thin-point spline to fit nonlinear age patterns while allowing for the simultaneous inclusion of parametric terms. Generalized additive models were fit with *gam* in the *mgcv* package and *gamm4* in the *gamm4* package. Mixed models were used to control for both individual variation in age trajectories and correlated errors between repeated samples.[19]

Longitudinal Rates of BP Change

Longitudinal analyses included only individuals with ≥5 years between first and last observation (please see the online-only Data Supplement). Repeat BP values were recoded as changes from the mean of a subject's BP measures (ΔBP); times were coded as days before or after the subject's median examination date. Linear models were fit to ΔBP including subject identification, a subject-by-time interaction term, season, and pregnancy status as controls. Parameter values for ΔBP were obtained from the subject-by-time interaction terms.

Two-Stage Mixed Model

To examine the effect of modernization on absolute BP levels and rates of BP change, we use a 2-stage mixed model (Tables 2 and S3). In the first stage, a standard mixed generalized additive model was run with a nonparametric age term, and individual variation in slope was modeled as a random effect. Individual slopes were obtained by adding the overall population slope for an individual's age plus that individual's random slope, both from the stage 1 model. These slopes were used as the dependent variable in model 2 to examine factors affecting rate of BP change.

Ethical Concerns

Informed consent was obtained for all of the protocols at 3 levels, Tsimane government, community, and individual. After explanation of protocols by bilingual Spanish-Tsimane research assistants, consent forms were either signed by literate participants or fingerprinted by nonliterate participants. All of the protocols have been approved by the institutional review boards at University of New Mexico and University of California-Santa Barbara.

Results

Sample Characteristics

Average age was 38.0 and 39.3 years for women and men, respectively (Table 1). Women represented 52.6% of observations. In comparison with normotensives, hypertensive men and women were older, shorter, had more body fat, were less likely to be nonsmokers, were less educated, and were more likely to speak Spanish.

Mean BP and Hypertension Prevalence

In the largest medical round (October 2008–2009), any observation of hypertension was followed with a confirmatory reading within a half hour. Mean BP for Tsimane men and women, respectively, was 113, 108 mm Hg (SBP); 70, 66 mm Hg (DBP); and 43, 41 mm Hg (PP). This cross-sectional analysis shows a notable increase in SBP and PP with age for women and a very modest increase in SBP for men (Figure S1). Prevalence of hypertension was 3.9% for women and 5.2% for men (Figure S2). It was highest among women over age 70 years (30.4%). Isolated systolic hypertension accounted for 49.3% of hypertensive cases, and isolated diastolic accounted for 22.3%. Prehypertension prevalence was 17.4% for women and 29.1% for men.

Prevalence of hypertension declined substantially if we required additional observations of elevated BP in other rounds. Among people sampled ≥3 times, only 38% were

Table 1. Sample Means by BP Status for Tsimane Adults Aged ≥20 y

	Women						Men						
	Blood Pressure Group			*P* Value§			Blood Pressure Group			*P* Value§			
Variable	Normal	Prehypertensive	Hypertensive	NvP	NvH	PvH	Normal	Prehypertensive	Hypertensive	NvP	NvH	PvH	Sex by BP Group‖
Age, y	38.0	56.0	66.5	‡	‡	‡	39.3	46.8	65.8	‡	‡	‡	‡
Height, cm	150.8	150.8	148.3	NS	†	†	162.7	162.2	159.5	NS	‡	†	NS
Weight, kg	53.6	56.3	52.5	†	NS	*	62.8	63.7	63.3	†	NS	NS	NS
Body fat, %	25.9	28.5	28.2	‡	†	NS	17.5	18.9	21.1	‡	‡	*	NS
BMI, kg/m^2	23.6	24.7	23.8	‡	NS	NS	23.6	24.2	24.8	‡	*	NS	NS
Years of schooling	1.4	0.5	0.5	‡	NS	NS	2.8	2.5	1.0	NS	NS	NS	NS
Distance to San Borja, km	37.7	35.0	35.9	NS	NS	NS	38.5	41.1	36.2	NS	NS	NS	NS
SBP, mm Hg	103.8	122.2	146.5	‡	‡	‡	107.9	122.5	144.3	‡	‡	‡	‡
DBP, mm Hg	64.4	73.9	80.0	‡	‡	‡	66.6	74.0	95.0	‡	‡	‡	‡
PP, mm Hg	39.2	47.0	65.2	‡	‡	‡	41.6	47.3	54.7	‡	‡	NS	‡
Smoking tertile, %													
None	78.9	69.3	58.8	*	*	NS	15.8	21.4	18.8	NS	NS	NS	NS
First	14.9	13.3	23.5				27.5	21.4	18.8				
Second	3.9	16.0	11.8				27.5	23.3	31.3				
Third	2.3	1.3	5.9				29.3	34.0	31.3				
Spanish fluency, %													
None	55.8	72.1	38.5	*	NS	*	24.6	31.4	16.7	NS	NS	NS	NS
Moderate	27.3	18.0	38.5				36.6	36.4	66.7				
Fluent	16.9	9.8	23.1				38.8	32.2	16.7				
n (cases)	942	158	44				838	288	51				

For each individual the median value of repeated measures on a given variable was used to calculate group means and determine hypertensive category. NvP indicates normal vs prehypertensive; NvH, normal vs hypertensive; PvH prehypertensive vs hypertensive; NS, not significant; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; BMI, body mass index; BP, blood pressure.

*$P \leq 0.05$.

†$P \leq 0.01$.

‡$P \leq 0.001$.

§*P* values for comparisons are from a Mann-Whitney U or χ^2 test.

‖*P* values indicate the significance of a sex×blood pressure group interaction in a linear model with Gaussian link or a geneneralized linear model with ordinal response and logit link function. Models also included main effect terms for sex and hypertension group (not shown).

hypertensive more than once, and only 1% were hypertensive for all of the readings (Table S1). Even among those sampled 8 times, 50% of those with a hypertensive measurement were hypertensive only once. It is, therefore, likely that the true prevalence of hypertension may be as low as one third the rates based on single measurements reported in Table S1 and preliminarily described in Reference 20. Among those sampled multiple times, frequency of ≥2 instances of hypertension was low (Figure 1). Only 7.7% and 27.3% of men and women, respectively, in the highest risk age category (aged ≥70 years) were hypertensive more than once, whereas an additional 18% of each sex were hypertensive only once. Overall, prevalence of repeat hypertension was 2.9% for both sexes.

Rise in BP With Age

We estimated age trajectories of SBP, DBP, and PP for Tsimane and a US comparison (National Health and Nutrition Examination Survey 2005–2006; Figure 2). Men's SBP is much flatter across adulthood than women's, whose SBP rises substantially around menopause. DBP increase with age is modest for women, whereas DBP decreases for men after age 60 years. This decrease in DBP is observed for both men and women in the U.S. PP increases for women after age 40 and less steeply for men after age 45. Despite these sex differences, Tsimane age profiles indicate substantially less change in BP with age than US age profiles, even after controlling for BMI (Figure 2). However, both populations show similarities, including lower SBP for women than men at younger ages and increasing BP in women after menopause. Although blunted, Tsimane males also show an increase in DBP early in life and a decrease later in life. PP increases at later ages in both populations.

The 2-stage mixed-modeling strategy tests for effects on both the intercept and rate of increase in BP for individuals (Tables 2 and S3). Stage 1 models main effects of predictors on BP, using random effects to control for repeated observations. Stage 2 assigns a slope to each individual consisting of the population slope for that age from stage 1 plus the individual's difference from the population mean obtained from the stage 1 random-effects model. These analyses include controls for sex, pregnancy status, season, BMI,

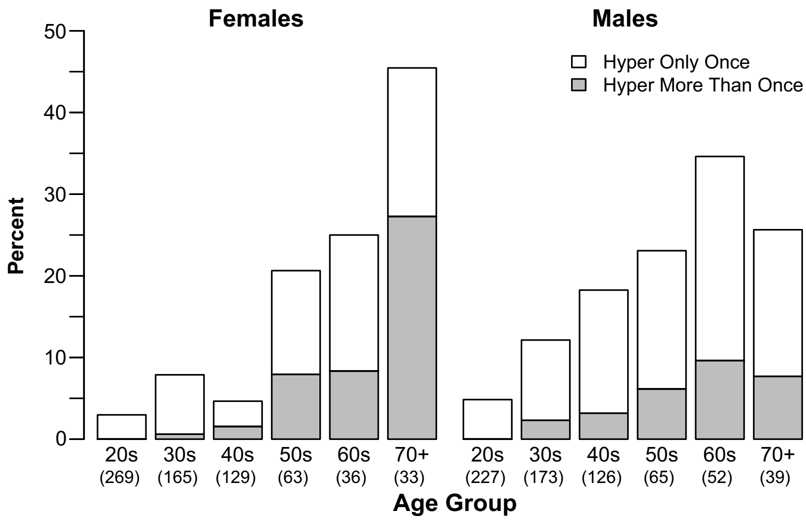

Figure 1. Prevalence of hypertension by age and sex among those sampled at least twice. □, hyper only once; ▩, hyper more than once.

Spanish fluency, years of schooling, and distance to San Borja. Substantial variability exists among individuals in ΔBP (Figure 3). Overall, SBP increases throughout life for women. Average ΔSBP increases significantly among women aged 40 to 55 years and then declines gradually (Figure 3A). The net ΔSBP for men increases from a negative slope to a positive one by the mid-30s, increases slightly for a few decades to a maximum of 2 mm Hg per decade, and then declines after age 50 years (Figure 3B). ΔDBP is constant and positive at ≈1 mm per decade for women but declines continuously with age in men (Figure 3C and 3D). ΔPP shows a similar pattern as ΔSBP in women, given the lack of age-related change in ΔDBP. ΔPP changes little before age 40 years given similar changes in ΔSBP and ΔDBP (Figure 3E). For men, ΔPP increases from negative before age 40 years to positive after age 40 years and close to 0 after age 60 years (Figure 3F).

Cross-Sectional Versus Longitudinal Analysis

Although analyses above include repeated measures, they are cross-sectional because they estimate the overall population pattern for a given segment of time. An explicit longitudinal analysis looks at within-individual changes. We estimated ΔBP for each individual with ≥5 years between first and last observation using linear regression models and controlling for season of measurement and pregnancy status. ΔBP varies somewhat among cross-sectional and longitudinal analyses, although less so when cross-sectional analyses are restricted to the same set of individuals with ≥5 observations (Table 3). Because of intraindividual lability of BP, SEs of longitudinally estimated slopes are much higher than those estimated cross-sectionally, and in many cases slopes were not significantly different from 0.

Across ages, men had positive but moderate ΔSBPs, ranging from 0.32 mm per decade in longitudinal to 1.23 mm per decade in the restricted cross-sectional analyses. Women had higher overall ΔSBP, ranging from 1.81 to 3.08 mm per decade. Men had little net increase in ΔDBP, with estimates ranging from −2.99 mm per decade in longitudinal to 0.93 mm per decade in the cross-sectional analysis. Similarly, female ΔDBP ranged from −1.86 mm per decade in longitudinal to 0.95 mm per decade in cross-sectional analysis. PP increased the most in longitudinal analyses, 3.31 and 3.67 mm per decade, but this increase was modest in cross-sectional analysis, with −0.02 and 1.95 mm per decade for men and women, respectively.

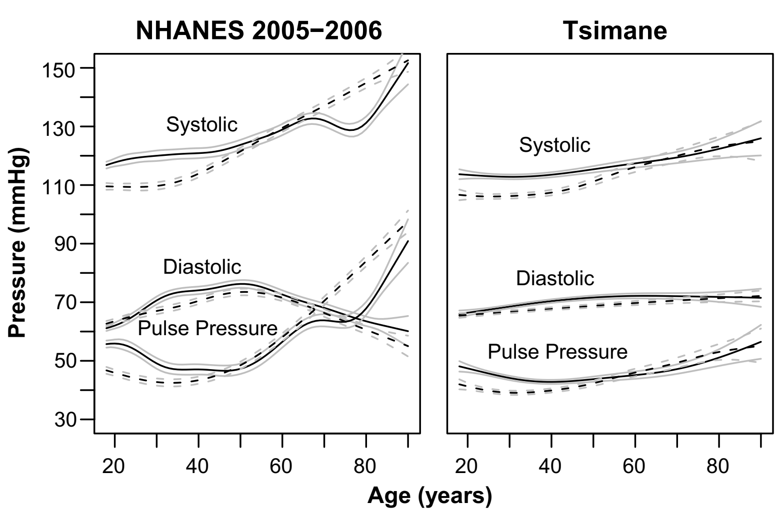

Figure 2. Blood pressure (BP) by age and sex. Generalized additive models of systolic BP (SBP), diastolic BP (DBP), and pulse pressure (PP) for males (solid lines) and females (dashed lines), controlling for body mass index (BMI) and pregnancy status. Tsimane models are mixed models to control for repeated observations (n=5528 observations, 1749 individuals). National Health and Nutrition Examination Survey (NHANES) models are based on a single time point (n=7359). Both models are illustrated at BMI=25.84, which is the midpoint between mean BMI for Tsimane (23.67) and NHANES (28.00). Gray lines are 95% CIs for the mean.

Table 2. Two-Stage Mixed Models

Parameter	Stage 1 Main Effects, mm Hg SBP	DBP	PP	Stage 2, ΔBP, mm Hg per Decade SBP	DBP	PP
Constant	94.5‡	57.6‡	36.3‡	2.0‡	0.9‡	0.6
Sex (male)	2.7‡	1.4*	1.1	−2.7‡	0.03	−3.0‡
BMI	0.6‡	0.4‡	0.3‡	0.02	0.01	0.03
Years of schooling	0.1	0.1	0.01	0.01	0.01	0.01
Distance to San Borja (per 10 km)	−0.3*	−0.1	−0.2	0.03	0.01	0.08‡
Pregnant	−2.8†	−3.3‡	0.4			
Smoking (tertile§)						
First	−1.2	−1.4*	0.2	−0.1	−0.03	−0.20
Second	1.1	0.5	1.1	−0.01	0.10	−0.10
Third	0.5	−0.4	1.2	−0.02	0.05	−0.08
Spanish fluency‖						
Moderate	1.1	0.5	0.5	0.05	0.07	0.01
Fluent	−1.1	0.4	−1.8*	0.08	0.06	0.2
Season¶						
Dry	3.9‡	2.8‡	1.0*			
Intermediate	−0.6	0.02	−0.6			

Stage 1 models have a random slope and intercept for each individual in the study, with blood pressure (BP) as the dependent variable. Stage 2 models use the individual random-effect slopes plus population main effect of age from stage 1 as the dependent variable. Age was included as a nonlinear thin-plate spline in both models. Only individuals with data for all of the variables and ≥2 observations were included (n=695 individuals; n=2876 observations). For more details please see the online-only Data Supplement. BMI indicates body mass index; SBP, systolic BP; DBP, diastolic BP; PP, pulse pressure.

*$P \leq 0.05$.
†$P \leq 0.01$.
‡$P \leq 0.001$.
§Data are relative to no smoking.
‖Data are relative to speaks no Spanish.
¶Data are relative to wet season.

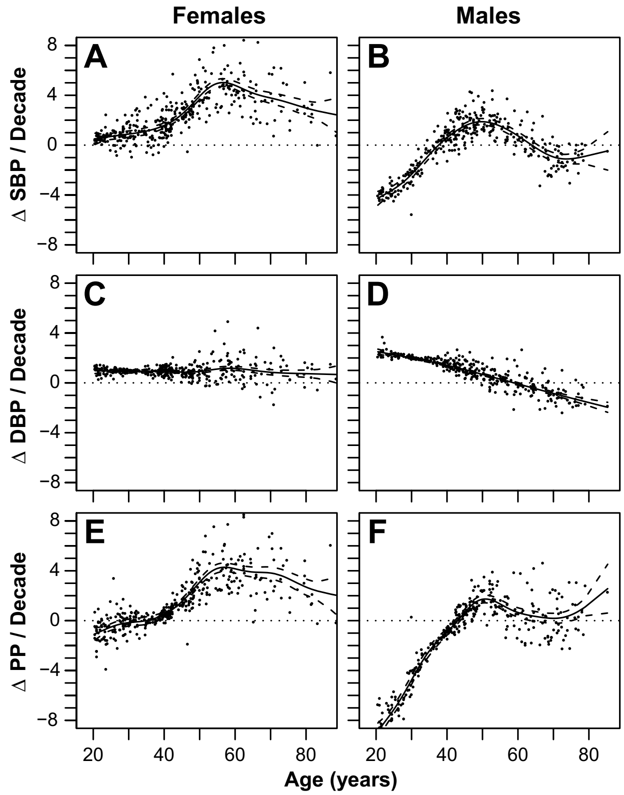

Figure 3. Change in systolic blood pressure (BP; SBP; **A** and **B**), diastolic BP (DBP; **C** and **D**), and pulse pressure (PP; **E** and **F**) per decade by sex and age. Points are ΔBP vs mean observation age (Table 2, step 1). Lines are spline fits and 95% CIs for the slopes as a function of mean observation age, estimated with a generalized additive model (Table 2, step 2).

After segregating the sample by age, cross-sectional and longitudinal analyses showed similarities but with notable exceptions. Men aged 20 to 39 years had significantly decreasing ΔPP in the cross-sectional model, including all Tsimane, but increasing ΔPP in the restricted sample. In all 3 of the models, male ΔPP increased between ages 40 and 59 years, but only ΔSBP in the full cross-sectional model increased significantly above 0. Male ΔDBP declined significantly in individuals aged ≥60 years in all of the analyses. Like men, women aged 20 to 39 years had increasing ΔPP in the restricted sample and no change in the full cross-sectional sample. ΔSBP increased in all 3 of the models, although not significantly in the longitudinal analysis. For women aged 40 to 59 years, ΔSBP, ΔDBP, and ΔPP increased in both cross-sectional analyses. Increases in ΔSBP and ΔPP in the longitudinal analysis were not statistically significant. Women aged ≥60 years showed increasing ΔSBP, declining ΔDBP, and increasing ΔPP, but only ΔPP changed significantly and only in the full cross-sectional sample.

Variance in BP

To test whether BP patterns were consistent for all of the individuals or affected subpopulations differentially, we examined differences in variance in BP and longitudinal slopes by sex, age, and population. Overall, variance in SBP, DBP, and PP was higher in women than in men and higher in Americans than in Tsimane, particularly after age 40 years (Figure 4 and Table S4). Variance in both sexes and populations increased with age; both Tsimane and American women showed higher variance in BP with age. Examining longitudinal slopes, Tsimane women had higher variance over age 40 years, but variance did not increase significantly at age ≥60 years compared with ages 40 to 59 years (Table S4). Tsimane men's SBP variance increased after age 40 years, and men's variance in slope also increased after age 60 years. Tsimane men's variance in DBP did not change significantly with age, whereas Tsimane and American women's DBP and PP variance increased with age (Figures 4 and S4). Overall variance was greatest for SBP, and the greater variance with age among women is evident. By age 60 years, although mean and median slopes for women were positive for SBP and PP, a significant portion of women showed slopes ≤0.

Effects of Modernization

We examined effects of modernization on SBP, DBP, and PP controlling for age, sex, season, and pregnancy status (Table 2, Stage 1). BMI was associated with higher SBP (β=0.61), DBP (β=0.39), and PP (β=0.25). BMI was not associated with significant differences in ΔBPs with age. Living farther

Table 3. Comparison of 10-y Increase in BP as Estimated From CS vs L Analyses

		Men			Women		
Variable	Pressure	CS All, β	CS≥5 y, β	L≥5 y, Mβ	CS All, β	CS≥5 y, β	L≥5 y, Mβ
Age, y							
20–39	ΔSBP	−0.33	3.65†	2.09	1.83†	2.59*	1.82
	ΔDBP	2.28‡	2.22*	−3.90	1.61‡	0.49	−1.93
	ΔPP	−2.71‡	1.32	5.99†	0.11	1.89†	3.75*
40–59	ΔSBP	2.03*	0.85	0.69	4.36‡	5.62‡	2.12
	ΔDBP	0.43	−0.87	−0.72	1.72†	1.91*	−0.97
	ΔPP	1.75†	1.67*	1.41	2.83‡	3.66‡	3.09
≥60	ΔSBP	−2.64	−2.86	−5.71	1.89	0.82	0.45
	ΔDBP	−4.08‡	−4.50†	−7.26*	−0.96	−2.03	−5.07
	ΔPP	1.4	1.65	1.55	3.09*	2.99	5.52
All	ΔSBP	0.91‡	1.23†	0.32	2.86‡	3.08‡	1.81
Ages	ΔDBP	0.93‡	0.23	−2.99*	0.95‡	0.72†	−1.86
	ΔPP	−0.02	0.97‡	3.31	1.95‡	2.38‡	3.67†

CS indicates cross-sectional; L, longitudinal; BP, blood pressure; SBP, systolic BP; DBP, diastolic BP; PP, pulse pressure. CS slopes were estimated on both the full sample and a subset with repeated observations ≥5 years apart, controlling for season, pregnancy, repeated measures, and subject identification. For values from CS analyses, parameter estimates (β) are shown; for values from L analyses, mean parameters (Mβ) are shown. Significance is given for a 1-sample *t* test for results from L analyses and for the model parameter from CS analyses.

**P*≤0.05.

†*P*≤0.01.

‡*P*≤0.001.

from town was associated with lower SBP (β=−0.30 per 10 km) and a greater ΔPP (β=0.08 mm/10 years per 10 km). Fluent Spanish speakers had lower PP than those with no Spanish fluency (β=−1.8 mm Hg). Individuals in the lowest smoking tertile had lower DBP than nonsmokers (β=−1.43), but other tertiles did not differ from nonsmokers. Smoking and Spanish fluency were not associated with significant ΔBPs, and schooling was not associated with significant changes in baseline BP or ΔBP.

Discussion

Age-related increases in BP are modest among Tsimane compared with Westerners. BP changes little with age among Tsimane men, whereas a larger increase occurs among Tsimane women. Such increases are not uniform across the population. Longitudinal analyses reveal variability in age-related slopes, and variability increases with age, particularly among women. Overall, hypertension prevalence is low among Tsimane, and point observations of hypertension are not sustained over time.

To place the Tsimane age-related increase in context, we compared Tsimane ΔSBP and ΔDBP with those from 52 populations from Intersalt,[21] a cross-sectional study of hypertension using standardized methodology among adults aged 20 to 59 years (Figure 5). Tsimane slopes were derived from a mixed model with the same controls over the age range 20 to 59 years. Tsimane ΔSBP and ΔDBP were among the lowest, comparable with those from 4 other subsistence populations, the Xingu and Yanomamo of Brazil, Papua New Guinean highlanders, and rural Kenyans. National populations show ΔSBPs that are 2 to 8 times higher and ΔDBPs that are 2 to 4 times higher than Tsimane. Given their median level of adult SBP and DBP, Tsimane ΔBPs were smaller than that predicted by the regression lines (Figure 5). Overall, Tsimane BP and ΔBPs were small compared with other populations, even after controlling for BMI (Figure S3).

Despite the minimal age-related increases in BP, Tsimane BP age profiles shared similarities with Western profiles. Women had lower BPs than men at young ages, but beyond age 50 years, women's BPs equaled men's. In addition, DBP declined at older ages across populations. Explanations for the late drop in DBP include "burned out" diastolic hypertension, reduced cardiac output, and increased large arterial stiffness.[6] Burned out hypertension seems unlikely given the DBP decrease in a population with minimal hypertension and longitudinal BP increase.

Effects of modernization were small and not consistent with the notion that greater exposure leads to poor health outcomes. Although no indicator of modernization predicted a greater age-related increase in BP, BMI had the most substantial effect on BP level. Cohort increases in BMI have been linked to reduced physical activity, poor diet, and other changes associated with modernization.[22] Indeed, >85% of hypertension diagnoses occur in overweight or obese individuals (BMI ≥25 kg/m^2) among Westerners.[23] It might be expected, therefore, that behavioral changes associated with modernization should impact BP primarily through an indicator of obesity, that is, BMI. BMI is almost universally positively and independently associated with morbidity and mortality from hypertension, cardiovascular, and other chronic diseases and type 2 diabetes mellitus.[24] Greater body mass increases blood volume and viscosity, impairs pressure natriuresis, and can lead to renal tubular sodium reabsorp-

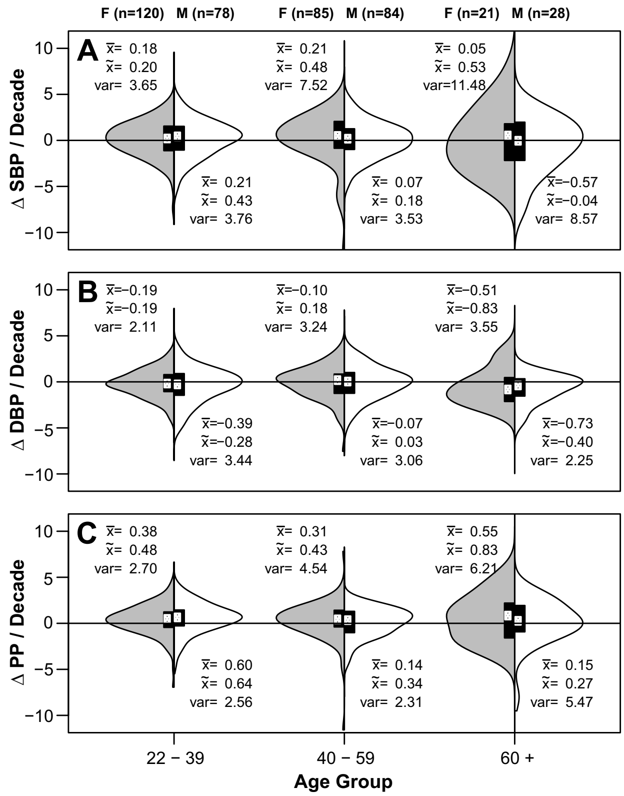

Figure 4. Distribution of individual systolic blood pressure (BP; ΔSBP; **A**), diastolic BP (ΔDBP; **B**), and pulse pressure (ΔPP; **C**) per decade by sex and age. Females are shown on the left (gray) and males on the right (white). Only individuals with ≥2 measures and ≥5 years between their earliest and latest BP measures were included. Box plots show the first to third quartile range. Distributions are smoothed density plots. White circles indicate medians.

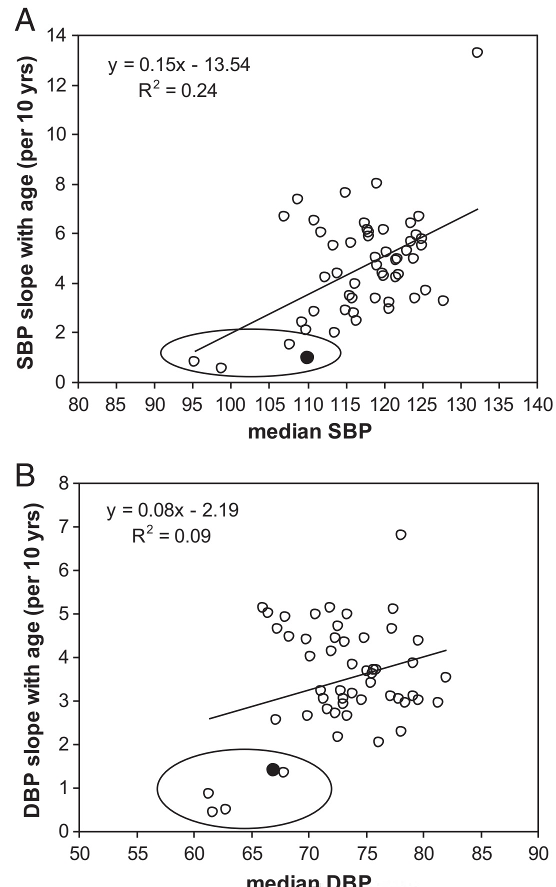

Figure 5. Increase in (**A**) systolic blood pressure (SBP) and (**B**) diastolic blood pressure (DBP) per decade. Cross-cultural sample includes 52 populations from the Intersalt study (ages 20–59 years).[21] Tsimane slope estimates are represented by black dots. Other populations inside ovals include the Brazilian Yanomamo and Xingu Amerindians, Papua New Guinea highlanders, and Kenyans.

tion.[25] Adipocytes also release angiotensinogen, a precursor of angiotensin.

The effect of a unit change in BMI on BP is similar among Tsimane and Americans (β=0.39, 0.13, and 0.26 for SBP, DBP, and PP from the National Health and Nutrition Examination Survey; β=0.61, 0.39, and 0.25 for Tsimane), but Tsimane BMI did not increase substantially throughout adulthood. Although obesity was rare among Tsimane (5.6% of women and 1.6% men age ≥20 years), overweight was not uncommon, including 27.8% of women and 21.9% of men. Heavy smokers and moderate Spanish speakers with greater schooling were more likely to be overweight or obese (Table S6). However, BMI was not greater in villages closer to town (Table S7), nor was overweight and obesity more prevalent (Table S6). Even if the average Tsimane was obese, Tsimane BP would not resemble US patterns. Based on the model from Table 2, a Tsimane woman with US average BMI at ages 40 and 70 years would have SBPs of 113 and 117 mm Hg, respectively, whereas an American woman with Tsimane average BMI at the same ages would have SBPs of 116 and 122 mm Hg, respectively (Table S8).

Despite the significant relationship between BMI and BP among Tsimane, Tsimane display lower median SBP and DBP and lower ΔSBP and ΔDBP than expected based on comparative BMIs of 52 Intersalt populations (Figure S3). Based on regressions using all of the Intersalt populations, Tsimane ΔSBP and ΔDBP from ages 20 to 59 years should be 339% and 134% greater, respectively, given their median BMI of 23.5. One possibility for the low BP given Tsimane BMI is that higher BMI among lean, active forager-horticulturalists reflects greater muscle rather than fat mass. However, this is not the case; BMI is highly correlated with body fat percentage in men and women across the BMI range (men, r=0.76, P<0.0001; women, r=0.55, P<0.0001; Figure S4). Body fat percentage per unit increase in BMI also appears similar among Tsimane and US adults (1.5% from BMI of 20–35; Figure S4 for Tsimane women; Reference 26 for US women).

Unlike patterns documented in the developed world,[23] Tsimane BMI reached its peak by age 45 years and then declined by 1.0 kg/m^2 by age 70 years (Table S6), although body fat percentage increased with age (men r=0.27, P<0.0001; women, r=0.13, P<0.0001). So, although we find evidence that modernization may lead to higher BMI among Tsimane, only cumulative smoking increased with age, whereas schooling and Spanish fluency were greater among younger adults. The net effect is a decline in BMI at late ages and only a minimal age-related increase in BP.

Distance to town showed minimal effect on BP and a positive effect on PP rise with age. However, indicators of modernization, such as smoking, Spanish fluency, and schooling, showed no consistent effects on BP. This finding contrasts with many published patterns of "0-slope" populations that underwent rapid modernization, where mean BP increased and also rose with age.[11] A meta-analysis of effects of modernization on BP shows universal positive effects with similar effect sizes worldwide (≈4 mm higher for SBP and 3 mm for DBP, on average).[14] That study, however, did not examine modernization effects on the rate of BP increase. Migration and initial contact (<3 years) in a modernized setting had the greatest positive impacts on BP, more than BMI or other variables. This high level of modernization is not representative of the Tsimane at present. Few Tsimane live in towns, and even those living in the most modernized villages still actively practice horticulture, fishing, and hunting. Most Tsimane have not given up their traditional lifestyle. Their diet remains rich in potassium, fiber, and omega-3 fatty acids and low in saturated fat.[20] Perhaps the greatest differences across regions is in access to market foods (eg, sugar, salt, and cooking oil), medical attention, and schools. A comparison of risk factors across regions does not show consistent high risk in more acculturated regions (Table S7). For example, whereas women near town and the mission show highest Spanish fluency, literacy, and schooling (Figure S5), women living downstream from San Borja show the highest body fat and BMI, whereas women living in remote villages smoke more (Table S7 and Figure S6). Despite increasing modernization, low hypertension prevalence and minimal age-related increase in BP among Tsimane are noteworthy given that Native Americans display higher susceptibility to hypertension; they show similar genetic profiles affecting salt avidity and cardiovascular reactivity as high-risk African populations, despite recent descent from cold-adapted north Asian populations.[15] This genetic propensity with rising obesity and changing diets is likely responsible for rising levels of cardiovascular disease and metabolic disease among native North Americans. However, among North American Indians from the Strong Heart Study, BP increased substantially with age but was minimally affected by obesity despite cardiovascular disease being the leading cause of death[27] (but see Reference 28). North American Indians show similar rates of hypertension compared with other US groups.[28] The nontrivial prevalence of prehypertension among Tsimane does suggest that imminent changes in cardiovascular risk factors are likely if physical activity, diet, or other hypertension-promoting conditions increase over time. Among "partially acculturated" island-dwelling Kuna, BP is also low and does not rise with age, whereas Kuna migrants to Panama City show relatively high prevalence of hypertension and rising BP with age.[29]

Finally, sex differences in Tsimane BP are striking. Most of the substantial rise in SBP and PP occurs in women, especially during the 40s and 50s (Figures S1 and 2–4). We find greater variation in women's BP and ΔBP with age (Figure 4 and Table S4). Unlike the sex profiles of BP among Westerners, Tsimane women have higher rates of hypertension and are at greater risk of BP-related morbidity than men. Although age profiles of BMI do not vary markedly by sex, body fat increases at a higher rate among women (Figure S4; 17.2% versus 12.2% per decade). BMI also has a 61% greater effect on SBP in women than in men (β=1.16 versus 0.72; Table S5). Postmenopausal increases in BP have been documented among Westerners and have been attributed to declines in estradiol production.[30] Estradiol influences vascular tone and structure and endothelial vasodilation and might inhibit vascular response to arterial injury.[31]

Strengths and Limitations

To our knowledge, the Tsimane are the only foraging-horticultural population sampled longitudinally. Their active lifestyle, lack of BP medication, and variable experience with modernization provided a unique opportunity to investigate BP change with age. Little bias is expected, because ≥90% of adults present were sampled per medical round. Few adults, however, were sampled ≥5 times, and the maximum time depth of the study was only 8 years. Although we include several measures of modernization, we did not consider its direct effects via individual-level measures of diet, physical activity, and other behavioral changes, although these are being collected in ongoing studies.

Perspectives

We found low levels of persistent hypertension and minimal age-related BP increase among Tsimane Amerindians compared with Westerners. Tsimane women were at greater risk of hypertension at late ages. Proximity to town affected SBP but not rate of BP increase in the predicted direction; BMI impacted BP level, but not BP slope, with age. Many aspects of traditional diet and activities were preserved even among more modern Tsimane, suggesting that they have not yet experienced severe changes that would otherwise promote greater hypertension and cardiovascular disease. Prehypertension prevalence was moderate, suggesting that further changes in diet and behavior could place Tsimane at elevated risk.

Acknowledgments

We thank Tsimane for their participation and collaboration and Tsimane Health and Life History Project personnel.

Sources of Funding

This research was supported by grants from the National Institutes of Health/National Institute on Aging (R01AG024119, R56AG024119, and R01AG024119-08) and the National Science Foundation (BCS-0422690).

Disclosures

None.

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Novelty and Significance

What Is New?

- We provide the first systematic test of whether blood pressure increases with age in a subsistence population using longitudinal and cross-sectional data.
- We test whether modernization affects blood pressure and its rise with age.

What Is Relevant?

- Persistent hypertension is minimal (<3%) among adults aged ≥40 years, despite high levels of inflammation and variable experience with modernization.
- Hypertension and age-related increase in blood pressure are more prevalent among Tsimane women, unlike sex differences observed in Western countries.

Summary

An increase in blood pressure with age is not a fundamental feature of human aging. Effects of age and modernization are minimal on blood pressure and its rise. The lean physique, active lifestyle, and traditional diet may protect against hypertension in spite of increasing socioeconomic change.

ONLINE SUPPLEMENT

DOES BLOOD PRESSURE INEVITABLY RISE WITH AGE? LONGITUDINAL EVIDENCE AMONG FORAGER-HORTICULTURALISTS

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Short title: Blood pressure change with age and modernization

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METHODS

Village sample. Villages can be grouped based on decreasing access to market: Near Town (n=752 adults, 17 villages, average 18 km from San Borja), Lower Maniqui River (n=330, 6 villages, 23 km), Central River (n=261, 16 villages, 40 km), road to Rurrenabaque (n=70, 8 villages, 48 km), Forest (n=318, 11 villages, 56 km), Upper Maniqui River (n=276, 9 villages, 64 km), Mission (n=203, 1 village, 66 km), and Quiquibey River (n=59, 8 villages, 74 km). The following villages were added in 2010 and only sampled once: all villages along the road to Rurrenbaque, all villages along the Quiquibey River, 12 of the Near Town villages, one Forest village, 15 Near River villages, and one Lower Maniqui River village.

Medical rounds. Data were collected during annual medical exams of the Tsimane Health and Life History Project. From 2002 to 2004, a mobile medical team made annual visits to 18 villages, obtaining blood pressure measurements during routine medical exams. Efforts were made to sample all present individuals. An additional 7 villages were sampled from 2005 to 2009. From 2010 to 2011, medical exams on all adults age 40+ were conducted in a clinic in San Borja. An additional 45 villages were added to the sample in 2010. Adults from these 45 villages were only sampled once. Clinical exams are given by Bolivian physicians with the assistance of bilingual Spanish-Tsimane translators. Additional details are given here[1].

Age estimation. Ages were assessed by cross-checked demographic interviews, as has been described elsewhere[2]. These include using known ages from written records, relative age lists, dated events, photo comparisons of people with known ages and cross-checking of information from independent interviews of kin. In constructing relative age lists, multiple informants were used for each five year age grouping of individuals, and inconsistencies were investigated and resolved. The photo comparison method used a sample of 70 photos of individuals with known ages. For older individuals, 50 photos of men and women from ages 50-75 were used. Each of these methods provides a roughly independent age estimate. When all estimates yield a date of birth within a 3-year range, the average was used unless one or two estimates were judged to be superior.

DATA ANALYSIS

Estimation of individual rates of blood pressure change. To estimate individual longitudinal rates of change, BP values and time points were first centered on the mean blood pressure value and median time-point for a given individual, such that blood pressures were recoded as positive or negative changes from the subject's mean, and times were recorded as days before or after the subject's median reading date. Linear models were fit to blood pressure change including subject PID, a subject-by-time interaction, season of exam, and pregnancy status as control variables. Fitting all slopes in one model, instead of separate models for each subject, facilitated estimation of population values for control variables. Parameter values for rates of blood pressure changes were then obtained from the subject-by-time interaction parameters. Slopes based on only two data points had large variances and showed evidence of regression to the mean. In order to analyze these slopes we therefore had to determine how many data points were required for an accurate slope estimate. To examine the effect of number of measures on slope estimates we performed a simple simulation. Beginning with individuals with six or more observations we randomly sampled different numbers of consecutive observations from each individual. We then examined the standard deviation of the slopes obtained. The results show that the standard deviation around the mean slope declines with increasing number of observations (Figure S7). For our data, however, requiring six or more observations would drastically decrease sample size. We therefore estimated the standard error of the mean that would be obtained from our sample, given different inclusion criteria to identify the “optimal” trade-off between accuracy and sample size. We found that the standard error was minimized by including only individuals with five or more observations. For longitudinal analyses we therefore use this inclusion criterion.

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2 Gurven, M., Kaplan, H. & Zelada Supa, A. Mortality experience of Tsimane Amerindians: regional variation and temporal trends. *American Journal of Human Biology*. 2007; 19:376-398.

Table S1. Number of repeat samples and hypertension diagnoses across repeat sampling

	# of Times Sampled									
Age Group	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**Total**
20-29	193	164	122	105	54	33	11	7	0	689
30-39	61	51	67	96	52	36	28	5	3	399
40-49	236	24	43	47	74	32	22	11	2	491
50-59	120	16	18	28	28	17	16	5	0	248
60-69	108	12	24	11	22	9	8	2	0	196
70+	153	12	10	21	20	3	3	3	0	225
Total	871	279	284	308	250	130	88	33	5	2248
Total Obs.	871	558	852	1232	1250	780	616	264	45	6468
Never Hyper	92.2%	93.5%	88.4%	91.9%	86.4%	80.0%	84.1%	72.7%	40.0%	89.8%
Hyper Only Once	7.8%	6.5%	7.7%	6.2%	10.0%	16.9%	9.1%	18.2%	40.0%	8.5%
Hyper More Than	-	0.0%	3.9%	1.9%	3.6%	3.1%	6.8%	9.1%	20.0%	2.9%
Hyper Always	7.8%	0.0%	0.4%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	3.1%

Table S2. Sample size for all variables by medical round

	Medical round and date (month/year)								
Variable	**(1) 8/03-12/03**	**(2) 1/04-6/04**	**(3) 7/04-12/04**	**(4) 1/05-8/05**	**(5) 10/05-7/06**	**(6) 8/06-8/07**	**(7) 9/07-8/08**	**(8) 10/08-10/09**	**(9) 12/09-12/10**
SBP	276	279	268	321	865	1117	1107	1186	1098
DBP	276	279	268	321	865	1117	1106	1186	1098
Pregnant	276	279	268	321	865	1117	1107	1186	1098
Height	184	143	250	115	840	1116	1104	1184	1057
Weight	184	142	247	115	852	1116	1103	1184	1057
BMI	183	141	246	115	839	1115	1102	1183	1056
Spanish fluency	193	201	210	247	658	863	945	1084	490
Years of schooling	192	197	209	241	648	851	934	1064	489
Smoking	179	182	172	199	586	759	700	712	508
Distance to San Borja	269	275	261	319	851	1100	1088	1168	1018

Table S3. Two-stage mixed models. Stage 1 models have a random slope and intercept for each individual in the study, with blood pressure (SBP, DBP, PP) as the dependent variable. Stage 2 models are generalized additive models that use the individual random-effect slopes plus population main effects from Stage 1 as the dependent variable to model associations with individual level slope, with the overall age-pattern in the slopes modeled with thin-plate splines. Parameter values are in units of change per decade. Only individuals with data for all variables and at least two observations were included (n=695 individuals, n=2,876 observations).

Stage 1 Main effects (mm Hg)		**SBP**			**DBP**			**PP**		
		B	**SE**	**p**	**B**	**SE**	**p**	**B**	**SE**	**p**
Constant		94.5	2.4	<0.01	57.6	1.6	<0.01	36.3	1.7	<0.01
Sex (Male)		2.7	1.0	<0.01	1.4	0.6	0.02	1.1	0.7	0.11
BMI		0.6	0.1	<0.01	0.4	0.06	<0.01	0.3	0.07	<0.01
Pregnant		-2.8	1.0	<0.01	-3.3	0.7	<0.01	0.4	0.8	0.63
Smoking tercile										
	1st	-1.2	0.9	0.21	-1.4	0.6	0.02	0.21	0.7	0.75
	2nd	1.1	1.2	0.34	0.5	0.8	0.55	1.1	0.8	0.21
	3rd	0.5	1.3	0.68	-0.4	0.9	0.62	1.2	0.9	0.19
Spanish fluency	None	0			0			0		
	Moderate	1.1	0.8	0.14	0.5	0.5	0.32	0.5	0.6	0.38
	Fluent	-1.1	1.0	0.27	0.4	0.7	0.51	-1.8	0.7	0.01
Years of Schooling		0.1	0.1	0.58	0.1	0.08	0.23	0.01	0.09	0.91
Distance to San Borja (per 10 km)		-0.3	0.1	0.04	-0.1	0.1	0.29	-0.2	0.1	0.13
Season	Wet	0			0			0		
	Dry	3.9	0.6	<0.01	2.8	0.4	<0.01	1.0	0.5	0.04
	Intermediate	-0.6	0.59	0.33	0.02	0.4	0.97	-0.6	0.5	0.26
		edf	**Ref.df**	**p**	**edf**	**Ref.df**	**p**	**edf**	**Ref.df**	**p**
Age Splines	Female	3.1	3.1	<0.01	1	1	<0.01	3.4	3.4	<0.01
	Male	3.4	3.4	0.03	2.6	2.6	<0.01	4.2	4.2	<0.01

Table S3 continued on next page

Table S3 continued

Stage 2 BP slopes (mm Hg/decade)		SBP			DBP			PP		
		B	**SE**	**p**	**B**	**SE**	**p**	**B**	**SE**	**p**
Constant		2.0	0.4	<0.01	0.9	0.2	<0.01	0.6	0.4	0.12
Sex (Male)		-2.7	0.1	<0.01	0.03	0.07	0.65	-3.0	0.1	<0.01
BMI		0.02	0.01	0.27	0.00	0.01	0.91	0.03	0.02	0.07
Smoking tercile										
	1st	-0.1	0.1	0.37	-0.03	0.07	0.63	-0.2	0.1	0.16
	2nd	-0.01	0.2	0.97	0.1	0.08	0.25	-0.1	0.2	0.41
	3rd	-0.02	0.2	0.90	0.05	0.09	0.59	-0.08	0.2	0.65
Spanish fluency	None									
	Moderate	0.05	0.1	0.65	0.07	0.06	0.26	0.01	0.1	0.93
	Fluent	0.08	0.1	0.55	0.06	0.07	0.41	0.2	0.2	0.28
Years of schooling		0.01	0.02	0.63	0.01	0.01	0.63	0.01	0.02	0.60
Distance to San Borja (per 10 km)		0.03	0.02	0.15	0.01	0.01	0.70	0.08	0.02	<0.01
		edf	**Ref.df**	**p**	**edf**	**Ref.df**	**p**	**edf**	**Ref.df**	**p**
Age Splines	Female	7.2	8.2	<0.01	6.1	7.3	0.184	7.5	8.4	<0.01
	Male	6.2	7.4	<0.01	2.7	3.4	<0.01	7.6	8.5	<0.01

Table S4. Variance in blood pressure and change in blood pressure by age and sex for Tsimane and NHANES 2005-2006. Cross-sectional (CS) Tsimane values are based only on the largest medical round; slopes were estimated from longitudinal (L) data on individuals with at least five years between first and last observations. P-values represent F-test comparison of variance with a Bonferroni correction for multiple comparisons. p<0.01 comparing Tsimane vs. NHANES BP variance, except for females aged 60+ (p=0.92).

		Variance						**P-value**		
		Tsimane				**NHANES**		**Males vs. Females**		
		Pressures (CS)		**Slopes (L)**		**Pressures (CS)**		**Pressure**	**Slopes**	**Pressure**
Measure	**Age**	**Females**	**Males**	**Females**	**Males**	**Females**	**Male**	**Tsimane**	**Tsimane**	**NHANES**
SBP	22 - 39	68.9	60.9	3.76	3.73	102.9	140.8	1.00	1.00	<0.01
	40-59	188.0	87.6	7.55	3.49	320.6	252.7	<0.01	<0.01	<0.01
	60+	454.7	115.7	11.52	8.55	600.4	426.9	<0.01	1.00	<0.01
DBP	22 - 39	46.3	70.1	2.12	3.31	119.4	167.8	<0.01	0.11	<0.01
	40-59	71.1	62.2	3.22	2.99	125.9	153.4	1.00	1.00	0.05
	60+	157.1	83.8	3.55	2.25	301.4	203.8	0.05	1.00	<0.01
PP	22 - 39	47.6	80.3	2.65	2.62	127.9	205.2	<0.01	1.00	<0.01
	40-59	95.1	69.0	4.55	2.30	241.2	189.3	0.17	<0.01	<0.01
	60+	190.5	89.7	6.27	5.46	685.1	444.5	0.01	1.00	<0.01

Table S5. Pairwise comparison of variance in blood pressure and change in blood pressure between age groups within each sex in the last medical round for Tsimane and NHANES 2005-2006. P-values represent F-test comparison of variance with a Bonferroni correction for multiple comparisons. CS refers to cross-sectional analysis and L refers to longitudinal analysis.

		p-value					
		Tsimane				**NHANES**	
		Pressures (CS)		**Slopes (L)**		**Pressures (CS)**	
Measure	**Comparison**	**Females**	**Males**	**Females**	**Males**	**Female**	**Males**
SBP	22 - 39 vs. 40 - 59	<0.01	0.03	<0.01	1.00	<0.01	<0.01
	22 - 29 vs. 60+	<0.01	<0.01	<0.01	0.02	<0.01	<0.01
	40 - 59 vs. 60+	<0.01	0.66	0.75	<0.01	<0.01	<0.01
DBP	22 - 39 vs. 40 - 59	<0.01	1.00	0.12	1.00	1.00	0.93
	22 - 29 vs. 60+	<0.01	1.00	0.36	0.87	<0.01	0.03
	40 - 59 vs. 60+	<0.01	0.54	1.00	1.00	<0.01	<0.01
PP	22 - 39 vs. 40 - 59	<0.01	1.00	0.04	1.00	<0.01	1.00
	22 - 29 vs. 60+	<0.01	1.00	0.02	0.04	<0.01	<0.01
	40 - 59 vs. 60+	<0.01	0.75	1.00	<0.01	<0.01	<0.01

TABLE S6. Probability of overweight or obesity (BMI>=25 kg/m2) and obesity (BMI>=30 kg/m2) in mixed-effects regression models with random intercept and age parameters, controlling for physician, medical round, season, and pregnancy status (n=3,411 observations for 1,136 individuals)

	Probability of overweight or obese				**Probability of obese**			
Predictor	Odds Ratio	95% Wald Confidence Limits		P	Odds Ratio	95% Wald Confidence Limits		p
Age	1.2			<0.01	1.2			<0.01
Age^2	0.99			<0.01	0.99			<0.01
Sex (Female)	1.8	1.4	2.5	<0.01	6.3	3.0	13.1	<0.01
Pregnant	1.7	1.2	2.5	<0.01	1.4	0.7	2.9	0.32
Region								
Downriver	1.7	1.3	2.4	<0.01	1.5	0.8	2.9	0.04
Mission	0.8	0.6	1.2	0.04	0.5	0.2	1.1	0.03
Forest	1.2	0.8	1.7	0.46	1.2	0.6	2.6	0.32
Upriver (vs. Near Town)	0.9	0.6	1.2	0.08	0.9	0.4	1.9	0.93
Spanish fluency								
None	0.5	0.4	0.7	<0.01	0.5	0.3	1.1	<0.01
Moderate (vs. Fluent)	1.1	0.8	1.4	<0.01	1.4	0.7	2.5	<0.01
Years of schooling	1.1	1.04	1.1	<0.01	1.1	1.01	1.2	0.03
Smoking								
Low	1.2	0.9	1.6	0.81	0.99	0.5	1.9	0.43
Moderate	1.1	0.8	1.6	0.77	0.5	0.2	1.5	0.03
High	1.1	0.8	1.6	0.66	1.3	0.5	3.3	0.8
Unknown (vs. None)	1.6	0.96	2.6	0.15	4.03	2.0	8.3	<0.01

TABLE S7. Regional differences in hypertension risk factors by sex. Yellow refers to region(s) with highest potential risk. Blue refers to region(s) with lowest expected risk.

	Females						Males					
	Forest	Upriver	Downriver	Fatima	Near Town		Forest	Upriver	Downriver	Fatima	Near Town	
Variable	(57 km)	(62 km)	(22 km)	(66 km)	(18 km)	p	(57 km)	(62 km)	(22 km)	(66 km)	(18 km)	p
Age (years)	38.6	37.2	38.5	37.0	38.3	ns	38.9	38.5	40.7	38.4	40.4	*
Height (cm)	151.0	150.4	150.9	150.9	150.9	ns	162.2	161.7	162.2	163.7	163.2	‡
Weight (kg)	54.3	52.2	55.6	53.7	54.8	‡	61.0	61.0	61.8	63.7	63.5	‡
Body fat (%)	25.7	24.1	26.3	24.8	24.9	‡	16.6	16.4	17.3	18.1	16.4	‡
BMI (kg/m^2)	23.8	23.1	24.4	23.5	24.0	‡	23.2	23.3	23.5	23.8	23.8	‡
Schooling (years)	0.2	0.8	0.8	2.3	2.1	‡	0.9	1.9	1.9	3.0	4.5	‡
Spanish fluency (%)												
None	88.5	71.3	65.4	49.9	30.2	‡	55.4	23.1	19.3	16.7	8.9	‡
Moderate	10.8	25.1	29.0	33.3	36.1		35.8	46.0	43.0	58.3	31.4	
Fluent	0.7	3.6	5.7	16.9	33.7		8.9	30.9	37.7	25.0	59.7	
Smoking (%)												
None	66.4	71.2	70.4	80.5	83.3	‡	4.2	21.0	14.8	16.8	12.6	‡
Low	22.9	13.5	13.2	7.1	8.3		17.8	21.6	19.6	12.4	25.0	
Moderate	7.3	5.5	6.4	3.7	5.0		33.0	17.7	30.7	23.5	33.5	
High	2.0	4.9	0.0	0.0	1.2		42.1	35.1	22.6	46.0	25.9	
SBP (mm Hg)	110.0	103.2	108.1	108.0	106.9	‡	113.9	110.3	113.3	113.0	112.0	‡
DBP (mm Hg)	68.5	64.2	66.4	68.1	66.1	‡	70.4	67.5	68.6	70.8	67.7	‡
PP (mm Hg)	41.5	39.0	41.7	39.9	40.9	‡	43.5	42.8	44.6	42.2	44.2	†
n (cases)	492	515	471	463	939		434	467	463	417	817	

*$p<0.05$, †$p<0.01$, ‡$p<0.001$, ns=not significant

Table S8. Blood Pressure at average U.S. and Tsimane body mass index (BMI), estimated from models in Table 2 and Figure 2.

Calculated With Tsimane Average BMI

Sex/Age	Average BMI	NHANES SBP	DBP	Tsimane SBP	DBP
Female					
Age 40	24.29	113.29	70.25	112.73	70.03
Age 70	23.07	135.98	65.99	117.02	70.99
Male					
Age 40	24.15	120.22	73.85	112.63	69.97
Age 70	23.20	131.02	67.76	117.11	71.05

Calculated With US Average BMI

Sex/Age	Average BMI	NHANES SBP	DBP	Tsimane SBP	DBP
Female					
Age 40	28.56	114.96	70.79	115.72	71.98
Age 70	29.66	138.56	66.82	121.64	74.01
Male					
Age 40	29.35	122.26	74.50	116.27	72.35
Age 70	28.55	133.11	68.43	120.86	73.50

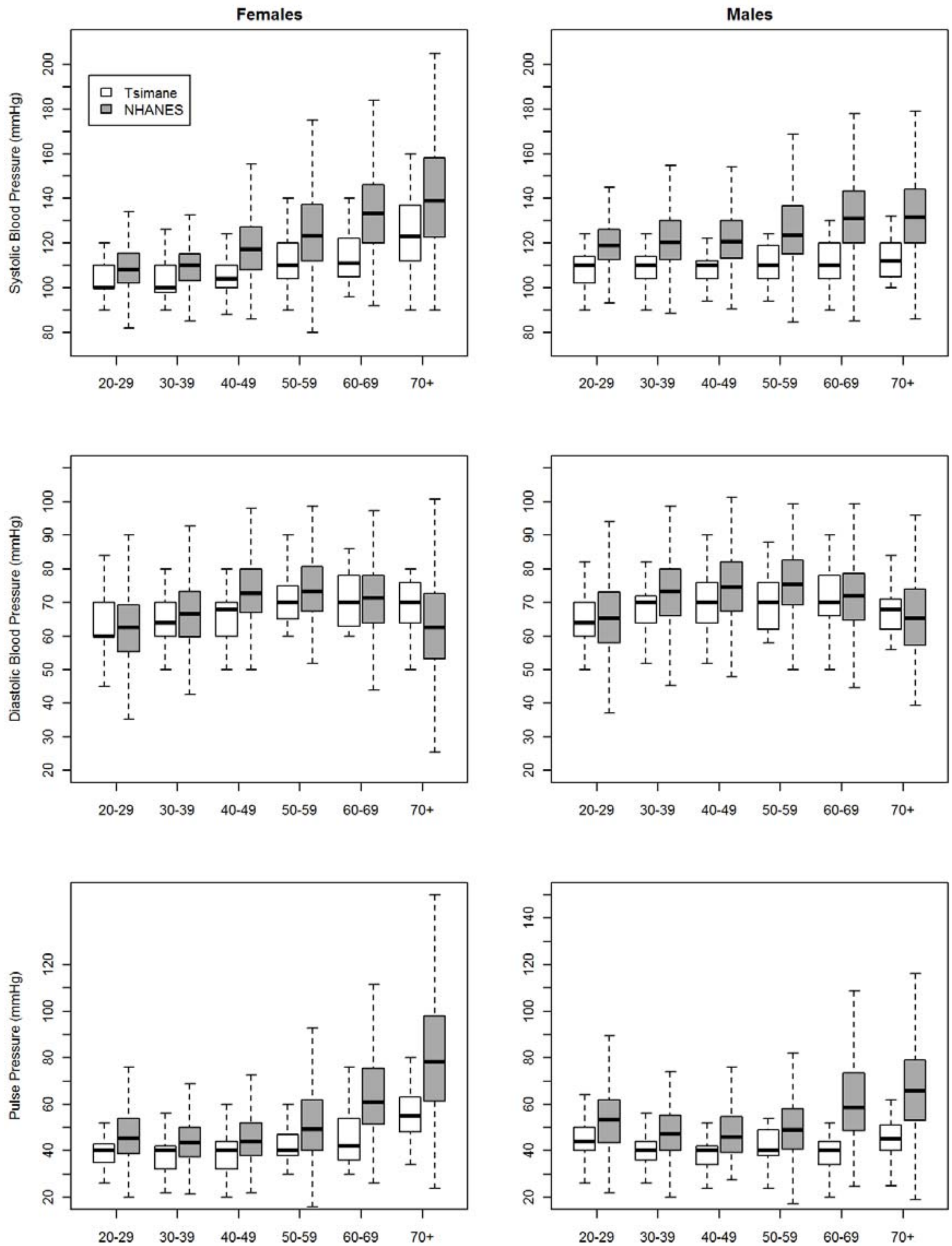

Figure S1. SBP, DBP and PP for last Tsimane medical round (Oct. 2008-2009) and NHANES 2005-2006 for females and males. Boxes encompass the 25th- 75th percentiles, lines indicate the median, and whiskers indicate either the extreme data points or 1.5 times the interquartile range, whichever produces a shorter whisker. Outliers are not shown.

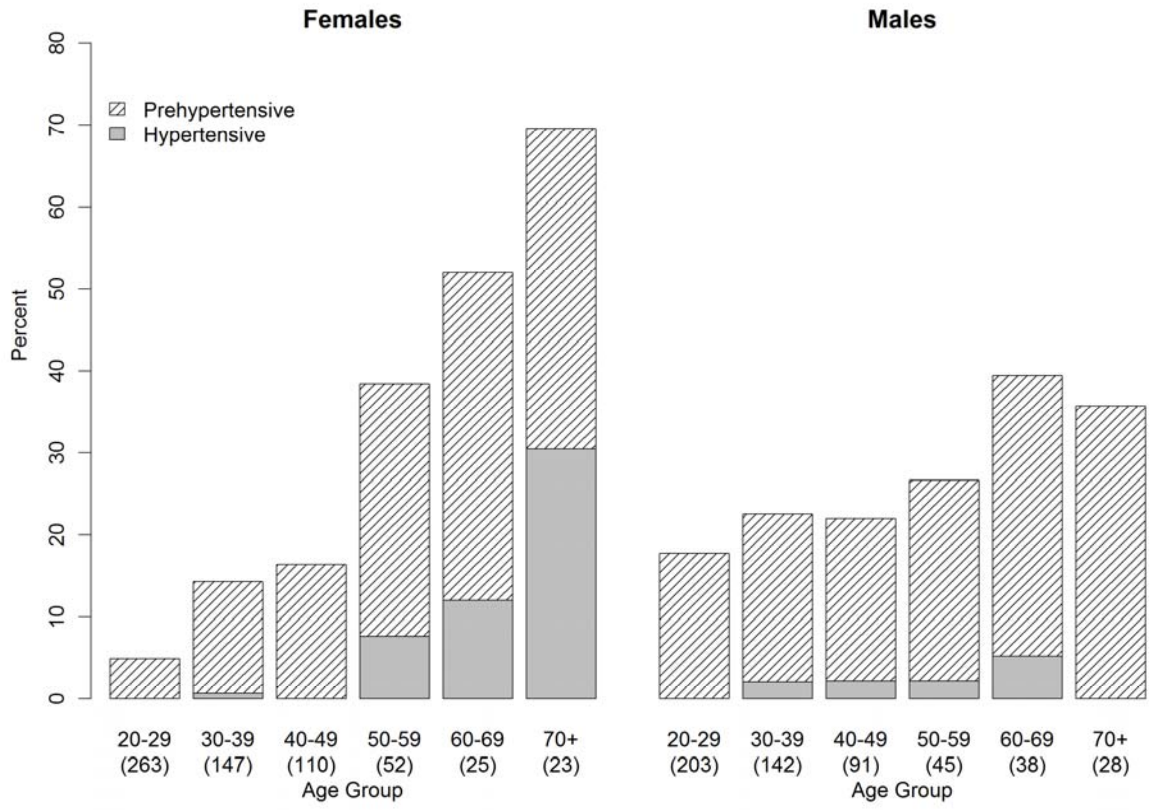

Figure S2. Prevalence of hypertension, pre-hypertension and normal tension among (a) females and (b) males during the last medical round (n=1,186 individuals). Sample sizes are in parentheses below age categories.

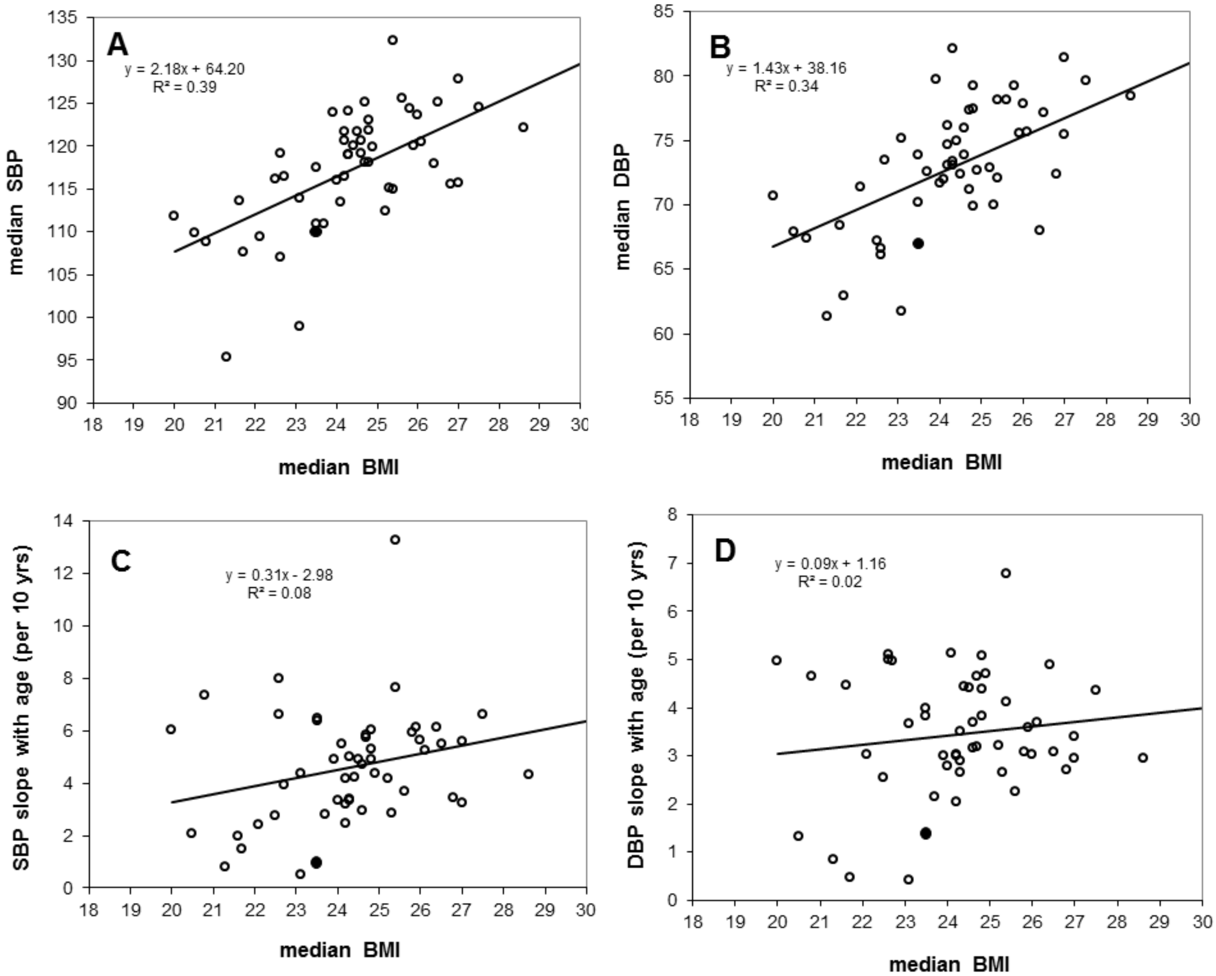

Figure S3. Effects of median adult body mass index (BMI) on median levels of (a) SBP and (b) DBP, and on age-related increases per 10 years of adult age in (c) SBP and (d) DBP, using INTERSALT study (ages 20-59). Tsimane estimates are represented as black dots.

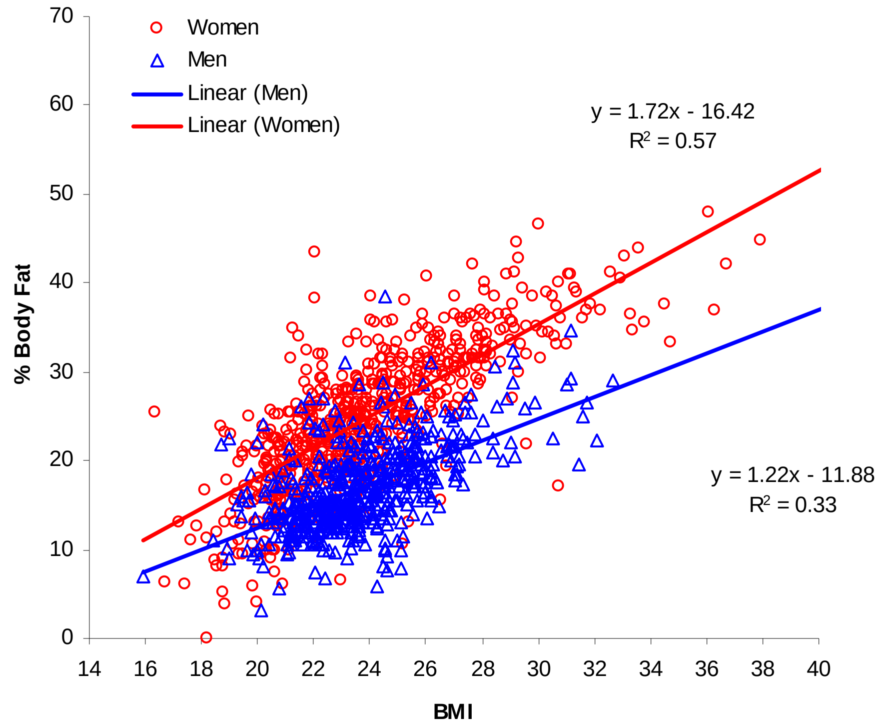

FIGURE S4. Body fat percentages as a function of body mass index (BMI) for women and men in largest medical round (Oct. 2008-2009).

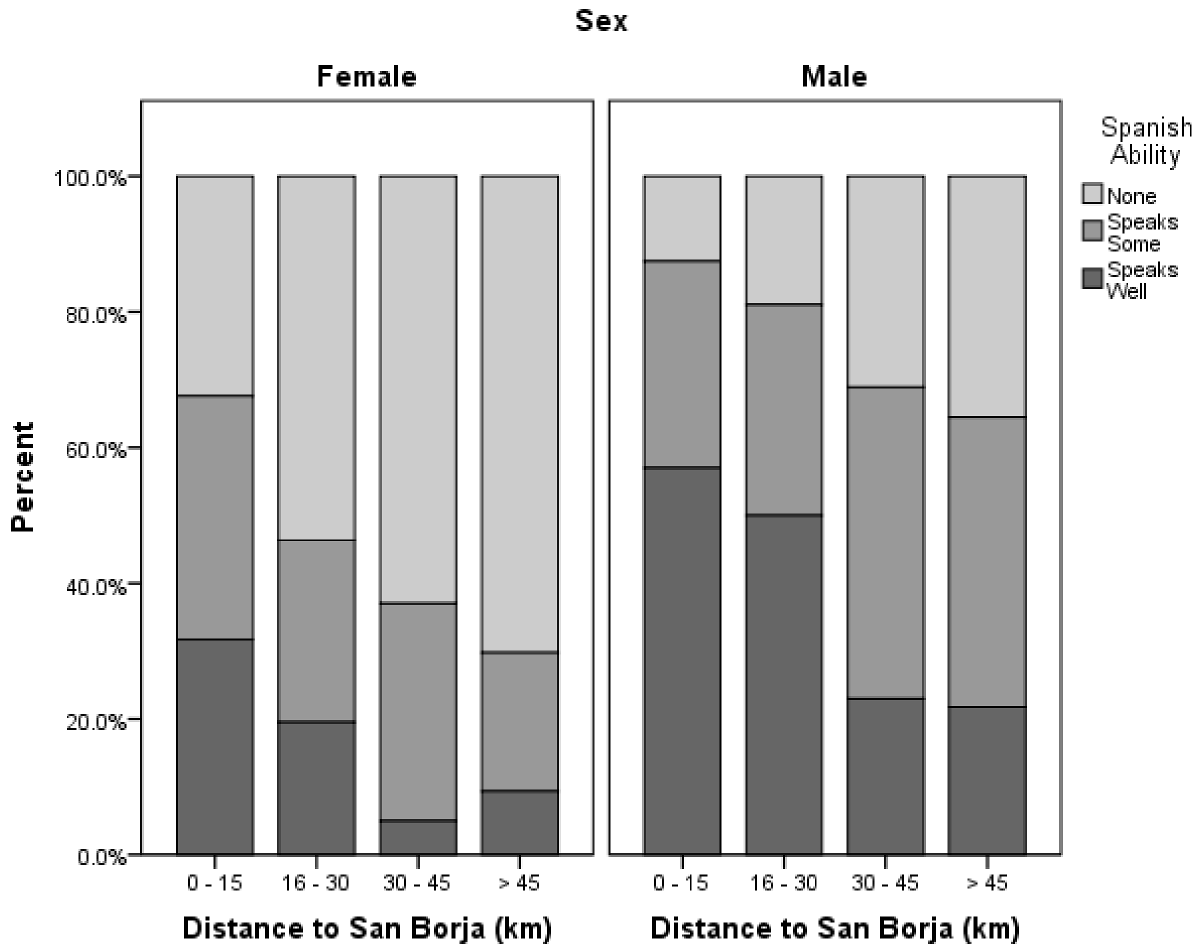

Figure S5. Spanish ability by sex and distance to San Borja

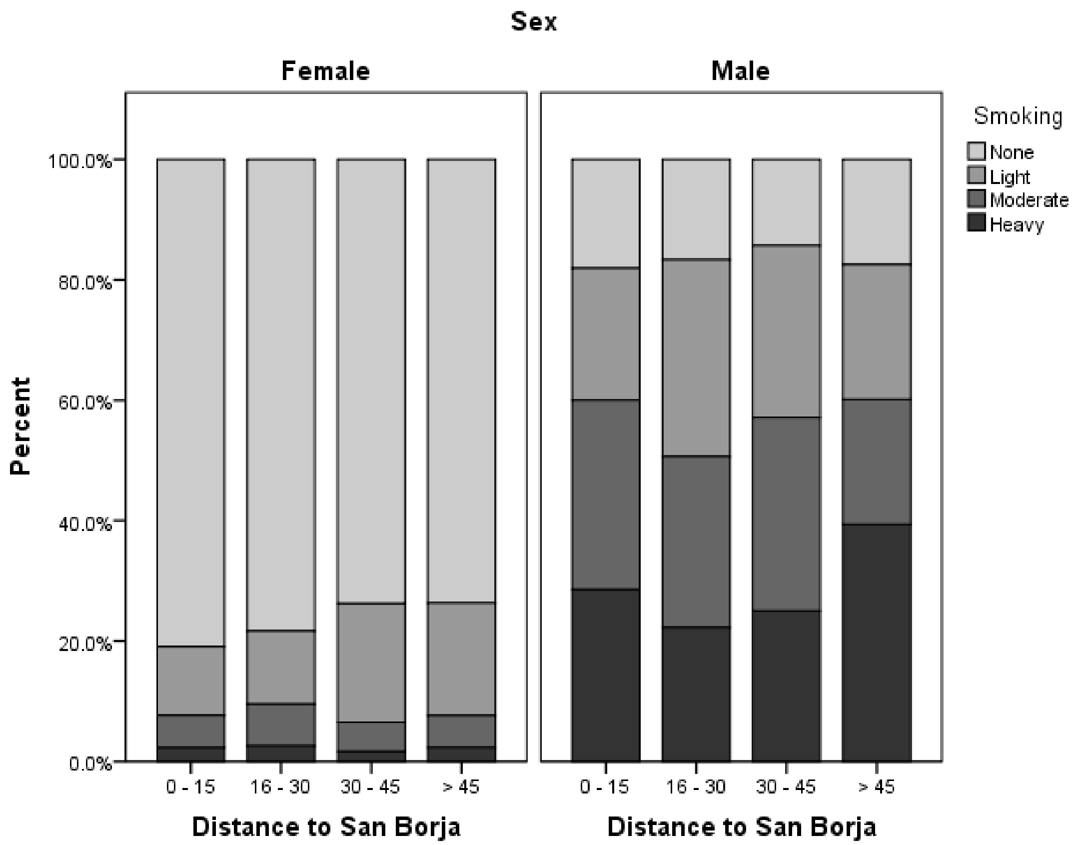

Figure S6. Smoking by sex and distance to San Borja

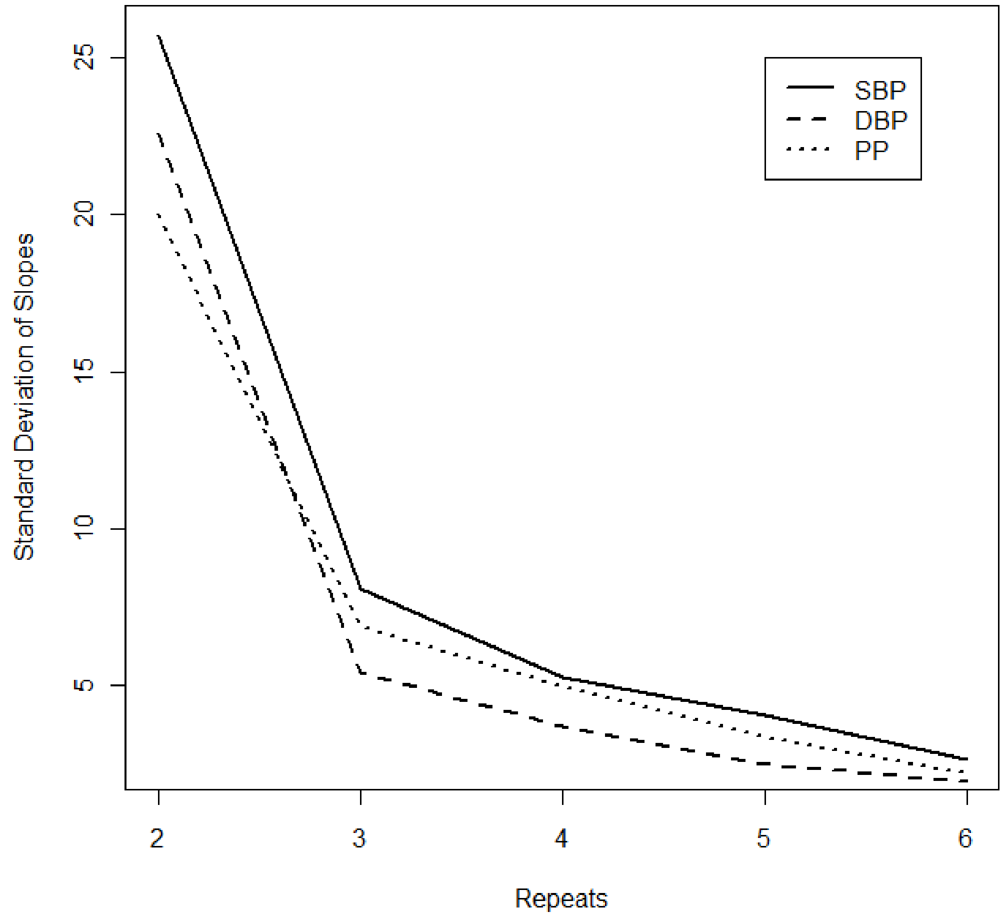

Figure S7. More observations lead to lower deviation in slope estimates. Pressure values from individuals with six or more observations were randomly resampled for 2-6 consecutive observations and a linear line was fit for each individual slope. The graph shows the sample standard deviation in slope estimates for a given number of observations. Note that sample size and subject identities are held constant.