

## **The association between blood pressure and the prevalence of hypertension with geographical latitude and solar radiation: results from the Chilean Health Survey 2009-2010**

*Short Title: Geographical latitude, solar radiation and blood pressure.*

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**Key Words:** Geographical latitude, solar radiation, hypertension, blood pressure, Chile.

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Abstract: 345 words Main text: 2580 words Tables: 4, Figures: 2.

Supplementary Files: 1

**Sources of Funding:** Dr Cabrera is supported by a joint International Society of Nephrology/Kidney Research UK Long-Term Fellowship and by grant support from Becas Chile. Dr Ferro is supported by a UK National Institute for Health Research Fellowship.

**Abstract**

**Importance** Hypertension is a major risk factor for cardiovascular disease. There are significant geographical differences in the prevalence of hypertension around the world. The reasons for this are not completely understood.

**Objective** To explore the relationship between geographical latitude and solar radiation with blood pressure and hypertension prevalence.

**Setting** Chilean general population.

**Participants** Adult population of the Chilean Health Survey 2009-2010 (n=4,634).

**Exposures** Solar radiation and geographical latitude.

**Main Outcome** Values of systolic and diastolic blood pressure and presence of hypertension.

**Results** The prevalence of hypertension was significantly higher in the South (37.4%) compared with the Central (34.0%) and North (29.3%) zones ( $P<.001$ ). Systolic pressure was significantly higher in the South (126.3 [Interquartile range (IQR) 113.7 – 143.0] mmHg) than Central (123.0 [IQR 112.7 – 139.0] mmHg) and North (121.0 [IQR 109.7 – 135.0] mmHg) zones ( $P<.001$ ). The prevalence of hypertension was associated with latitude (Odds Ratio (OR), 1.014 [95% Confidence Intervals (CI) 1.007, 1.021]  $P<.001$ ) and solar radiation (OR, 0.963 [95% CI 0.944, 0.982],  $P<.001$ ). These associations persisted after adjustment for multiple variables (latitude OR, 1.012 [95% CI 1.002, 1.021],  $P=.02$  and solar radiation OR, 0.973 [95% CI 0.949, 0.999],  $P=.04$ ). Blood pressure was associated with latitude (systolic  $\beta$  coefficient 0.194 [95% CI 0.117, 0.271],  $P<.001$  and diastolic  $\beta$  coefficient 0.080 [95% CI 0.043, 0.118],  $P<.001$ ) and solar radiation (systolic  $\beta$  coefficient -0.533 [95% CI -0.744, -0.322],  $P<.001$  and diastolic  $\beta$  coefficient -0.197 [95% CI -0.301, -.094],  $P<.001$ ). The association between systolic pressure and latitude ( $\beta$  coefficient 0.109 [95% CI 0.047, 0.172],

$P=.001$ ) and solar radiation ( $\beta$  coefficient  $-0.276$  [95% CI  $-0.448, -0.103$ ],  $P=.002$ ) persisted after adjustment. However, after adjustment, the association between diastolic pressure and latitude ( $\beta$  coefficient  $0.033$  [95% CI  $-0.003, 0.070$ ],  $P=.07$ ) and solar radiation ( $\beta$  coefficient  $-0.067$  [95% CI  $-0.167, 0.033$ ],  $P=.19$ ) was no longer significant.

***Conclusion and Relevance*** In the Chilean population the prevalence of hypertension and higher systolic pressure are associated with living further from the Equator and reduced exposure to solar radiation. Future work should investigate the potential mechanisms of this association as well as the potential impact on public health.

## Introduction

Hypertension is an important risk factor for cardiovascular (CV) disease. Mean systolic and diastolic blood pressures, as well as the prevalence of hypertension, vary widely throughout the world.<sup>1</sup> A number of potential explanations, including genetic factors, ethnicity, socio-economic factors, diet (e.g. salt intake, fruit and vegetable consumption) and a more “Westernised” lifestyle, have been postulated to contribute to this variation.<sup>2,3</sup> Geographical latitude has also been cited as a possible explanation for this variability<sup>4,5,6</sup> with increasing distance from the Equator being associated with higher blood pressure and an increased prevalence of hypertension. However, these statements are often not referenced<sup>5</sup> or refer to a post-hoc analysis of the INTERSALT study<sup>4,6</sup> published as a hypothesis paper without reporting adequate methodology to assess the validity of the results.<sup>7</sup> Other studies have suggested that blood pressure increases with distance from the Equator. However, the differences observed are either explained by factors such as salt intake<sup>8</sup> or were confounded by significant differences such as renal function, diabetes prevalence, lifestyle and diet.<sup>9,10</sup>

Humans have evolved exposed to solar radiation for most of the day. An increasing body of evidence suggests an important and positive effect of solar radiation on health and cardiovascular risk.<sup>4,11</sup> Small clinical studies on healthy and hypertensive subjects have demonstrated significant reductions in blood pressure in subjects exposed to ultraviolet radiation (UVR).<sup>6,12-14</sup> However, no studies have yet examined the association of solar radiation or UVR in a large population.

Chile is the longest country in the world: it runs almost perfectly North-South for 4250 km. In terms of latitude, the southern tip of mainland Chile is equivalent to south Alaska, with a

sub-polar climate, whereas the northern tip corresponds to the Mexican-Guatemalan border, with a dry desert climate (Figure 1). Thus the geography of Chile, together with a predominantly white and relatively genetically homogeneous population with low levels of immigration and emigration,<sup>15-17</sup> make it an ideal country to study the effect of latitude and solar radiation on human health. In this study we examined the association of geographical latitude and solar radiation with blood pressure and the prevalence of hypertension in a Chilean nationally representative sample.

## **Methods**

### ***Participants***

The 2009-2010 Chilean National Health Survey (CNHS2009/2010) is a cross-sectional survey using a multistage, stratified probability design to produce a representative sample of the Chilean population (estimated population). A total of 5,293 participants were recruited, of whom 5,069 (96%) were 18 or more years of age. Blood pressure was measured in 4,634 subjects (91.4%).<sup>18</sup> This study was approved by the ethical committee of the Pontificia Universidad Católica de Chile.

Brachial blood pressure was measured three times in the morning after 5 minutes of rest using a validated oscillometric monitor (Omron HEM 742 ®).<sup>19</sup> The average of these three readings are presented. Results were also analysed using the average of the 2<sup>nd</sup> and 3<sup>rd</sup> readings. Hypertension was defined as having a systolic blood pressure (SBP)  $\geq 140$ mm/Hg and/or a diastolic blood pressure (DBP)  $\geq 90$ mm/Hg and/or taking antihypertensive medication.<sup>20</sup>

Weight and height were measured according to the World Health Organisation recommendations.<sup>21</sup> Body mass index (BMI) was calculated using the formula of  $\text{weight(kg)/height}^2(\text{m}^2)$ . Normal BMI, overweight and obesity were defined as BMI of 18.5-24.9, 25-29.9 and  $\geq 30\text{kg/m}^2$ , respectively.<sup>21</sup> Fruit and vegetable consumption was evaluated using portion cards showing different fruit and vegetables.<sup>18</sup> Salt consumption was estimated by measuring urinary sodium excretion from a spot sample.<sup>22</sup> Educational level was classified as low (<5 years), medium (5-10 years) and high (>10 years in full-time education).<sup>23</sup> Alcohol consumption was assessed using a drinking short scale (Escala Breve de Beber Anormal, EBBA), which has been previously validated in the Chilean population. A definite alcohol excess intake is defined as an EBBA score  $\geq 2$ .<sup>24</sup>

### ***Biochemical analyses***

The four variable-modification of diet in renal disease (MDRD) equation, with serum creatinine recalibrated to be traceable to an isotope-derived mass spectroscopy method, was used to determine estimated glomerular filtration rate (eGFR).<sup>25</sup> The presence of chronic kidney disease (CKD) was defined as an eGFR of  $< 60 \text{ ml/min/1.73m}^2$ .<sup>26</sup> Blood glucose was measured the by glucose hexokinase enzymatic methodology. Glycosylated haemoglobin was evaluated by HPLC. Diabetes was defined as recommended by the American Diabetic Association (a fasting glucose  $\geq 126\text{mg/dL}$ , or a haemoglobin A1c  $\geq 6.5\%$ , or having a self-reported diagnosis of diabetes).<sup>27</sup>

### ***Geographical Latitude***

Chile is divided into three different geographical zones: North, Central and South, which in turn are divided into a total of 15 administrative regions, each with a capital city. The latitude

of the capital city was used as an index of latitude for participants living in that administrative region.

### ***Solar Radiation***

Solar radiation data was obtained from the Solar Radiation Laboratory of the Republic of Chile.<sup>28</sup> Solar radiation was measured using bimetallic actinographs (Robitzsch-Fuess Type 58dc).<sup>28</sup> Annual radiation data from all measuring stations in each administrative region were collected and averaged to show average daily regional and geographical zone solar irradiation values. Solar radiation was expressed as MJ/m<sup>2</sup>/day.

### ***Statistical Analyses***

Summary statistics results for continuous and categorical variables are presented as medians with interquartile range (25<sup>th</sup>-75<sup>th</sup> percentile) and percentages respectively.

Differences between categorical variables were compared with the Pearson- $\chi^2$  test.

Continuous variables were compared using the Kruskal-Wallis test. Linear regression was used to examine the relationships between blood pressure and geographical latitude and solar radiation. Logistic regression was used to examine the independent determinants of hypertension prevalence. All the variables used in the analyses had <5% of the values missing and were therefore treated as missing completely at random with case-wise deletion.

The two potential determinants of interest, geographical latitude and solar radiation are strongly correlated with each other, thus separate models were created to examine their associations with blood pressure and hypertension prevalence. Similarly, SBP and DBP are



strongly correlated and separate models for each variable were created. Independent variables were pre-specified for analyses based on previous studies showing a relationship with blood pressure (gender, age, BMI, fruit and vegetable consumption, eGFR, family income, smoking status, diabetes and prior CV event).<sup>29</sup> The proportion of variance explained by the adjusted models was estimated by the coefficient of Nagelkerke and the R-square to the logistic and lineal regression analysis, respectively. Age-adjusted hypertension prevalence estimates were adjusted by the direct method to the WHO World Standard population 2000-2025.<sup>30</sup> A p-value <0.05 was considered statistically significant. All statistical analyses were performed using SPSS software V21.0 (IBM, SPSS Inc, Chicago, IL).

## **Results**

The latitude limits and average solar radiation for the three geographical zones and the whole of Chile are shown in Table 1. There was a North to South decrease of solar radiation with a high inverse correlation between geographical latitude and solar radiation ( $r = -0.952$ ,  $P < .001$ ). Participant demographic characteristics of the 4,634 participants for the whole cohort and divided by geographical zone are presented in Table 2. There were proportionally more women in the central zone as well as higher fruit and vegetable consumption. Family income, educational level and eGFR were all higher in the North zone. The prevalence of current smokers was highest in the Central zone, whereas more participants in the South of the country were obese.

### ***Blood Pressure***

Both SBP and DBP significantly increased from the North to the South zone (Table 2). These relationships persisted for SBP, but not DBP, when separate analyses were performed for men and women, age <50 and  $\geq 50$  years and BMI < 25 or  $\geq 25$  kg/m<sup>2</sup> (Supplementary Figure 1).

The unadjusted and adjusted associations between SBP and DBP with geographical latitude and solar radiation are shown in Table 3 for the whole cohort. Both SBP and DBP were directly and inversely associated with geographical latitude and solar radiation in the unadjusted analyses. However, these relationships persisted only for SBP in the adjusted analyses, with DBP losing significance. The proportion of variance of SBP explained for by both these models was 38%. These associations did not change significantly, despite the use of the average of second and third measure of SBP and DBP (Supplementary Table 1).

### ***Prevalence of Hypertension***

The prevalence of hypertension in the entire cohort was 33.8% and increased from North (29.3%) to South (37.4%) ( $P < .001$ ; Table 2). This increase persisted when separate analyses were performed for men and women (Figure 2A), age <50 and  $\geq 50$  years (Figure 2B) and BMI < 25 or  $\geq 25$  kg/m<sup>2</sup> (Figure 2C).

The unadjusted and adjusted associations between the prevalence of hypertension with geographical latitude and solar radiation are shown in Table 4. Geographical latitude was positively and solar radiation inversely associated with the prevalence of hypertension in both the unadjusted and adjusted analyses. The proportion of variance of hypertension explained by both these models was 44%.

## **Discussion**

In this study we have demonstrated clear relationships between SBP and the prevalence of hypertension with geographical latitude and with solar radiation. Living further away from the Equator and being exposed to lower levels of solar radiation are associated with higher blood pressure even after adjustment for multiple factors. The prevalence of hypertension also increased with greater distance from the Equator and with reduced exposure to solar radiation.

The existence of a relationship of latitude in blood pressure is often mentioned in the literature. However, the studies quoted either do not report the methodology clearly,<sup>7</sup> or make comparisons between countries with different geographical longitude, without adequately controlling for socio-economic factors and other variables that could influence blood pressure.<sup>7,9</sup> The Chilean Health Survey is an ideal resource to investigate the associations between geographical latitude and blood pressure. Chile is the longest country in the world (4,250km), is thin (90 to 240 km wide, excluding the offshore islands) and runs almost perfectly North-South. In addition it has a relatively homogenous population with most inhabitants being descended from both the aboriginal population and European immigrants. Thus, Chile is an ideal country for a study into the effect of geographical latitude and solar radiation on health. Furthermore, the Chilean Health Survey collected data on a large number of demographic, clinical and biochemical variables known to be associated with blood pressure differences. A further strength is that the survey was conducted over a relatively short timeframe (one year) and all blood and urine tests were performed in a central laboratory.<sup>18</sup> All of these factors we believe increase the robustness of our findings.

The overall prevalence of hypertension in the Chilean Health Survey 2009-2010 was 33.8%, similar to that found in North America (USA 25.8% and Canada 23.8%).<sup>1</sup> This similarity is maintained even when we standardised the populations by age (Chile 19%, USA 16% and Canada 18%). The results suggest that the prevalence of blood pressure in Chile is not different to North America, and comparisons are feasible.

The relationship we have observed between geographical latitude and blood pressure is similar to that observed with cardiovascular disease (CVD)<sup>31</sup> and its surrogate markers such as carotid intima-media thickness.<sup>10</sup> An analysis of European populations demonstrated a higher incidence of CVD and mortality in countries further away from the Equator.<sup>31</sup> Hypertension is one of the most important risk factors for CVD, and the differences in geographical latitude and/or solar radiation might explain some of the regional variations in CVD. Differences in diet have also been postulated to contribute to the different incidence of CVD, especially in Europe. Indeed, there is a significant body of evidence that suggests that the Mediterranean diet is associated with lower cardiovascular morbidity and mortality.<sup>32</sup> However, the Mediterranean diet comes from countries closer to the Equator with higher levels of solar radiation, and may be an epiphenomenon of the geographical location and not the origin.

There is emerging evidence to suggest that the relationship between geographical latitude and blood pressure could be mediated by UVR, an important component of solar radiation (wavelength 10-400nm) with two main components: UVA (315 to 400nm) and UVB (200 to 315nm). While several clinical studies have demonstrated an acute/sub-acute effect of UVA on blood pressure reduction,<sup>6,13,14</sup> the effect of UVB on blood pressure is less clear. Whereas one study demonstrated a clear 6 mmHg decrease in SBP<sup>12</sup> another showed no difference.<sup>33</sup>

The potential mechanisms by which UVR might reduce blood pressure are not well understood. Recently, UVA radiation has been shown to release preformed cutaneous nitric oxide (NO) into the circulation<sup>4</sup> with no increase in cutaneous NO synthase activity.<sup>6</sup> In addition, Vitamin D synthesis is dependent on UVB radiation and low levels of exposure to solar radiation are associated with decreased production of vitamin D.<sup>11</sup> Low levels of calcitriol are associated with increased activation of the renin-angiotensin-aldosterone system and vascular smooth cell proliferation leading to potential increases in blood pressure. However, the actions of vitamin D on blood pressure have so far been inconclusive.<sup>34</sup> The results of the on-going VITamin D and OmegA-3 Trial (VITAL) with over 20,000 healthy participants are eagerly awaited (NCT 01169259).<sup>34</sup>

Further support for our findings comes from the seasonality of blood pressure with blood pressure being generally higher in the months with fewer hours of light.<sup>35,36</sup> However, this observation is confounded by the difference in temperature that also occurs as the seasons change, with higher temperatures being associated with lower blood pressure. Although the exact mechanism(s) are not known, activation of catecholamine synthesis by lower temperatures increasing peripheral resistance is a potential mediator.<sup>36</sup> Unfortunately we could not address this issue in our study. However, a recent study in healthy volunteers demonstrated that UVR decreased blood pressure acutely, independently of temperature.<sup>6</sup>

In this study we found that the average SBP in adults living in the North of the country was 5.3 mmHg lower than those in the South. A decline of SBP of 5-6mmHg is associated with a decrease in cardiovascular mortality of 9-13%.<sup>8</sup> Furthermore, the prevalence of hypertension was 8.1% higher in the South of the country compared with the North. These observations could have significant public health implications. Awareness of these geographical difference

in prevalence of hypertension suggest that directing resources into the diagnosis and treatment of hypertension to areas further away from the Equator could be more cost-effective. Another interesting point is the potential use of solar or UV radiation (heliotherapy or phototherapy) for the treatment of hypertension. However, this would need to be explored with caution, given that solar radiation exposure is the principal factor associated with a number of skin cancers including melanoma. Nevertheless, the overall mortality from CVD is much higher than from skin cancer. Indeed, it has been suggested that increased exposure to solar radiation could be potentially more beneficial than harmful for overall public health.<sup>6,37</sup>

Our study has a number of limitations. The cross-sectional design means that causality cannot be attributed. Nevertheless, there are biologically plausible mechanisms to explain our findings. We were also unable to adjust for the ethnic background of the population studied. However, as previously stated, the population of Chile is relatively homogeneous compared with other countries such as the USA.<sup>15</sup> Furthermore, the relationship between ethnicity and hypertension is greatly reduced once socio-economic factors such as family income are controlled for as we did in this study.<sup>38</sup>

### **Perspectives**

This work has shown that higher blood pressure and an increased prevalence of hypertension are associated with increasing distance from the Equator and reduced exposure to solar radiation. Although biologically plausible, the potential mechanisms for this relationship require further investigation. Future research should be done to prove the utility of programs for the best recognition of hypertension in regions with high geographical latitude and less

solar radiation; additionally of investigate the possibility of safely use solar or UV radiation as an adjunct to the pharmacological treatment of hypertension in the general population.

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**Table 1. Geographical Zone Characteristics**

	<b>North</b>	<b>Centre</b>	<b>South</b>	<b>Chile</b>	<b><i>P-Value</i></b>
<b>Latitude limits (degrees)</b>	17.5 to 29.1	29.1 to 8.5	38.5 to 56.5	17.5 to 56.5	
<b>Median Solar Radiation (MJ/m<sup>2</sup>/day)</b>	19.0 (18.2-19.1)	14.9 (14.8-15.2)	11.0 (10.8-12.9)	14.9 (12.8-15.3)	<.001

Results is presented as median (interquartile range) and percentage respectively. Analysis made using Kruskal-Wallis test for all groups.

Table 2. Participant Demographics and Cardiovascular risk factors.

	North (n=1,350)	Centre (n=1,678)	South (n=1,606)	All (n=4,634)	
Female (%)	61.0	62.3	58.0	60.4	.03
<b>Age groups (%)</b>					
18-24 years	11.3	11.5	11.9	11.2	.47
25-34 years	19.1	15.0	14.9	16.1	
35-44 years	17.3	19.7	18.4	18.5	
45-64 years	33.8	34.9	34.7	34.5	
>65 years	18.5	19.0	20.8	21.2	
<b>Nutritional Status</b>					
Body Mass Index (kg/m <sup>2</sup> )	27.3 (24.5-30.4)	27.0 (24.3-30.3)	28.1 (24.9-31.3)	27.4 (24.5-30.8)	<.001
Normal (%)	27.4	30.1	25.7	27.7	<.001
Overweight (%)	44.6	42.2	38.8	41.0	
Obese (%)	28.1	27.7	35.5	30.0	
Emaciated (%)	2.0	1.4	0.7	1.3	
<b>Level of Study (%)</b>					
>10 years	59.0	55.9	52.5	55.6	<.001
5-10 years	27.8	32.0	29.9	30.1	
< 5 years	10.6	9.3	14.0	11.2	
No formal education	2.5	2.7	3.6	3.0	
<b>Monthly Family Income (%)</b>					
<US\$500	50.4	55.1	58.8	55.0	<.001
US\$500-1300	31.6	31.7	29.2	30.8	
>US\$1300	12.8	9.0	9.1	10.1	
Unknown	5.1	4.2	2.9	4.0	
<b>Fruit and Vegetable Consumption</b>					
g/day	182.9 (125.7-320.0)	205.7 (125.7-320.0)	160.0 (91.4-251.4)	171.4 (114.3-320.0)	<.001
Portion/day	2.3 (1.6-4.0)	2.6 (1.6-4.0)	2.0 (1.1-3.1)	2.1 (1.4-4.0)	<.001
<b>Salt Consumption</b>					
g/day	9.9 (8.4-11.4)	9.8 (8.2-11.4)	9.6 (8.1-11.4)	9.8 (8.2-11.4)	.57
<b>Renal Function</b>					
GFR (ml/min/1.73m <sup>2</sup> )	92.8 (80.1-105.8)	87.1 (72.7-100.3)	89.0 (76.4-102.4)	89.6 (76.1-102.8)	<.001
Chronic Kidney Disease (%)	3.7	4.6	4.5	4.3	.45

<b>Sedentary Free Time (%)</b>	93.4	92.7	92.2	92.7	.46
<b>Diabetes (%)</b>	4.7	4.3	4.5	4.5	.84
<b>Actual Smoker (%)</b>	25.6	28.1	23.6	25.8	.008
<b>Problem Drinker (%)</b>	14.9	16.2	13.4	14.8	.09
<b>Blood Pressure</b>					
<b>Hypertension Prevalence (%)</b>	29.3	34.0	37.4	33.8	<.001
<b>Systolic Blood Pressure (mmHg)</b>	121.0 (109.7-135.0)	123.0 (112.7-139.0)	126.3 (113.7-143.0)	123.7 (112.0-139.3)	<.001
<b>Diastolic Blood Pressure (mmHg)</b>	74.3 (67.3-82.3)	76.0 (69.3-83.3)	76.0 (69.7-83.7)	75.3 (68.7-75.3)	<.001

Results for continuous and categorical variables are presented as median (interquartile range) and percentage respectively.

Analyses of categorical variables was made using Pearson- $\chi^2$  test. Analyses of continuous variables was made using Kruskal-Wallis test for all groups.

**Table 3. Unadjusted and adjusted associations between systolic and diastolic blood pressures with geographical latitude and solar radiation**

	Systolic Blood Pressure		Diastolic Blood Pressure	
	$\beta$ Coefficient (95% Confidence Intervals)	P-value	$\beta$ Coefficient (95% Confidence Intervals)	P-value
<b>Geographical Latitude</b>				
<b>Unadjusted</b>	0.194 (0.117, 0.271)	<.001	0.080 (0.043, 0.118)	<.001
<b>Adjusted<sup>a</sup></b>	0.109 (0.047, 0.172)	.001	0.033 (-0.003, 0.070)	.07
<b>Solar Radiation</b>				
<b>Unadjusted</b>	-0.533 (-0.744, -0.322)	<.001	-0.197 (-0.301, -0.094)	<.001
<b>Adjusted<sup>a</sup></b>	-0.276 (-0.448, -0.103)	.002	-0.067 (-0.167, 0.033)	.19

<sup>a</sup>Adjusted for sex, age, body mass index, fruit and vegetable consumption, estimated glomerular filtration rate, family income, smoking status, diabetes and previous cardiovascular event.

**Table 4. Association between the prevalence of hypertension with geographical latitude and solar radiation.**

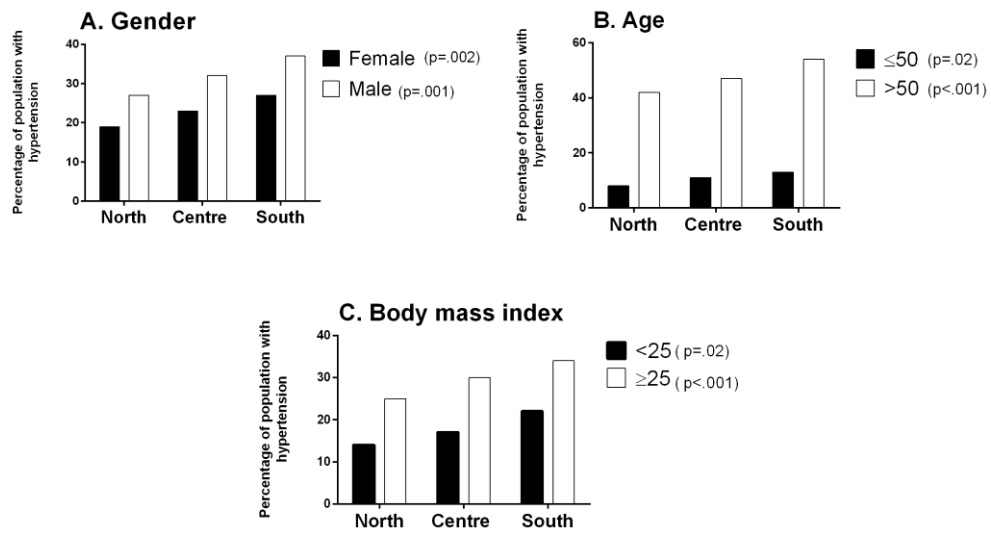
	<b>Odds Ratio (95% Confidence Intervals)</b>	<b>P-value</b>
<b>Geographical Latitude</b>		
<b>Unadjusted</b>	1.014 (1.007,1.021)	<.001
<b>Adjusted<sup>a</sup></b>	1.012 (1.002,1.021)	.02
<b>Solar Radiation</b>		
<b>Unadjusted</b>	0.963 (0.944, 0.982)	<.001
<b>Adjusted<sup>a</sup></b>	0.973 (0.949, 0.999)	.04

<sup>a</sup>Adjusted for gender, age, body mass index, fruit and vegetable consumption, estimated glomerular filtration rate, family income, smoking status, diabetes and prior cardiovascular event.

**Figure 1:** Geographical map of North America and Chile. Chile has been inverted and placed so that the southern latitude of Chile corresponds to the same northern latitude in North America. The southern tip of Chile is almost equivalent to south Alaska or north of Canada. The northern tip of Chile corresponds to southern Mexico.



**Figure 2.** Hypertension prevalence by geographic zone. Analysis according to sex, age, and body mass index.



Results are presented as percentage.  
Analyses were made using Pearson- $\chi^2$  test.  
Age is in years. Body mass Index is in  $\text{kg}/\text{m}^2$