UNIVERSIDAD SAN FRANCISCO DE QUITO USFQ

Colegio de Ciencias de la Salud

Cardiovascular Risk Assessment in Ecuadorian Elderly Population: Yield of four different models

Proyecto de investigación

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Medicina

Trabajo de titulación presentado como requisito
para la obtención del título de Médico

Quito, 15 de julio de 2017

UNIVERSIDAD SAN FRANCISCO DE QUITO USFQ
Colegio de Ciencias de la Salud

HOJA DE CALIFICACIÓN
DE TRABAJO DE TITULACIÓN

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Quito, 15 de julio de 2017

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Lugar y fecha: Quito, 15 de julio de 2017

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DEDICATION

To God, to look at me with eyes of mercy from the womb of my mother and to make me the man that I am,

To my parents and grandparents, whose unconditional support has been a *sine qua non* requirement for the fulfillment of my life goals,

To my professors, who motivate me as referents of constant self-improvement.

ABSTRACT

Objectives

The present study aims to: i) calculate the cardiovascular disease (CVD) risk profile of an Ecuadorian hypertensive elderly sample using four different models: (1) the 2003 Systematic Coronary Risk Evaluation (SCORE) risk model, (2) the 2008 Framingham Risk Score (FRS, both using lipids profile and body mass index - BMI), (3) the 2013 AHA/ACC Pooled Cohort Equations model, and (4) the 2015 SCORE for Older Population - O.P., and; ii) assess the relationship between several independent variables: (1) dependence; (2) abuse; (3) creatinine; (4) estimated glomerular filtration rate (eGFR); (5) glucose; (6) HOMA-IR index; (7) albumin; (8) thyroid stimulating hormone (TSH); (9) high-sensitivity C-reactive protein (hsCRP); and (10) vitamin D (25OHD) serum levels and predicted CVD risk in the elderly according to each of the four tested models.

Methods

This cross-sectional study analyzed the Ecuadorian National Dataset of Health, Welfare and Aging in the Elderly (SABE-ECU) conducted in 2009. From 5235 subjects belonged to the original database, a sample of 951 participants was selected after excluded missing values. We estimated the predicted 10-year risk of CVD based on the four model equations previously mentioned. In addition, logistic regression models were used to find odds ratios (OR) and corresponding 95% confidence intervals (CI) between proposed novel cardiovascular risk factors and predicted CVD risk.

Results

In 2009, one-third of the Ecuadorian hypertensive elderly population is allocated in the "high CVD risk" category according to the four equations used. In the adjusted logistic regression model, low eGFR (<60 ml/min, OR 0.23, [0.06-0.92]), low albumin serum level (<3.5 g/dl, OR 8.09, [1.63-40.04]), high HOMA-IR index (≥3.2, OR 2.01, [1.22-3.30]), and high hsCRP serum level (≥1.1 mg/L, OR 2.00, [1.12-3.58]) showed association with CVD risk when using FRS and SCORE O.P. models.

Conclusion

We found that low eGFR, high HOMA-IR index, low albumin and high hsCRP serum levels are independently and significantly associated with CVD risk in the study individuals. These laboratory variables could be included as predictor markers for CVD risk in future elder-validated scores. More studies are needed to assess the complex interaction between aging, hypertension, nutritional status, insulin resistance, inflammation, and CVD risk in the aged population.

Key words: coronary heart disease, cardiovascular risk, elderly, hypertension, kidney disease, nutritional status, insulin resistance, inflammation, predictive model, multinomial logistic regression.

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INTRODUCTION

Background

Between 2015 and 2030, the number of older persons — those aged 60 years or over — in the world is projected to grow by 56 percent, from 901 million to more than 1.4 billion [1]. With this change in demographics, the risk of age-related, non-communicable diseases will increase. Given the presence of known risk factors, it is not surprising to find metabolic syndrome (MetS) [2] and coronary heart disease (CHD) [3] within this age group, conditions which increase the relative risk to develop cardiovascular disease (CVD), a disorder that accounts for 30% of deaths worldwide [4]. In order to predict the future development of CVD, several risk scores and equations have been established [5-16]. However, most of these models were developed in middle-aged populations. It is uncertain whether risk estimates based on these scores can be generalized to the elderly. Indeed, recent work from a number of studies has shown that these conventional models, validated in middle-aged populations, perform poorly in predicting cardiovascular risk in the elderly, tending to overestimate actual risk [17, 18].

The absolute risk of vascular disease increases with advancing years, being *age* a massively recognized CVD risk factor [19]. However, the relative contribution of age and other conventional risk factors to overall CVD risk decreases in the elderly [20, 21]. Moreover, it has been proposed that traditional CVD risk factors in the old population show a phenomenon termed "reverse epidemiology" or "risk factor paradox", according to which body mass index (BMI), serum cholesterol, and blood pressure (BP) are also found to relate to CVD outcomes in the geriatric population, but in an opposite direction [22]. This fact does alter the mathematical behavior and, consequently, the logarithmic coefficients used to

predict CVD risk in the elderly when incorporating these independent factors into multivariate risk prediction equations.

A number of studies have attempted to validate existing models in older populations [23-26]. Overall, these have found the tool unsuitable for use in the majority of older adults, particularly those at lower risk. Therefore, there is a need to assess the relationship between non-classical clinical and laboratory parameters and CVD risk in the elderly population. At the moment, some of those "potential" CVD risk factors (already proposed to be related with CVD risk profile, but uncertainly explored in the elderly population yet), include: (1) dependence/frailty status [27]; (2) elder abuse [28]; (3) creatinine [29, 30]; (4) estimated glomerular filtration rate (eGFR) [31]; (5) glucose [32]; (6) HOMA-IR [33]; (7) albumin [34-36]; (8) thyroid stimulating hormone (TSH) [37-39]; (9) high-sensitivity C-reactive protein (hsCRP) [40-42]; and (10) vitamin D (25OHD, 25-hydroxivitamin D) [43, 44]. In addition, it does not exist data about the risk of CVD among the elderly population of Ecuador.

Objectives

The present study aims to: i) calculate the CVD risk in an Ecuadorian elderly sample using four different models: (1) the 2003 Systematic Coronary Risk Evaluation (SCORE) European Project CVD risk model [8], (2) the 2008 Framingham CVD risk model (FRS) [13], (3) the 2013 AHA/ACC Pooled Cohort Equations model [14], and (4) the 2015 SCORE for Older Persons - O.P. [26]; and ii) assess the relationship between several independent variables: (1) dependence/frailty status -for basic activities of daily living (BADL) determined by Katz scale [45], and for instrumental activities of daily living (IADL) determined by Lawton & Brody scale [46]; (2) elder abuse -either physical, psychological, neglect or exploitation, determined by Bass AAT- [47]; (3) creatinine; (4) estimated glomerular filtration rate (eGFR); (5) glucose; (6) HOMA-IR, (7) albumin; (8) thyroid stimulating hormone (TSH); (9)

high-sensitivity C-reactive protein (hsCRP); and (10) vitamin D and CVD risk in elderly hypertensive patients.

METHODOLOGY

Setting

The geographic setting of this study was the country of Ecuador, located in South America. In 2009, the Ecuadorian government conducted a national survey, entitled *Encuesta sobre Salud, Bienestar y Envejecimiento* (SABE-ECU – Survey of Health, Wellbeing and Aging), to investigate the health and well-being of elderly people, based on a representative sample (n= 5235) of persons aged from 60 years and over [48]. The modules included in the survey were demographic and household characteristics; self-reported health and chronic conditions; anthropometric measures; mobility status, abuse and cognitive states; use and access of health services; medication use; family and social support, and labor force and retirement.

Study Design, Participants and Data Sources

This cross-sectional study analyzed the national dataset of Health, Welfare and Aging in Ecuadorian elderly population conducted during 2009 [48]. Participants included in this study were man and women older than 60 years of age, living in urban and rural areas of the coast and highlands of Ecuador. The model under which the representative sample for the study was selected included a probabilistic and two-stage design, proportional to the size of the existing elderly Ecuadorian population according to the final data and mapping of the VI Census of Population and V Census of Housing, held in November 2001. Overall, 5235 subjects belonged to the original database, but 4284 subjects were progressively excluded due to missing values (Figure #1).

Testing Instruments

This study applied two elder-validated scales to evaluate dependence status. The Katz Basic Activities of Daily Living Scale (BADL) consists of six items (bathing, dressing, toileting,

transferring, continence, and feeding), hierarchically ordered according to the sequence in which patients lose and regain independence to perform them [45]. The scale assigns each item one point if done independently by the subject or with little assistance, or zero points if required a great help to be done or directly not realized. According to the total score, patients are classified into seven groups, where A is the maximum independency and G at the maximum dependency. In the present study, a summary score of zero was considered to be *independency*, with any other value allocated as *dependency*.

The Lawton Instrumental Activities of Daily Living Scale (IADL) is an appropriate instrument to assess independent living skills, measuring eight domains of functional status (using the telephone, shopping, preparing food, housekeeping, doing laundry, using transportation, handling medications, and handling finances) [46]. Women are scored on all 8 areas of function; historically, for men, the areas of food preparation, housekeeping, laundering were excluded. However, current recommendations are to assess all domains for both genders [49]. In the present study, all individuals were scored according to their highest level of functioning in each category, with a summary score of 8 considered *independency* and any other value catalogued as *dependency*.

In addition, an elder-validated questionnaire was used to assess physical-psychological abuse, as well as neglect and exploitation. The Bass Actual Abuse Tool (AAT) provides a list of the major forms of abuse and violence, with a single check already indicating domestic maltreatment [47]. In the present study, the existence of one or more of the indicators from the AAT list was already considered elder abuse.

Estimated glomerular filtration rate (eGFR) was calculated using the validated Modification of Diet in Renal Disease (MDRD) equation (see *Appendix C*) [59]. Insulin resistance was quantified applying the well-known Homeostatic Model Assessment (HOMA) index [92].

Finally, four different equations to calculate CVD risk in the elderly were used: (1) the 2003 SCORE European Project CVD risk model [8], (2) the 2008 Framingham CVD risk score (FRS, with both sub-equations using the lipids profile or BMI) [13], (3) the 2013 AHA/ACC Pooled Cohort Equations model [14], and (4) the 2015 SCORE for Older Population – O.P. model [26]. In general, these models are derived multivariable mathematical functions that assign weights to major CVD risk factors such as sex, age, race, blood pressure, total cholesterol, high-density lipoprotein cholesterol, smoking behavior, and diabetes status, to produce a probability estimate of developing CHD within a certain period (e.g., the next 10 years). However, many features differentiate each one of the equations. FRS was developed based on a population 30-74 years old [13], while SCORE model was applied for 19-80 years old patients [8]. The 2013 ACC/AHA model pooled several cohorts with 40-79 years old subjects, and includes "race" as risk factor [14]. The "high risk" threshold for FRS and 2013 AHA/ACC models is 20% [14], whereas for SCORE model is only 5% [8]. Additionally, FRS model is only intended to predict CHD risk [13], whilst 2003 SCORE model prognosticates total-CVD risk (particularly fatal events occurrence probability) [8]. The 2015 SCORE for Older Persons – O.P. is an adaptation proposed by Cooney et al. intended to provide improved accuracy in total-CVD risk estimation than original SCORE in old patients [26]. The 2013 ACC/AHA model predicts atherosclerotic cardiovascular disease (ASCVD), defined as coronary death or nonfatal myocardial infarction, or fatal or nonfatal stroke [14].

Variables and Statistical Analysis

Descriptive statistics were used to characterize the demographic and CVD risk (low-moderate vs. high) data retrieved from the study participants. Continuous variables are described as mean ± standard deviation (SD), and categorical variables as counts and percentages. To
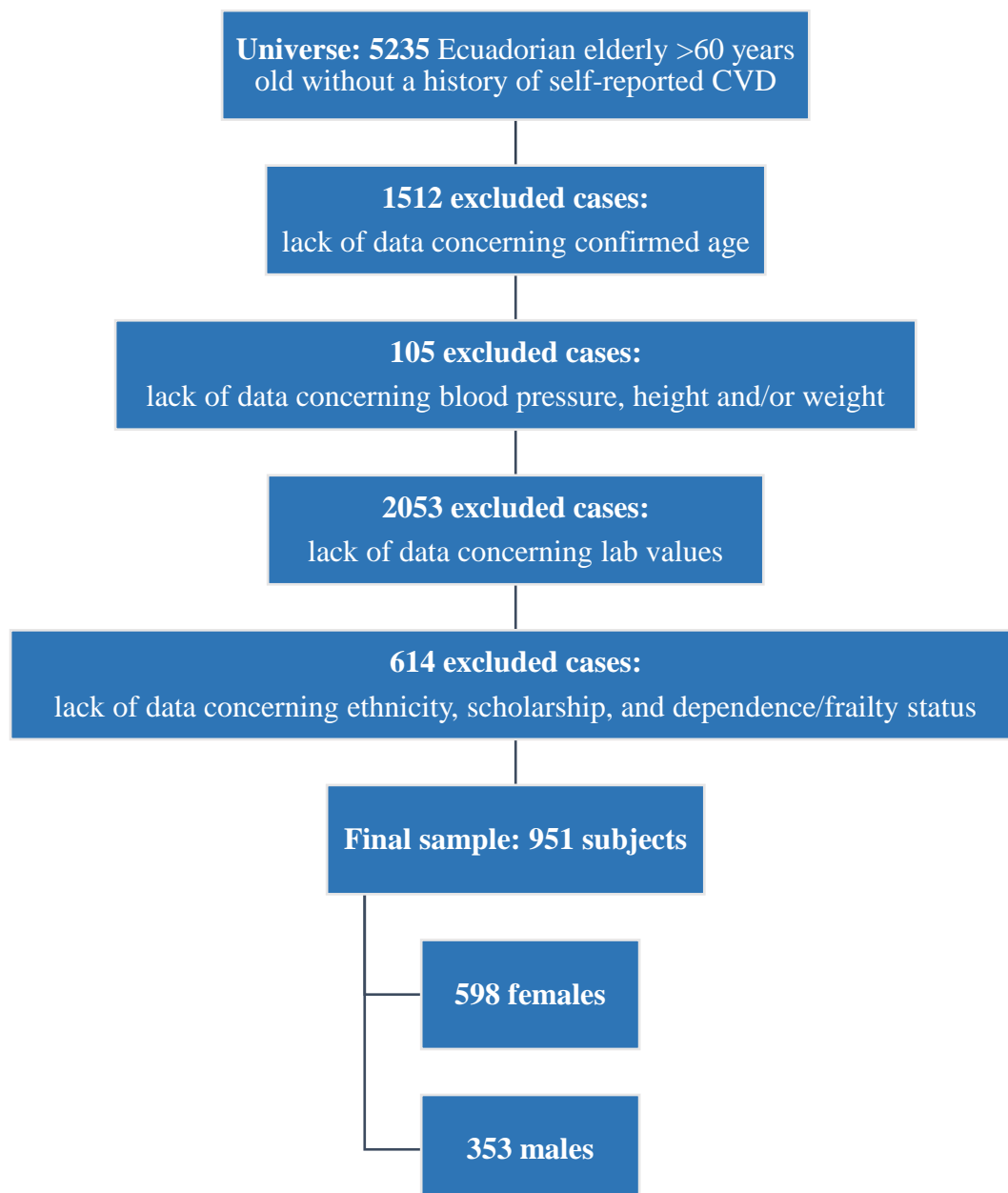
predict the 10-year risk of developing CVD in this elderly population we used the four model equations and regression coefficients as described in the *Appendix A*. Unless otherwise specified, we used a knowledge of prior studies and univariate screen (Chi Square test, independent sample t-test or Fisher's exact test, as appropriate) approach at a level of p-value <0.05 to identify the potential independent variables to be included in the adjusted model.

Multinomial logistic regression was used to quantify the odds ratios (OR) and corresponding 95% confidence intervals (CI) between proposed independent variables and CVD risk according to each of the four used model equations. When necessary, laboratory continuous variables were transformed to categorical variables according to most widespread Merck Manual cut-offs [50]. Results with statistical significance were those with a p-value less than 0.05. The software used was SPSS 22.0 Software Statistics Platform.

RESULTS

This cross-sectional study analyzed information from the SABE-ECU national dataset. All SABE-ECU participants aged 60 years and older without a history of self-reported CVD were studied. The final study population consisted of 951 subjects (Figure #1).

Figure #1: Flowchart describing selection of subjects and final sample of the study.

Universe: 5235 Ecuadorian elderly >60 years old without a history of self-reported CVD

1512 excluded cases:
lack of data concerning confirmed age

105 excluded cases:
lack of data concerning blood pressure, height and/or weight

2053 excluded cases:
lack of data concerning lab values

614 excluded cases:
lack of data concerning ethnicity, scholarship, and dependence/frailty status

Final sample: 951 subjects

598 females

353 males

In the univariate analysis, we found differences between gender and place of residence, education level, dependence status (both for BADL and IADL), elder abuse, antihypertensive treatment, smoking status, prior diabetes mellitus diagnosis, creatinine, glucose, HOMA-IR, hsCRP, and vitamin D serum levels of the subjects (Table #1). The percentages of dependency according to Katz BADL scale and Lawton IADL scale found in the sample are considerable, with 313 (32.9%) being dependent for BADL and 372 (39.1%) being dependent for IADL.

Moreover, the distribution of elder abuse in the study population was as follow: 90 (9.5%) suffer physical abuse, 209 (22%) endure psychological abuse, 101 (10.6%) bear exploitation, and 78 (8.2%) withstand neglect by other, with a final prevalence of 277 (29.1%) individuals suffering some form of abuse, exploitation and/or neglect. Finally, despite all the participants of the sample were previously diagnosed with hypertension, 391 (41.8%) of the subjects did not receive appropriate antihypertensive therapy.

Descriptive statistics regarding general CVD risk profile of the elderly Ecuadorian population according to all four tested CVD risk models can be found in Figure #2. Briefly, each one of the four tested CVD risk equations found different results. This phenomenon can be partially justified by the fact that, although all the four equations used have many variables in common, the outcome predicted by each one is slightly different (see *Methodology*, section *Tested Instruments*).

Our results show that: (1) sixty nine percentage (when using FRS with lipids) and ~76% (when using FRS with BMI) of the Ecuadorian elderly population is at high 10-year risk of developing coronary heart disease (CHD); (2) 36.9% (when using SCORE) and 58.8% (when using SCORE O.P.) of the population is at high total-CVD risk; and (3) according to AHA/ACC model, approximately 59.7% of the old adults in Ecuador is at high 10-year risk of suffering atherosclerotic cardiovascular disease (ASCVD).

Each one of the selected independent variables, with respective odds ratios (OR) and confidence intervals of 95% (CI 95%) for both unadjusted and adjusted multinomial logistic regression models, are showed in Table #2. There are several interesting findings derived from this statistical analysis. First, there were many variables not usually related to CVD risk found in this model to be significant:

(1) place of residency for AHA/ACC equation (*rural* as protective factor);

(2) education level for FRS using lipids equation (*High school or higher* as protective factor);

(3) Lawton scale for AHA/ACC and SCORE O.P. equations (*dependent for IADV* as risk factor);

(4) Bass Scale for FRS using BMI equation (*elder abuse* as risk factor);

(5) creatinine serum level for all four CVD risk equations (*≥1.3 mg/dl* as risk factor);

(6) eGFR for FRS using BMI, SCORE, AHA/ACC, and SCORE O.P. equations (*≥60 ml/min* as protective factor);

(7) glucose serum level for FRS using lipids, using BMI and AHA/ACC equations (*≥126 mg/dl* as risk factor);

(8) albumin for FRS using BMI equation (*<3.5 g/dl* as risk factor);

(9) HOMA-IR for FRS using lipids, SCORE, and SCORE O.P. equations (*≥3.2* as risk factor); and

(10)   hsCRP for FRS using lipids equation (*≥1.1 mg/dl* as risk factor).

Second, of all these variables found to be related to CVD risk through unadjusted analysis, only four of them showed statistical significance when examined with the multinomial logistic regression model adjusted for covariates:

(1) eGFR for SCORE O.P. equation (*≥60 ml/min* as protective factor);

(2) albumin for FRS using BMI equation (*<3.5 g/dl* as risk factor);

(3) HOMA-IR for FRS using lipids equation (≥*3.2* as risk factor); and

(4) hsCRP for Framingham using lipids equation (≥*1.1* mg/dl as risk factor).

Therefore, might be interesting to include each of these variables into its corresponding CVD risk equation, in order to predict an accurate CVD risk in elderly patients and perhaps a novel equation can be proposed incorporating these variables.

Third, there were some variables not associated at all with CVD risk (not even in the multinomial logistic regression unadjusted model):

(1) ethnicity,

(2) living alone status,

(3) Dependence status for BADV according to Katz scale,

(4) TSH serum level, and

(5) vitamin D serum level

Interestingly, although 2013 AHA/ACC model uses "ethnicity" as a "breaking point" to classify subjects into Afro-American and non-Afro-American categories, when applied to our population, this equation did not correlate with significant p-values for this independent variable.

Variables	Gender		p-value
	Female (n=598)	Male (n=353)	
Age (Mean ± SD), years	71.22 ± 8.195		0.845**
Age (categories)			
≤70 years old	322 (53.8%)	184 (52.1%)	
71-80 years old	183 (30.6%)	110 (31.2%)	0.846*
> 80 years old	93 (15.6%)	59 (16.7%)	
Place of residence			
Urban	451 (75.4%)	227 (64.3%)	<0.001*
Rural	147 (24.6%)	126 (35.7%)	
Ethnicity			
Indigenous/Native	28 (4.7%)	26 (7.4%)	
Afro-American	18 (3.0%)	14 (4.0%)	
Mixed	414 (69.2%)	244 (69.1%)	0.304*
White	74 (12.4%)	39 (11%)	
Other	64 (10.7%)	30 (8.5%)	
Education level			
None/Primary	367 (81.4%)	250 (83.9%)	
Secondary/Technical	68 (15.1%)	27 (9.1%)	0.01*
College/Postgraduate	15 (3.3%)	21 (7.0%)	
Living alone/accompanied			
Alone	55 (9.2%)	32 (9.1%)	0.946*
Accompanied	543 (90.8%)	321 (90.9%)	
Dependence status for BADL (Katz) α			
0 (independence)	367 (61.4%)	271 (76.8%)	<0.001*
≥1 (dependence)	231 (38.6%)	82 (23.2%)	
Dependence status for IADL (Lawton) β			
8 (independence)	322 (53.8%)	257 (72.8%)	<0.001*
<8 (dependence)	276 (46.2%)	96 (27.2%)	
Elder abuse (AAT) γ			
Yes	191 (31.9%)	86 (24.4%)	0.01*
No	407 (68.1%)	267 (75.6%)	
Hypertension previously diagnosed			
Yes	598 (100%)	353 (100%)	N/A
No	0 (0%)	0 (0%)	
Antihypertensive treatment			
Yes	371 (62%)	189 (53.5%)	0.01*
No	227 (38%)	164 (46.5%)	
Smoking status			
Never	500 (83.6%)	97 (27.5%)	
Former	85 (14.2%)	204 (57.8%)	<0.001*
Current	12 (2%)	51 (14.4%)	
Diabetes mellitus previously diagnosed			
Yes	134 (22.4%)	55 (15.6%)	0.01*
No	464 (77.6%)	298 (84.4%)	
Creatinine (Mean ± SD), mg/dl	0.8795 ± 0.4188		<0.001**
Creatinine categories (mg/dl)			
≤1.3	581 (97.2%)	319 (90.4%)	<0.001*
>1.3	17 (2.8%)	34 (9.6%)	
eGFR (ml/min/1.73m²)μ			
<15	4 (0.7%)	0 (0%)	
15-29.9	7 (1.2%)	5 (1.4%)	
30-59.9	64 (10.7%)	40 (11.3%)	0.712***
60-89.9	293 (49%)	169 (47.9%)	
≥90	230 (38.5%)	139 (39.4%)	
Glucose (Mean ± SD), mg/dl	113.77 ± 45.495		<0.001**
Glucose categories (mg/dl)			
<126	481 (80.4%)	308 (87.3%)	0.007*
≥126	117 (19.6%)	45 (12.7%)	
HOMA-IR			
<3.2	318 (53.2%)	261 (73.9%)	<0.001*
≥3.2	280 (46.8%)	92 (26.1%)	
Albumin (g/dl)			
<3.5 (low)	8 (1.3%)	10 (2.8%)	0.102*
≥3.5 (normal)	590 (98.7%)	343 (97.2%)	
TSH mIU/L			
<5 (low-normal)	382 (63.9%)	206 (58.4%)	0.09*
≥5 (high)	216 (36.1%)	147 (41.6%)	
hsCRP (Mean ± SD), mg/L	5.52 ± 9.67		0.942**
hsCRP categories (mg/L)			
<1.1 (normal)	108 (18.1%)	97 (27.5%)	0.001*
≥1.1 (high)	490 (81.9%)	256 (72.5%)	
Vitamin D (Mean ± SD), ng/ml	26.246 ± 10.65		<0.001**
Vitamin D categories (ng/ml)π			
<15 (low)	63 (10.5%)	15 (4.2%)	0.001*
≥15 (normal)	535 (89.5%)	338 (95.8%)	

Table #1. Baseline characteristics of the sample.

*p-value found using chi-square test.

**p-value found using independent samples t-test

***p-value found using Fischer's exact test.

α Dependence for basic activities of daily living (BADL) using Katz scale [42].

β Dependence for instrumental activities of daily living (IADL) using Lawton scale [43].

γ Elder abuse using Bass Actual Abuse Tool (AAT) [44].

μ Estimated glomerular filtration rate (eGFR) calculated using MDRD formula [48].

π Vitamin D measured in serum as 25-hydroxyvitamin D (25OHD).

N/A p-value could not be calculated because all the cases were positive for only one possible option (everybody in the sample has been previously diagnosed with hypertension).

Figure #2. Comparison of cardiovascular risk categories among the 2003 SCORE model, the 2008 Framingham Risk Score (FRS) using lipids and BMI equations, the 2013 AHA/ACC model, and the 2015 SCORE O.P. model.*
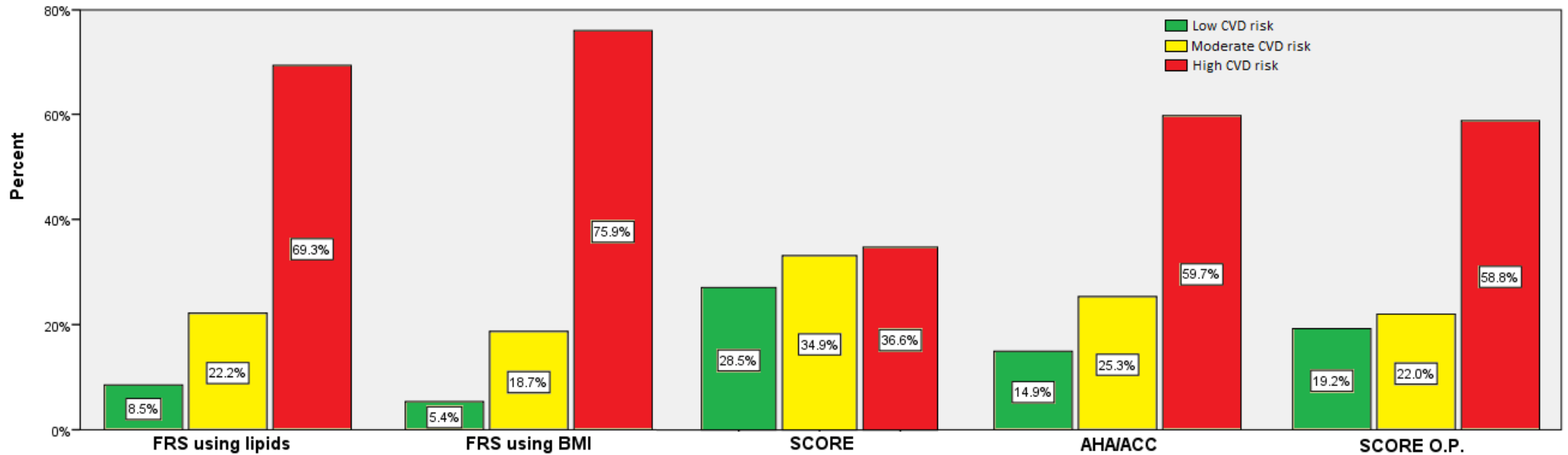
The y-axis reflect percentage of individuals. To compute both SCORE and SCORE O.P. European Project CVD risk models, Ecuador was assumed to be a "high CVD risk European land", and that schema was used in the equation codification for SPSS (see Appendix A). The cut-off point between low, moderate and high CVD risk was determined, respectively, to be <10%, 10-20%, >20% for FRS and 2013 AHA/ACC models; and <1%, 1-5%, >5% for SCORE model; and <5%, 5-10%, >10% for SCORE O.P. model, agreeing with the references [7, 12, 13, 49].

Table #2. Odds Ratios between significant independent variables and the general CVD risk according to each of the four tested equations.*

Tested Equation[β]	10-year Framingham CVD risk model (using lipids profile)		10-year Framingham CVD risk model (using BMI)		SCORE European Project CVD risk model[α]		2013 AHA/ACC ASCVD risk Pooled Cohort Equations model		SCORE O.P.	
Variables	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Place of residency (rural/urban)	0.75 (0.56-1.01)	1.11 (0.63-1.93)	0.79 (0.58-1.1)	0.78 (0.42-1.46)	0.81 (0.59-1.08)	0.65 (0.38-1.11)	**0.74 (0.56-0.99)**	0.65 (0.34-1.24)	0.93 (0.7-1.24)	0.72 (0.29-1.79)
Ethnicity (Afro-American/Non-Afro-American)	1.13 (0.52-2.49)	0.87 (0.28-2.77)	1.39 (0.56-3.42)	0.87 (0.25-3.09)	1.36 (0.67-2.77)	0.86 (0.29-2.58)	1.13 (0.55-2.35)	2.44 (0.52-11.31)	1.18 (0.57-2.43)	*0.93 (0.10-8.64)*
Education level (High-school or higher/Primary or less)	**0.73 (0.55-0.97)**	0.69 (0.47-1.02)	0.83 (0.61-1.13)	0.81 (0.52-1.26)	0.94 (0.71-1.24)	0.92 (0.62-1.36)	0.89 (0.68-1.16)	0.82 (0.51-1.31)	0.98 (0.74-1.28)	0.87 (0.45-1.67)
Living alone status (yes/no)	0.90 (0.55-1.47)	0.71 (0.34-1.49)	0.81 (0.47-1.39)	0.69 (0.29-1.59)	0.76 (0.49-1.19)	0.83 (0.39-1.74)	0.81 (0.51-1.27)	0.68 (0.29-1.57)	0.86 (0.55-1.35)	0.83 (0.24-2.88)
Katz scale (dependent/non-dependent)	0.96 (0.72-1.28)	1.10 (0.69-1.75)	0.98 (0.72-1.35)	1.14 (0.68-1.93)	1.01 (0.76-1.34)	1.29 (0.81-2.08)	1.09 (0.83-1.44)	0.81 (0.47-1.41)	1.15 (0.87-1.51)	0.66 (0.31-1.44)
Lawton scale (dependent/non-dependent)	0.98 (0.74-1.31)	0.92 (0.57-1.47)	1.06 (0.78-1.45)	0.84 (0.49-1.43)	1.21 (0.92-1.58)	0.77 (0.47-1.29)	**1.6 (1.22-2.09)**	0.81 (0.46-1.44)	**1.97 (1.50-2.59)**	0.52 (0.22-1.22)
Elder abuse (non-abused/ abused)	0.75 (0.56-1.02)	0.94 (0.58-1.51)	**0.66 (0.48-0.91)**	0.65 (0.38-1.12)	1.11 (0.83-1.48)	1.22 (0.76-1.95)	0.83 (0.62-1.09)	1.08 (0.6-1.94)	0.92 (0.69-1.23)	0.77 (0.34-1.76)
Creatinine (mg/dl) (≥1.3/<1.3)	**4.31, (1.69-10.96)**	0.99 (0.28-3.44)	**5.37 (1.66-17.39)**	0.68 (0.15-3.09)	**2.21 (1.25-3.9)**	1.24 (0.54-2.83)	**3.86 (1.79-8.3)**	1.79 (0.51-6.35)	**3.02 (1.5-6.11)**	1.44 (0.32-6.59)
eGFR (ml/min/1.73m2) (≥60/<60)	0.65 (0.42-1.02)	0.84 (0.38-1.84)	**0.52 (0.31-0.88)**	0.83 (0.32-2.14)	**0.57 (0.39-0.84)**	1.22 (0.57-2.62)	**0.41 (0.26-0.63)**	0.49 (0.18-1.31)	**0.32 (0.19-0.50)**	**0.23 (0.06-0.92)**
Glucose (mg/dl) (≥126/<126)	**2.96 (1.87-4.68)**	1.62 (0.76-3.45)	**1.91 (1.21-3.01)**	0.81 (0.34-1.91)	0.76 (0.53-1.09)	1.51 (0.71-3.22)	**1.59 (1.11-2.28)**	1.98 (0.78-5.02)	1.16 (0.82-1.64)	1.84 (0.52-6.47)
Albumin (g/dl) (<3.5/≥3.5)	0.87 (0.31-2.45)	2.16 (0.49-9.56)	1.22 (0.43-3.45)	**8.09 (1.63-40.04)**	1.51 (0.53-4.28)	2.24 (0.24-21.43)	1.19 (0.46-3.03)	0.81 (0.15-4.31)	1.42 (0.57-3.65)	0.82 (0.03-20.41)
TSH (mIU/L) (<5/≥5)	1.05 (0.79-1.4)	1.34 (0.85-2.09)	0.94 (0.69-1.27)	1.18 (0.71-1.96)	1.26 (0.96-1.65)	1.29 (0.84-1.99)	1.07 (0.82-1.39)	1.28 (0.75-2.18)	1.01 (0.78-1.32)	0.76 (0.35-1.64)
HOMA-IR (≥3.2/<3.2)	1.14 (0.86-1.51)	**2.01 (1.22-3.30)**	0.84 (0.62-1.13)	1.61 (0.92-2.80)	**0.59 (0.45-0.78)**	0.99 (0.61-1.64)	0.84 (0.64-1.09)	1.50 (0.83-2.71)	**0.73 (0.56-0.94)**	0.93 (0.41-2.12)
hsCRP (mg/L) (≥1.1/<1.1)	1.19 (0.86-1.65)	**2.00 (1.12-3.58)**	0.86 (0.59-1.24)	1.06 (0.55-2.06)	1.28 (0.92-1.78)	1.61 (0.96-2.70)	0.98 (0.72-1.34)	1.24 (0.67-2.33)	0.96 (0.70-1.32)	1.26 (0.49-3.21)
Vitamin D (ng/ml) (<15/≥15)	1.07 (0.65-1.76)	0.62 (0.30-1.28)	1.09 (0.64-1.86)	0.99 (0.43-2.31)	0.82 (0.51-1.31)	0.58 (0.28-1.23)	0.77 (0.47-1.24)	0.74 (0.29-1.89)	0.74 (0.45-1.19)	1.35 (0.34-5.41)

*p-value, OR and IC 95% were found using several multinomial logistic regressions for each variable and adjusted or unadjusted for sex and the remaining significant variables (see Methodology). Significant p-values are depicted in bold, those of interest for the lector in red (found to be significant in the adjusted model). The reference category for the dependent variable is always high CVD risk/low-moderate CVD risk.

DISCUSSION

General CVD risk profile of the Elderly Ecuadorian Population

The predicted CVD risk profile of the elderly Ecuadorian population varies widely depending on the equation model used. As mentioned before, this phenomenon can be partially justified by the fact that, although all the four equations used have many variables in common, the outcome predicted by each one is slightly different (see *Methodology*, section *Tested Instruments*). However, one-third of this population is allocated in the "high CVD risk" category. A similar proportion of elders endures some form of dependence/frailty (either for BADL or IADL) and suffers abuse, exploitation and/or neglect.

Demographics, Dependence Status, Elder Abuse and CVD risk

In relation with our results, place of residency (urban/rural) and education level (primary or less/high-school or higher) were the only demographic variables found to be significantly related to CVD risk. Living in urban areas was found to be a CVD risk factor. This relationship could be explained by the fact that there are significant differences for anthropometric, metabolic, and blood pressure variables between rural and urban areas [51-53]. As proposed by Das et al. (2008), living in urban/rural areas has a significant impact on central adiposity, lipid serum profile, lipoproteins, and blood pressure measures even after adjusted for age and sex [51]. In terms of education level, elderly who have completed only primary education or less were found to be statistically at higher 10-year CVD risk when compared with those with higher schooling. This finding could be attributed to the fact that people with higher education have a better capacity to understand their comorbidities, as well as the seriousness of their health-disease condition, being more empowered of their situation

and more capable of taking preventive measures to lower their CVD risk. So far, this is the first study to describe that association.

Dependence status only for IADL (not for BADL) predicted by Lawton & Brody scale did correlate well with ASCVD risk when applying 2013 AHA/ACC model. Being dependent was found to be a significant CVD risk factor. In fact, this is the first study trying to correlate dependence status measured by Katz and Lawton scales with CVD risk, since most existing studies evaluate frailty and pre-frailty using Fried phenotype instead of Katz and Lawton ADL scales [27, 54-56].

In the context of elder abuse, the International Network for the Prevention of Elder Abuse (INPEA) 2008 report of Elder Abuse in the Family in Spain, [57] found a prevalence of 10.5% for CVD in abuse victims, without testing the existence of a statistically significant relationship between both factors. A previous study found that elder abuse is associated with increased risk for metabolic syndromes, especially for those subjects who were younger elders, female, and had higher BMI [58]. To the present, our study is the first aimed to seek for a relationship between elder abuse (assessed by Bass AAT) and CVD risk, and found a predictable association when applying FRS using BMI equation. However, the potential causal mechanisms and temporal relations between specific subtypes of elder abuse and CVD risk are still not clearly understood, and require exhaustive cohort investigation.

Low eGFR and CVD risk

Four laboratory clinical measures were found to be significantly linked with CVD risk in multinomial logistic regression adjusted model. High eGFR (≥60 ml/min, measured with MDMR equation [59]) was found to be a protective factor for CVD risk predicted by SCORE O.P. equation, suggesting its potential usefulness to be included in elderly-modified versions of original SCORE model. Many plausible studies and pathophysiologic mechanism have

tried to sustain the relationship between low eGFR and CVD risk. According to Ghonemy et al. (2016), the increased inflammation and oxidative stress, which have an important role in the pathophysiology of coronary artery disease progression, could be associated with poorer renal function [60]. In addition, renal dysfunction may be associated with multiple other physiological changes, including high levels of hypercalcemia, hyperuricemia, homocysteine, anemia, and uremia, all of which have detrimental cardiovascular effects [60, 61]. Elevated asymmetric dimethyl arginine, reduced nitric oxide bioavailability, and endothelial dysfunction in kidney disease, which are associated with atherosclerosis, are also defined as factors linking impaired kidney function and CVD risk [61]. Additionally, in patients with chronic kidney disease (CKD), the renin-angiotensin and the sympathetic nervous systems are over stimulated and result in the increased production of superoxide, interleukin 6, and other pro-inflammatory cytokines. In addition, the activity of renalase, an enzyme produced by the kidneys that inactivates catecholamines, is decreased in patients with CKD [62].

Certainly, patients with end-stage renal failure have greatly accelerated vascular disease and a high cardiac risk [60-63]. Consistently with results derived from this study, it has been already suggested that, given the effects of vascular disease on kidney function, it may serve as an essential indicator of vascular health [63].

Low albumin serum level and CVD risk

Although the relationship between low albumin levels and CVD risk is not completely understood, several mechanism have been proposed. Hypoalbuminemia has been attributed to a variety of factors, including exogenous albumin loss, albumin distribution, catabolism rate of proteins, and the presence of inflammatory cytokines. Serum albumin concentrations are associated with increased inflammatory burden in the body. Inflammation has been associated with decreasing albumin synthesis rate and increasing catabolism [64].

Experimental studies have suggested that high IL-6 and TNF-α levels, usually found in patients with low albumin levels, are associated with left ventricular remodeling, fetal gene expression, myocyte hypertrophy, and myocyte apoptosis [65].

Another alternative explanation for albumin and CVD risk correlation is that comorbidities associated with development of CVD are also associated with worsening serum albumin profile (such as, for example, kidney disease). However, the multinomial logistic regression models proposed in this study have carefully assessed many possible confounding variables, which could potentially influence the association. In fact, controlling for all such predictors through an adjusted analysis did not change the association. These observations suggest an interesting role for serum albumin as a strong surrogate marker for CVD risk in the elderly, a marker that possibly integrates both known and unexplored pathways. Further insights are needed into anti-thrombotic, and anti-oxidant - oxidative stress mechanisms (due to the nitric oxide reservoir capabilities of albumin) [66], in order to fully characterize this association.

High HOMA index, Insulin Resistance, Metabolic Syndrome and CVD risk

The present study also found a statistically significant relationship between high HOMA-IR index (indicating insulin resistance) and CVD risk. Although establishing the pathophysiologic pathways linking insulin resistance to CVD is beyond the scope of the present study, it seems not out of place to mention that a number of mechanisms were identified through which an impaired insulin sensitivity could result in atherosclerosis. These mechanisms include the anti-aggregating platelet effect of insulin [67], the effect of the hormone on nitric oxide release from the endothelium [68], the inhibition by insulin of migration of vascular smooth muscle cells [69], and the inhibitory effect of the hormone on

fibrinogen synthesis [70]. These potentially anti-atherogenic properties of insulin seem to be impaired in insulin-resistant states, and this might contribute to explain our results.

On the other hand, many studies demonstrated that hyperinsulinemia, which generally coexists with insulin resistance, might promote atherosclerosis and CVD risk, through a potentially pro-atherogenic effect. The hormone enhances LDL cholesterol susceptibility to oxidation [71], promotes plasminogen activator inhibitor 1 [72] and endothelin-1 [73] release by several cells, and stimulates connective matrix and cholesterol synthesis and LDL receptor expression in the arterial wall [74]. Therefore, it can be suggested that the increased CVD risk observed in insulin-resistant states could stem from the perverse combination of the deficiency of anti-atherogenic effects of insulin, on the one side, and the presence of pro-atherogenic effects of hyperinsulinemia on the other side. This hypothesis defines insulin resistance as a "selective phenomenon" that *differently* impairs multiple endocrine pathways, which finally enhance CVD risk. Such observation could also explain the finding that HOMA-IR index, for some equations, showed OR in the protective range (when applying SCORE and SCORE O.P.), whereas for other models showed OR in the risk range (when applying FRS with lipids).

High hsCRP serum level and CVD risk

High hsCRP serum levels also demonstrated statistically significant relationship with CHD risk predicted by FRS using lipids equation, being another potential independent CVD risk factor to be incorporated in that model. There are many large studies that have linked high hsCRP serum levels with CVD risk, including the Physicians Heart Study (PHS) [75], the Texas Coronary Atherosclerosis Prevention Study (CAPS) [76], the Women's Health Initiative (WHI) [77], the Women's Health Study (WHS) [78], the Cardiovascular Health Study (CHS) [79], the Framingham Heart Study (FHS) [80], and the Prospective Study of

Pravastatin in the Elderly at Risk (PROSPER) [81]. On the other hand, various other trials failed to find those significant associations, including the Multiple Risk Factor Intervention Trial (MRFIT) [82], the Québec Cardiovascular Study [83], the Rotterdam Study [84], and the Nurses' Health Study (NHS) [85]. Based on evidence that has accrued, hsCRP serum measurement has been integrated into the Reynolds risk score (RRS) [11, 12], which has not been validated in the elderly population yet, but could eventually constitute a reliable alternative for old patients [86].

In the context of the elderly population, the findings are still controversial. Jalal et al (2012) demonstrated that high hsCRP levels provide prognostic CVD risk information in elderly patients with chronic kidney disease (CKD) [41]. In the PROSPER (Prospective Study of Pravastatin in the Elderly at Risk) analysis of 5,804 elderly individuals, hsCRP levels minimally enhanced risk prediction (3.64 mg/l in those who had a CV event vs. 3.01 mg/l in those who remained event free) [81]. Halil et al (2008), in an extensive analysis aimed to investigate the link between CHD risk determined by FRS and serum levels of ferritin, CRP, homocysteine, creatinine, and uric acid, did not find any significance for CRP [87].

There are many other immunological-mediated proposed mechanisms to justify CRP and CVD risk association [88]. Zwaka et al. (2001) concluded that foam cell formation in human atherogenesis might be caused in part by uptake of CRP-opsonized native LDL [89]. Calabro et al. (2005) demonstrated in-vitro production of CRP by adipocytes isolated from human adipose tissue in response to inflammatory cytokines (IL-1-beta, IL-6, and resistin), thereby suggesting a new link between obesity and vascular inflammation [90]. More recently, Devaraj et al. (2011) provided data that CRP, via nitric oxide deficiency, promotes endothelial dysfunction by inducing release of circulating endothelial cells and endothelial micro particles, which are biomarkers of endothelial dysfunction [91].

Strengths and Limitations

This study has several strengths. We used a risk estimation model validated for older men and women (SCORE O.P). Hence, overestimation of CVD risk is less likely to have occurred compared to the other risk-assessment models used in the analysis. Our study used data from a national survey that is representative of the Ecuadorian elderly population, which maximizing its external validity.

On the other hand, this research was limited by its cross-sectional design, thus making impossible to propose a new mathematical model for predicting CVD risk in the elderly by monitoring occurrence of new CVD fatal and non-fatal cases over time. Also, all subjects included in the sample were previously diagnosed with hypertension, leaving concerns about the influence of proposed CVD risk factors in non-hypertensive elderly patients.

CONCLUSIONS

In summary, one-third of the Ecuadorian elderly population is allocated in the "high CVD risk" category. Four laboratory measures (eGFR, HOMA-IR index, albumin, and hsCRP serum levels) were independently correlated with CVD risk in hypertensive elderly patients when using FRS and SCORE O.P. models. The inclusion of these laboratory tests as predictor variables to estimate future CVD events might be useful.

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APPENDIX A: SPSS STATISTICS INFORMATICS

The following is a detailed description of the process used to estimate the CVD risk applying three different models: (1) the 2008 FRS model [12], (2) the 2003 SCORE model [7], and (3) the 2013 AHA/ACC Pooled Cohort Equations model [13]. The main objective of this section is to make easily reproducible to other researchers the informatics procedure behind this study. All the models previously described use many logarithmical expressions that are multiplied by specific coefficients, according to the subject's sex, race and treated-untreated hypertension specific condition. Here the lector will find the codes introduced in the SPSS 22.0 Statistical Analysis Software in order to calculate the CVD risk with each model. We strongly recommend referring to Appendix B to adequately interpret those codes.

Equations used to calculate 10-year Framingham CVD risk in subjects according to D'Angostino et al. (2008)

As proposed by D'Angostino et al. (2008), the Framingham Heart Study offered two different equations to estimate CVD risk, one based on the subject's lipid profile and the other based on the subject's BMI.

Using Lipids:

Step 1: Obtain the general $\sum\beta x$ real subtotal, according to each case:

- **Male not receiving antihypertensive treatment:**

$\sum\beta x$ REAL = (LN_EDAD * 3.06117) + (LN_PA_SIST * 1.93303) + (LN_COLEST_TOTAL * 1.1237) + (LN_COLEST_HDL*(-0.93263)) + (FUMAR_RECOD * 0.65451) + (DIAB_DX_RECOD * 0.57367)

     o **Male receiving antihypertensive treatment:**

∑βx REAL = (LN_EDAD * 3.06117) + (LN_PA_SIST * 1.99881) + (LN_COLEST_TOTAL * 1.1237) + (LN_COLEST_HDL*(-0.93263)) + (FUMAR_RECOD * 0.65451) + (DIAB_DX_RECOD * 0.57367)

     o **Female not receiving antihypertensive treatment:**

∑βx REAL = (LN_EDAD * 2.32888) + (LN_PA_SIST * 2.76157) + (LN_COLEST_TOTAL * 1.20904) + (LN_COLEST_HDL*(-0.70833)) + (FUMAR_RECOD * 0.52873) + (DIAB_DX_RECOD * 0.69154)

     o **Female receiving antihypertensive treatment:**

∑βx REAL = (LN_EDAD * 2.32888) + (LN_PA_SIST * 2.82263) + (LN_COLEST_TOTAL * 1.20904) + (LN_COLEST_HDL*(-0.70833)) + (FUMAR_RECOD * 0.52873) + (DIAB_DX_RECOD * 0.69154)

Step 2: Calculate the risk score, depending on the subject's sex:

     o **Male:**

$$\text{Risk Score} = 1 - 0.88936^{\exp(\sum \beta x\ REAL - 23.9802)}$$

FRAM_RS1 = 1-(0.88936 ** EXP(Bx_REAL1-23.9802))

     o **Female:**

$$\text{Risk Score} = 1 - 0.95012^{\exp(\sum \beta x\ REAL - 26.1931)}$$

FRAM_RS1 = 1-(0.95012 ** EXP(Bx_REAL1-26.1931))

Using BMI

Step 1: Obtain the general ∑βx real subtotal, according to each case:

     o **Male not receiving antihypertensive treatment:**

∑βx REAL = (LN_EDAD* 3.11296) + (LN_PA_SIST * 1.85508) + (LN_IMC * 0.79277) + (FUMAR_RECOD * 0.70953) + (DIAB_DX_RECOD * 0.5316)

o **Male receiving antihypertensive treatment:**

∑βx REAL = (LN_EDAD* 3.11296) + (LN_PA_SIST * 1.92672) + (LN_IMC * 0.79277) + (FUMAR_RECOD * 0.70953) + (DIAB_DX_RECOD * 0.5316)

o **Female not receiving antihypertensive treatment:**

∑βx REAL = (LN_EDAD* 2.72107) + (LN_PA_SIST * 2.81291) + (LN_IMC * 0.51125) + (FUMAR_RECOD * 0.61868) + (DIAB_DX_RECOD * 0.77763)

o **Female receiving antihypertensive treatment:**

∑βx REAL = (LN_EDAD* 2.72107) + (LN_PA_SIST * 2.88267) + (LN_IMC * 0.51125) + (FUMAR_RECOD * 0.61868) + (DIAB_DX_RECOD * 0.77763)

Step 2: Calculate the risk score, depending on the subject's sex:

o **Male:**

$$\text{Risk Score} = 1 - 0.88431^{\exp(\sum \beta x \text{ REAL} - 23.9388)}$$

FRAM_RS2 = 1-(0.88431 ** (EXP(Bx_REAL2-23.9388)))

o **Female:**

$$\text{Risk Score} = 1 - 0.94833^{\exp(\sum \beta x \text{ REAL} - 26.0145)}$$

FRAM_RS2 = 1-(0.94833 ** (EXP(Bx_REAL2-26.0145)))

Equations used to calculate 10-year SCORE European Project CVD risk in subjects according to Conroy et al. (2008)

Step 1: Calculate the underlying risks for coronary heart disease and for non-coronary cardiovascular disease separately for the person's age now and for their age in ten years time. In this study, we assumed Ecuador to be equivalent to a "high CVD risk European land". The underlying survival probability is calculated depending on each case:

o **Male coronary heart disease underlying risk**

S0AGE_HRC = EXP(-(EXP(-21))*(EDAD_VERIF-20) ** 4.62)

S0AGE10_HRC = EXP(-(EXP(-21))*(EDAD_VERIF-10) ** 4.62)

- o **Male non-coronary heart disease underlying risk**

S0AGE_HRNC = EXP(-(EXP(-25.7))*(EDAD_VERIF-20) ** 5.47)

S0AGE10_HRNC = EXP(-(EXP(-25.7))*(EDAD_VERIF-10) ** 5.47)

- o **Female coronary heart disease underlying risk**

S0AGE_HRC = EXP(-(EXP(-28.7))*(EDAD_VERIF-20) ** 6.23)

S0AGE10_HRC = EXP(-(EXP(-28.7))*(EDAD_VERIF-10) ** 6.23)

- o **Female non-coronary heart disease underlying risk**

S0AGE_HRNC = EXP(-(EXP(-30))*(EDAD_VERIF-20) ** 6.42)

S0AGE10_HRNC = EXP(-(EXP(-30))*(EDAD_VERIF-10) ** 6.42)

Step 2: Calculate the weighted sum, *w*, of the risk factors cholesterol, smoking and systolic blood pressure. Two weighted sums will have to be calculated, one for coronary heart disease and one for non-coronary cardiovascular disease. Smoking is coded as 1 for current and 0 for non-smoker, so no value for smoking has to be entered if the person is a non-smoker. Cholesterol is measured in mmol/L and SBP is measured in mmHg.

- o **Weighted sum for coronary heart disease underlying risk**

W_C = (0.24*(COLEST_TOTAL_MMOL-6)) + (0.018*(PA_SIST_PROM -120)) + (0.71*FUMAR_RECOD)

- o **Weighted sum for non-coronary heart disease underlying risk**

W_NC = (0.02*(COLEST_TOTAL_MMOL-6)) + (0.022*(PA_SIST_PROM-120)) + (0.63*FUMAR_RECOD)

Step 3: Combine the underlying risks for coronary heart disease and for non-coronary cardiovascular disease, at the person's age and at their age ten years from now (four

calculations) which were calculated in step 1 with the weighted sum of a person's risk factors from step 2 for the two end-points, coronary heart disease and non-coronary cardiovascular disease to get the probability of survival at each age for each cause.

- **Male/Female combined coronary heart disease underlying risk**

S0AGE_HRC2 = S0AGE_HRC ** W_C

S0AGE10_HRC2 = S0AGE10_HRC ** W_C

- **Male/Female combined non-coronary heart disease underlying risk**

S0AGE_HRNC2 = S0AGE_HRNC** W_NC

S0AGE10_HRNC2 = S0AGE10_HRNC** W_NC

Step 4: For each cause, calculate the 10-year survival probability based on the survival probability for the person's current age and their age in 10 years time:

- **Male/Female 10-year survival probability for coronary heart disease**

S10_C = S0AGE10_HRC2/S0AGE_HRC2

- **Male/Female 10-year survival probability for coronary heart disease**

S10_NC = S0AGE10_HRNC2/S0AGE_HRNC2

Step 5: Calculate the 10 year risk for each end-point as follows:

- **Male/Female 10-year risk for coronary heart disease**

RISK10_C = 1 - S10_C

- **Male/Female 10-year risk for coronary heart disease**

RISK10_NC = 1 - S10_NC

Step 6: Combine the risks for coronary heart disease and non-coronary cardiovascular disease by adding them:

o   **Male/Female 10-year CVD risk**

SCORE_RISK = RISK10_C + RISK10_NC

Equations used to calculate the 2013 AHA/ACC 10-year race- and sex-specific ASCVD risk (Pooled Cohort Equations) in subjects according to Goff et al. (2013)

Step 1: Obtain the "individual sum value", depending on the subject's race and sex:

o   **Non-black female not receiving antihypertensive treatment:**

NBF_INDIV_SUM = (LN_EDAD * (-29.799)) + ((LN_EDAD **2)*4.884) + (LN_COLEST_TOTAL * 13.540) + (LN_EDAD*LN_COLEST_TOTAL*(-3.114)) + (LN_COLEST_HDL*(-13.578)) + (LN_EDAD*LN_COLEST_HDL*3.149) + (LN_PA_SIST*1.957) + (FUMAR_RECOD * 7.574) + (LN_EDAD* FUMAR_RECOD*(-1.665)) + (DIAB_DX_RECOD * 0.661)

o   **Black female not receiving antihypertensive treatment:**

BF_INDIV_SUM = (LN_EDAD * 17.114) + (LN_COLEST_TOTAL * 0.940) + (LN_COLEST_HDL*(-18.920)) + (LN_EDAD*LN_COLEST_HDL*4.475) + (LN_PA_SIST*27.820) + (LN_EDAD* LN_PA_SIST*(-6.087)) + (FUMAR_RECOD * 0.691) + (DIAB_DX_RECOD * 0.874)

o   **Non-black female receiving antihypertensive treatment:**

NBF_INDIV_SUM = (LN_EDAD * (-29.799)) + ((LN_EDAD **2)*4.884) + (LN_COLEST_TOTAL * 13.540) + (LN_EDAD*LN_COLEST_TOTAL*(-3.114)) + (LN_COLEST_HDL*(-13.578)) + (LN_EDAD*LN_COLEST_HDL*3.149) + (LN_PA_SIST*2.019) + (FUMAR_RECOD * 7.574) + (LN_EDAD* FUMAR_RECOD*(-1.665)) + (DIAB_DX_RECOD * 0.661)

- **Black female receiving antihypertensive treatment:**

BF_INDIV_SUM = (LN_EDAD * 17.114) + (LN_COLEST_TOTAL * 0.940) + (LN_COLEST_HDL*(-18.920)) + (LN_EDAD*LN_COLEST_HDL*4.475) + (LN_PA_SIST*29.291) + (LN_EDAD* LN_PA_SIST*(-6.432)) + (FUMAR_RECOD * 0.691) + (DIAB_DX_RECOD * 0.874)

- **Non-black male not receiving antihypertensive treatment:**

NBM_INDIV_SUM = (LN_EDAD * 12.344) + (LN_COLEST_TOTAL * 11.853) + (LN_EDAD*LN_COLEST_TOTAL*(-2.664)) + (LN_COLEST_HDL*(-7.990)) + (LN_EDAD*LN_COLEST_HDL*1.769) + (LN_PA_SIST*1.764) + (FUMAR_RECOD * 7.837) + (LN_EDAD* FUMAR_RECOD*(-1.795)) + (DIAB_DX_RECOD * 0.658)

- **Black male not receiving antihypertensive treatment:**

BM_INDIV_SUM = (LN_EDAD * 2.469) + (LN_COLEST_TOTAL * 0.302) + (LN_COLEST_HDL*(-0.307)) + (LN_PA_SIST*1.809) + (FUMAR_RECOD * 0.549) + (DIAB_DX_RECOD * 0.645)

- **Non-black male receiving antihypertensive treatment:**

NBM_INDIV_SUM = (LN_EDAD * 12.344) + (LN_COLEST_TOTAL * 11.853) + (LN_EDAD*LN_COLEST_TOTAL*(-2.664)) + (LN_COLEST_HDL*(-7.990)) + (LN_EDAD*LN_COLEST_HDL*1.769) + (LN_PA_SIST*1.797) + (FUMAR_RECOD * 7.837) + (LN_EDAD* FUMAR_RECOD*(-1.795)) + (DIAB_DX_RECOD * 0.658)

- **Black male receiving antihypertensive treatment:**

BM_INDIV_SUM = (LN_EDAD * 2.469) + (LN_COLEST_TOTAL * 0.302) + (LN_COLEST_HDL*(-0.307)) + (LN_PA_SIST*1.916) + (FUMAR_RECOD * 0.549) + (DIAB_DX_RECOD * 0.645)

Step 2: Calculate the final total ASCVD risk, according to the following equations:

- **Non-black female (either receiving antihypertensive treatment or not)**

NBF_ASCVD_RISK = 1-(0.9665 ** EXP(NBF_INDIV_SUM-(-29.18)))

- **Black female (either receiving antihypertensive treatment or not)**

BF_ASCVD_RISK = 1-(0.9533 ** EXP(BF_INDIV_SUM-86.61))

- **Non-black male (either receiving antihypertensive treatment or not)**

NBM_ASCVD_RISK = 1-(0.9144 ** EXP(NBM_INDIV_SUM-61.18))

- **Black male (either receiving antihypertensive treatment or not)**

BM_ASCVD_RISK = 1-(0.8954 ** EXP(BM_INDIV_SUM-19.54))

NOTE: SCORE O.P. CVD risk was calculated based on the same variables used for SCORE CVD risk estimation, only doing appropriate arrangements in the coefficients used according to Cooney et al. (2015) [26].

APPENDIX B: IMPORTANT SPSS CODE'S GLOSSARY

The following is the list of the most important variables necessary to adequately comprehend the informatics process explicated in Appendix A. Many codes depicted before have not been included in this chart, since their interpretation can be easily understood from the explanation paragraphs.

SPSS Code	Type of variable	Label
COLEST_TOTAL_MMOL	Scale	Total serum cholesterol (in mmol/L)
CREA	Scale	Serum creatinine (in mg/dl)
DIAB_DX_RECOD	Nominal	Diabetes mellitus previously diagnosed (yes/no)
EDAD_VERIF	Scale	Verified age of the subject (using personal ID birth date)
FUMAR_RECOD	Nominal	Smoking status of each subject (yes/no)
LN_IMC	Scale	Ln of BMI of each subject (in kg/m^2)
LN_COLEST_HDL	Scale	Ln of serum HDL cholesterol (in mg/dL)
LN_COLEST_TOTAL	Scale	Ln of total serum cholesterol (in mg/dL)
LN_EDAD	Scale	Ln of EDAD_VERIF
LN_PA_SIST	Scale	Ln of PA_SIST_PROM
PA_SIST_PROM	Scale	Mean systolic blood pressure (of two different measures) of the subject in mmHg
PESO_PROM	Scale	Mean weight (of two different measures) of the subject in kg

APPENDIX C: GFR ESTIMATION EQUATIONS

We used the 4-variable MDMR Equation to estimate the GFR of the sample, as follows [48]:

- **Non-black male**

NBM_GFR = 186 * (CREA ** -1.154) * (EDAD_VERIF ** -0.203)

- **Black male**

BM_GFR = 186 * (CREA ** -1.154) * (EDAD_VERIF ** -0.203) * 1.210

- **Non-black female**

NBF_GFR = 186 * (CREA ** -1.154) * (EDAD_VERIF ** -0.203) * 0.742

- **Black female**

BF_GFR = 186 * (CREA ** -1.154) * (EDAD_VERIF ** -0.203) * 0.742 * 1.210