Gender differences in cardiovascular risk assessment in elderly adults in Ecuador: evidence from a national survey

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ABSTRACT

The present study aimed to predict the risk of developing cardiovascular disease (CVD) over a 5-year period and how it might vary by sex in an ethnically diverse population of older adults. We used a novel CVD risk model built and validated in older adults named the Systematic Coronary Risk Evaluation in Older Persons (SCORE OP). A population-based study analyzed a total of 1307 older adults. Analyses were done by various risk categories and sex. Of the study population, 54% were female with a mean age of 75±7.1 years. According to the SCORE OP model, individuals were classified as having low (9.8%), moderate (48.1%), and high or very high risk (42.1%) of CVD-related mortality. Individuals at higher risk of CVD were more likely to be male compared with females, 53.9% vs 31.8%, respectively (p<0.01). Males were more likely to be younger, living in rural areas, had higher levels of schooling, and with the exception of smoking status and serum triglycerides, had lower values of traditional risk factors than females. In addition, males were less likely to require blood pressure-lowering therapy and statin drugs than females. This gender inequality could be driven by sociocultural determinants and a risk factor paradox in which lower levels of the cardiovascular risk factors are associated with an increase rather than a reduction in mortality. These data can be used to tailor primary prevention strategies such as lifestyle counseling and therapeutic measures in order to improve male elderly health, especially in low-resource settings.

Significance of this study

What is already known about this subject?

- Traditional risk assessment models tend to overestimate the cardiovascular disease (CVD) risk among the elderly.
- Evidence of CVD gender difference built mostly in middle-aged populations.
- Scarce information exists about the risk of developing CVD among elderly population in low-resource settings and how it varies according to sex.

What are the new findings?

- At a national level, this study found that older males were at higher risk of CVD compared with females.
- The higher risk among males is present despite possessing lower values of traditional cardiovascular risk factors.

How might these results change the focus of research or clinical practice?

- This study suggests that CVD gender inequality in low-resource settings might be driven by sociocultural determinants and a risk factor paradox phenomenon.

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death worldwide and represents more than 75%–80% of mortality in people over 65 years of age.[1] According to the Global Burden of Disease estimates, CVD represented ~175 million diasbility-adjusted life-years (DALY) of the total disease burden for 2010 in older people.[2] Most of this disease burden is higher in low-income and middle-income regions (827 DALYs per 1000) compared with high-income regions (590 DALYs per 1000).[2]

Despite the magnitude and impact of CVD in older adults, significant knowledge gaps exist in CVD management in the elderly. Due to the incorrect assumption that outcomes reported in medical literature involving younger and healthier patients are applicable to older adults,[3] there is a need for better risk stratification tools to identify individuals most likely to derive benefit from preventive and aggressive interventions.[3 4] Recently, a risk estimation function, referred to as the Systematic Coronary Risk Evaluation in Older Persons (SCORE OP), which predicts the risk of CV mortality over a 5 and 10-year period in people aged 65 years and older, was derived and validated using data from 4 European cohort studies.[5]

It is predicted that the death rate from CVD will increase markedly in Latin American countries due to their faster aging population compared with other regions in the world.[6 7] However, there is very little information regarding the CVD status of the elderly,[8 9] in particular about the risk of developing CVD and how it varies according to sex.

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The published literature has consistently shown a female disadvantage in CV risk factor assessment and management compared with males.[10–12] This evidence base, however, was mostly built in middle-aged populations, with little data among those >75 years of age.[3 13]

Using the SCORE OP model and a national survey data, we determined whether the risk of developing CVD and treatment gaps are different for elderly men and women residing in Ecuador.

MATERIALS AND METHODS

Data source

In 2009, the consortium research integrated by the University of San Francisco de Quito, the National Institute of Statistics and Census, and the Ministry of Public Health of Ecuador conducted the Encuesta sobre Salud, Bienestar y Envejecimiento (hereafter, SABE-ECU) to investigate the health and well-being of older individuals in the country. Based on a probabilistic and representative sample, SABE-ECU interviewed 5235 subjects of 60 years of age and older.[14] Overall, 5100 households in the highlands and 5268 in the coastal region were randomly selected based on the 2001 national census cartography.[14]

The survey included questions about personal and household information; health conditions; anthropometric measures; functional status, cognitive states; physical abuse history; use and accessibility to health services; medication intake; family and social network support, and work history and income. Further information such as manuals and survey instruments has been described elsewhere.[14]

The deidentified results of SABE-ECU are reported and publicly available at http://www.ecuadorencifras.gob.ec/encuesta-de-salud-bienestar-del-adulto-mayor/. In addition, it is important to note that SABE-ECU allows international comparisons with other similar studies because it used standardized measures of social and health components.[15]

Applied model and study design

The SCORE OP model was developed due to the inaccuracy of available models to estimate the risk of CVD over a period in time in older people.[16] Thus, using data of 20,704 men and 20,121 women aged 65 years and over without prior coronary disease from 4 European cohorts, a risk equation was developed for use in older individuals.[5] In performance measures, SCORE OP model showed good discrimination (area under the receiver operating characteristic curve: 0.74) and calibration (Hosmer-Lemeshow goodness-of-fit test: 17.16 for men and 22.70 for women).[5]

To estimate individual 5 or 10-year risk of CVD, the SCORE OP model uses a composite of CVD risk factors that remained statistically significant in Cox proportional hazards models, which were: total cholesterol, high-density lipoprotein cholesterol, systolic blood pressure (SBP), smoking status, and diabetes.[5] Furthermore, SCORE OP allows an estimation of CVD risk estimates according to sex and whether a country is considered to be a high or low CVD risk region.[5] Based on the European Society of Cardiology (ESC) and European Atherosclerosis Society guidelines and WHO statistics, Ecuador would be considered as a low-risk country.[17 18] After estimated specific individual

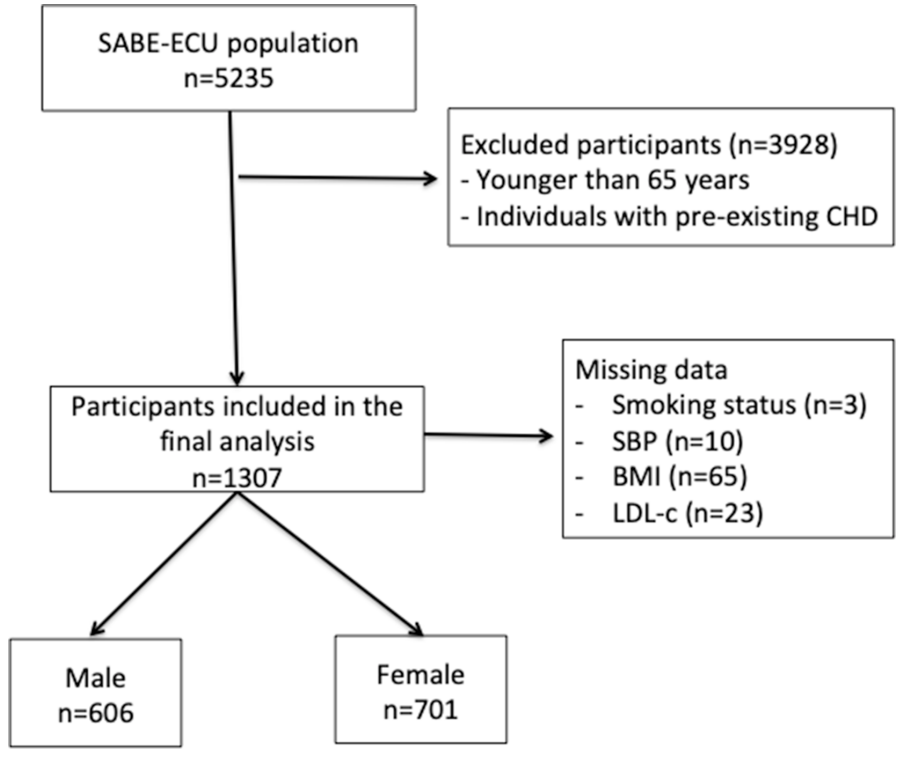

Figure 1 Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) flow chart of the study population. BMI, body mass index; CHD, coronary heart disease; LDL, low-density lipoprotein; SABE-ECU, Encuesta sobre Salud, Bienestar y Envejecimiento; SBP, systolic blood pressure.

Table 1 Characteristics of the study population at baseline by sex

Variables	Overall n=1307	Female n=701	Male n=606	P value
Age (y)	75±7.1	75±7.2	75±6.9	0.8
Age, n (%)				<0.01
65–70	431 (33)	242 (34.5)	189 (31.2)	
71–75	323 (24.7)	177 (25.3)	146 (24.1)	
76–80	263 (20.1)	117 (16.7)	146 (24.1)	
>80	290 (22.2)	165 (23.5)	125 (20.6)	
Residence, n (%)				<0.001
Rural	440 (33.7)	206 (29.4)	234 (38.6)	
Urban	867 (66.3)	495 (70.6)	372 (61.4)	
Race, n (%)				0.2
White	177 (13.5)	109 (15.5)	68 (11.2)	
Indigenous	107 (8.2)	51 (7.3)	56 (9.2)	
Mixed	847 (64.8)	444 (63.3)	403 (66.5)	
Black (Afro-Ecuadorians)	42 (3.2)	23 (3.3)	19 (3.1)	
Mulatto	47 (3.6)	26 (3.7)	21 (3.5)	
Education, n (%)				0.01
No schooling	25 (1.9)	14 (2.7)	11 (1.8)	
Primary (≤6 y)	826 (63.2)	415 (59.2)	411 (67.8)	
Secondary (7–12 y)	102 (7.8)	65 (9.3)	37 (6.1)	
Tertiary (≥13 y)	34 (2.6)	12 (1.7)	22 (3.6)	
Self-assessed health status, n (%)				<0.01
Poor	267 (20.4)	157 (22.4)	110 (18.2)	
Fair	733 (56.1)	407 (58.1)	326 (53.8)	
Good	265 (20.3)	125 (17.8)	140 (23.1)	
Very good	27 (2.1)	8 (1.1)	19 (3.1)	
Excellent	13 (1)	3 (0.4)	10 (1.6)	
Occupational status, n (%)				
Yes	627 (48)	240 (34.2)	387 (63.9)	<0.01
Living arrangements, n (%)				
Alone	137 (10.5)	73 (10.4)	64 (10.6)	1
Smoking status				<0.01
Never	810 (62)	608 (86.7)	202 (33.3)	
Former	364 (27.8)	71 (10.1)	293 (48.3)	
Current	130 (1)	20 (2.8)	110 (18.2)	
Hypertension, n (%)*				<0.01
Yes	730 (55.8)	442 (63.1)	288 (47.5)	
Systolic blood pressure (mm Hg)	139.2±23.4	140.6±24.8	137.3±22.7	<0.01
Diabetes mellitus†, n (%)				
Yes	147 (11.2)	98 (14)	49 (8)	0.5
BMI (kg/m^2)‡	26±4.6	26.5 (14.9–30)	24.7 (14.5–27.2)	<0.01
Total cholesterol (mg/dL)	200.2±41.8	207.9±43.6	191.2±37.8	<0.001
HDL-cholesterol (mg/dL)	48.3±14.5	50.2±14.4	46.2±14.3	<0.001
LDL-cholesterol§ (mg/dL)	116 (96–140)	119 (29–144)	114 (34–137)	<0.001
Triglycerides§ (mg/dL)	136 (99–190)	146 (105–199)	127 (93–177)	<0.001
hs-CRP (mg/dL)	2.3 (1.1–5)	2.5 (1.3–5.4)	2.1 (1–4.6)	<0.01

Plus-minus values are means±SD. Percentages may not sum to 100 due to missing data or rounding.
*Hypertension was defined as a systolic blood pressure ≥140 mm Hg.
†The presence of diabetes was based on a fasting plasma glucose level ≥126 mg/dL.
‡The body mass index is the weight in kilograms divided by the square of the height in meters.
§Expressed as median (25%–75%), because of skewed distribution.
BMI, body mass index; HDL, high-density lipoprotein; hs-CRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein.

risks by using baseline survival rates and β-coefficients for a low-risk country, we stratified individuals into 4 five-year risk categories as follows: low (<1%), moderate (1%–5%), high (5%–10%), and very high (>10%) CVD-related mortality as previously reported.[5] For purposes of this analysis, we combined high and very-high-risk individuals into a single category.

This study used a population-based, cross-sectional design. Interviewed patients in SABE-ECU survey were selected to calculate the predicted 5-year risk of developing

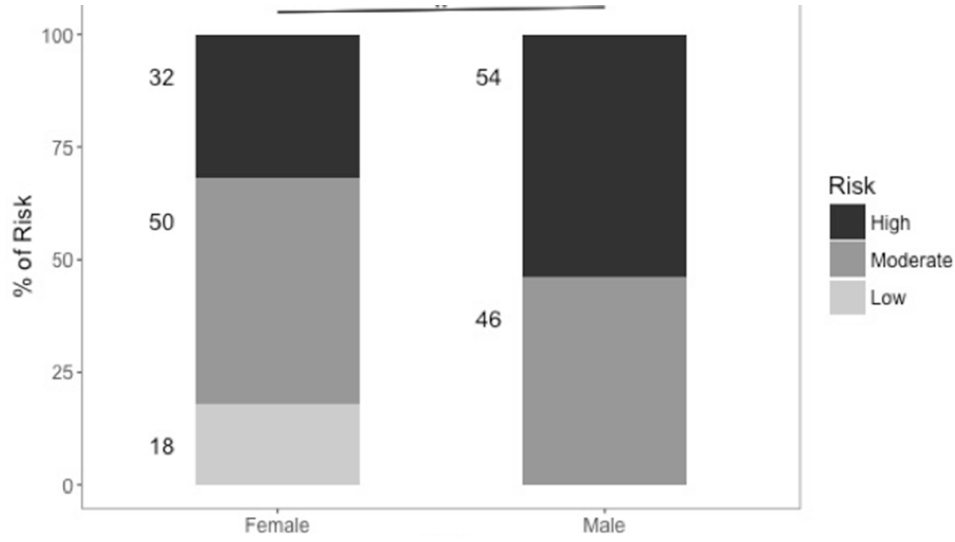

Figure 2 Distribution of risk categories according to Systematic Coronary Risk Evaluation in Older Persons (SCORE OP) model for men and women without cardiovascular disease (CVD). **P<0.01 for comparison of men and women.

CVD in elderly adults. All individuals aged <65 years and with pre-existing coronary heart disease were excluded. Age was grouped into 65–70, 71–75, 76–80, and >80 years.

Statistical analysis

All statistical analyses were performed using R for Mac, V.3.3.2. Parametric (χ^2 and t-test) and non-parametric (Wilcoxon rank-sum and Fisher's exact test) tests were used to evaluate the distribution of categorical and continuous variables by sex. In addition, we applied multiple imputation according to Rubin rules[19] for missing information about smoking status, SBP, body mass index (BMI) and low-density lipoprotein cholesterol (Ldl_c) which represented 0.2%, 0.8%, 4.9%, and 1.8% of the sample study, respectively. A two-tailed p value <0.05 was considered to indicate statistical significance.

RESULTS

The final study population for this cross-sectional analysis consisted of 1307 subjects (figure 1). Table 1 shows the distribution of sociodemographic and health variables by sex. The study participants had a mean age of 75±7.1 years, 46% were male, and ~77% of the population were 70 years and older. Compared with females, males were more likely to live in rural areas, had higher school achievements, were employed, perceived themselves as healthier, and with the exception of smoking status, all classical risk factors for CVD had lower values in men than in women.

In addition, we did not find differences among the imputed values for smoking status, SBP, BMI, and Ldl_c between females and males. According to the SCORE OP model, individuals were classified as having low (9.8%), moderate (48.1%), and high or very high (42.1%) risk of CVD-related mortality. Individuals with higher CVD risk were more likely to be male compared with females, 53.9% vs 31.8% (p<0.01), respectively. Furthermore, the model only categorized males as a moderate or high-risk individuals (figure 2). Individuals with higher risk of CVD were more likely to be male, younger, living in rural settings, having higher levels of education, and with the exception of smoking status and serum triglycerides, having lower values of traditional risk factors than females (table 2).

Based on the Eighth Joint National Committee and the 2013 ESC guidelines value of 150 mm Hg to define hypertension in elderly population, 25.8% (338/1307) of the study population had hypertension, suggesting that these individuals would benefit from a first antihypertensive medication prescription or appropriate monitoring of the current therapy. In addition, ~3.1% (40/1307) of the study population would benefit from a newly statin therapy and female individuals requiring a higher prescription rate than males (table 3).

Overall, males were less likely to require pharmacologic intervention as blood pressure-lowering and statin drugs than females.

DISCUSSION

Principal findings

The present study provides contemporary gender comparisons of the risk of developing CVD over a 5-year period and needed pharmacology intervention in elderly adults living in Ecuador. Our results show that males have a higher risk of suffering CVD than females despite possessing lower values of traditional CV risk factors and requiring less pharmacologic drug management.

Comparison with other studies

Our percentage of individuals categorized as high or very high risk was lower (72% vs 42.1%, respectively) compared with a publication from Spain that also used SCORE OP model.[20] As well as our findings, this study found that males obtained a higher risk of suffering CVD compared with females. Similarly, a study carried out in Finland found that in elderly people the prevalence of high CVD risk was higher in men although using a different risk prediction model.[12] In addition, in the original cohort population

Table 2 Comparison between moderate and high cardiovascular risk categories

	Moderate			High*		
	Female	Male		Female	Male	
Variables	n=350	n=279	P value	n=223	n=327	P value
Age (y)	72±3.5	69±2.9	<0.001	84±4.9	80±5.7	<0.001
Residence, n (%)			<0.001			0.04
Rural	91 (26)	128 (45.9)		54 (24.2)	106 (32.4)	
Urban	259 (74)	151 (54.1)		169 (75.8)	221 (67.6)	
Race, n (%)						0.04
White	44 (12.6)	32 (11.5)	<0.001	50 (22.4)	36 (11)	
Indigenous	25 (7.1)	35 (12.5)		10 (4.5)	21 (6.4)	
Mixed	237 (67.7)	176 (63.1)		132 (59.2)	227 (69.4)	
Black (Afro-Ecuadorians)	10 (2.8)	10 (3.6)		9 (4)	9 (2.7)	
Mulatto	10 (2.8)	10 (3.6)		9 (4)	11 (3.4)	
Education, n (%)			0.05			0.04
No schooling	5 (1.4)	7 (2.5)		7 (3.1)	4 (1.2)	
Primary (≤6 y)	219 (62.6)	193 (69.2)		120 (53.8)	218 (66.7)	
Secondary (7–12 y)	36 (10.3)	19 (6.8)		18 (8.1)	18 (5.5)	
Tertiary (≥13 y)	6 (1.7)	13 (4.6)		2 (0.8)	9 (2.7)	
Self-assessed health status, n (%)			<0.01			0.2
Poor	85 (24.3)	52 (18.6)		46 (20.6)	58 (17.7)	
Fair	206 (58.8)	145 (52)		134 (60.1)	181 (55.3)	
Good	54 (15.4)	69 (24.7)		38 (17)	71 (21.7)	
Very good	4 (1.1)	10 (3.6)		4 (1.8)	9 (2.7)	
Excellent	1 (0.3)	3 (1.1)		1 (0.5)	7 (2.1)	
Living arrangements, n (%)			1			0.6
Accompanied	314 (89.7)	251 (90)		195 (87.4)	291 (89)	
Alone	36 (10.3)	28 (10)		28 (12.6)	36 (11)	
Diabetes mellitus†, n (%)			<0.001			0.1
Yes	63 (18)	13 (4.6)		35 (15.7)	36 (11)	
Smoking			<0.001			<0.001
Yes	11 (3.1)	31 (11.1)		8 (3.6)	79 (24.1)	
Systolic blood pressure (mm Hg)	141±23	132±18	<0.001	147±25.1	142±24.8	0.01
BMI (kg/m^2)‡	27.2±4.7	25.1±4.1	<0.001	26±4.5	24.8±3.9	<0.001
Total cholesterol (mg/dL)	209.4±46.3	192.8±36.5	<0.001	204.8±43.3	190±39	<0.001
HDL-cholesterol§ (mg/dL)	45 (37–54)	46 (40–56)	0.08	51±14.3	45±13.3	<0.001
LDL-cholesterol§ (mg/dL)	116 (99–146)	114 (93–136)	0.01	120.5±32.6	115.7±32	0.09
Triglycerides§ (mg/dL)	152 (108–228)	130 (92–178)	<0.001	126 (94–174)	142 (105–183)	0.01
hs-CRP (mg/dL)	2.6 (1.4–5.20)	1.6 (0.8–3.9)	<0.001	2.5 (1.3–5.8)	2.5 (1.3–5.1)	0.7

Plus-minus values are means±SD. Percentages may not sum to 100 due to missing data or rounding.
*Includes individuals with high and veryhighrisk categories of developing cardiovascular disease (CVD) in a 5-year period.
†The presence of diabetes was based on a fasting plasma glucose level ≥126 mg/dL.
‡The body mass index is the weight in kilograms divided by the square of the height in meters.
§Expressed as median (25%–75%), because of skewed distribution.
BMI, body mass index; HDL, high-density lipoprotein; hs-CRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein.

used to derive and validate the SCORE OP model, a higher average risk of CVD was observed in males compared with females (15.7% vs 12.8%, respectively), although it analyzed a 10-year period.[5]

Explanations and implications

CVD is often considered a male disease, especially prior to the menopause.[12 21] Estrogen may explain some of these sex differences yet it is less clear in older adults.[22] Currently, a phenomenon termed 'risk factor paradox' might explain this, where lower levels of the classical CV risk factors (blood pressure, BMI, and cholesterol) are associated with an increase rather than a reduction in mortality.[23] One possible hypothesis suggested to explain this phenomenon is the 'catabolic' syndrome, which is closely linked to frailty and sarcopenia.[23 24]

In this state of frailty and sarcopenia, loosing adipose tissue decreases the release of beneficial substances such as adiponectin and soluble tumor necrosis factor-α receptors that can potentially offset the typical chronic inflammatory state that categorizes elderly people.[25] In addition, there is evidence, which shows that individuals with higher BMI can tolerate better CVD adverse events.[26] Based on this evidence, there might be possibilities that males in our

Table 3 Comparison of pharmacological intervention needed in the study population by sex and CVD risk category

	Male (n=606) n (%)	Female (n=701) n (%)	P value
Blood pressure-lowering therapy*, n (%)			0.02
Low (<1%)	–	12 (9.4)	
Moderate (1%–5%)	40 (14.3)	101 (28.8)	
High (>5%)	99 (30.3)	86 (38.5)	
Statin treatment Ldl_c†			0.04
Low (<1%)	–	3 (2.3)	
Moderate (1%–5%)	5 (1.8)	21 (6)	
High (>5%)	6 (1.8)	5 (2.2)	

*Defined as having systolic blood pressure of >150 mm Hg based on Eighth Joint National Committee (JNC 8) and the 2013 European Society of Cardiology/European Society of Hypertension (ESC/ESH) guidelines.
†Defined as having low-density lipoprotein cholesterol (Ldl_c) ≥190 mg/dL based on 2016 Task Force for the Management of Dyslipidaemias of the European Society of Cardiology/European Atherosclerosis Society (ESC/EAS) Guidelines.
CVD, cardiovascular disease.

study are facing a complex catabolic syndrome, which could translate into a higher CVD risk than females.

We were surprised to find this gender inequality in CVD risk towards males, especially, because males compared with females in our study are more likely to be younger, more educated, and perceived themselves as healthier. Nevertheless, certain health determinants of our study population may support these differential findings. For instance, males were more likely to live in rural Ecuador compared with females. Evidence shows that individuals living in rural settings have less access to healthcare services to prevent and treat CVD and related comorbid conditions.[27] Further, among older adults living in rural areas there is insufficient awareness of CVD risk factors and its prevention.[8 9 28] Thus, a study showed that 24.5% of elderly adults who possessed high CVD risk were not aware of their risk and consider themselves as individuals with little or no risk at all.[28 29] Finally, an important health determinant that could explain our findings is that males tend to judge sickness and healthcare use as a sign of weakness and vulnerability against their masculinity. Therefore, women are more aware of their health and are more likely to seek healthcare.[30]

In low/middle-income countries there is a scarcity of national guidelines on CVD risk assessment compared with developed nations.[31] Thus, in order to prevent CVD in an appropriate and cost-effective manner in low-resource settings, the total CVD risk calculation instead of screening for and treating single risk factors approach has been proven to lead to better CVD prevention and clinical outcomes.[32] Moreover, based on a clinical trial using the SCORE OP model, it is suggested that the implementation of multicomponent interventions including lifestyle counseling, motivational interviewing techniques, and therapeutic measures may have a greater effect if executed in countries with relatively low standards of vascular care in combination with projected increases in incident CVD.[33]

Literature shows that risk assessment[11 34] to inform management decisions, and non-pharmacology strategies reduce the risk of primary CVD events in older individuals especially among those younger than 80 years of age.[35–37] Hence, being able to quantitatively predict the absolute risk of developing a CVD event would enhance and enable elderly people to take more control over their health.[28 35] However, in light of our results and the unique condition that underlies ageing with CVD, one possibility to improve elderly male population survival should focus on interventions that address wasting disease by nutritional and anti-inflammatory interventions.[38]

Strengths and limitations of the study

Our study has several strengths. We used a CVD risk score built and validated in older adults. Thus, overestimation of CVD risk is less likely to have occurred compared with other risk estimation systems that were derived from a different age group to which it is to be applied.[5 16] To the best of our knowledge, this is the first study that evaluates the risk of developing CVD using SCORE OP model in an ethnically diverse population compared with the white middle-class population where it was originally developed.[5] Further, SCORE OP model is a straightforward and feasible calculator to be implemented at a community level in a low-resource setting. However, there are several limitations in this study. First, due to the absence of outcome data we were not able to conduct performance measure of the model. Second, in this study, we excluded individuals based on self-reported CVD status, a misclassification bias could have occurred, due to cognitive issues especially among the oldest individuals and those living in rural areas.[8 9 15] Third, we cannot exclude the possibility of exposure misclassification of statin intake among the study participants since SABE-ECU data set only disaggregated data about antihypertensive drug intake. However, using biomarkers of lipid profile we were able to ascertain which individuals will benefit most of this preventive strategy and reduce the risk of this bias.[28]

In summary, men have higher risk of developing CVD in a 5-year period than females among elderly adults in Ecuador. This gender inequality could be driven by sociocultural determinants and a complex catabolic syndrome. These data can be used to tailor primary prevention strategies to improve male elderly health especially in low-resource settings.

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