

Cardiovascular risk in the elderly population of Spain. The EPICARDIAN risk score

Riesgo cardiovascular en la población anciana española. Escala de riesgo EPICARDIAN

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Abstract

Background and objectives. Cardiovascular risk estimation in people over 70 years of age is problematic. Most scores have been created based on cohorts of middle-aged people, with an underrepresentation of older adults. The predictive power of classical cardiovascular risk factors declines with age. The aim of this work is to develop a specific score for estimating cardiovascular risk among the elderly population in Spain.

Methods. This work is a population-based cohort established in 1995. Setting: Three geographical areas of Spain (Madrid, Ávila, and Lugo). Participants: 3,729 people older than 64 years with no cardiovascular diseases (CVD) at baseline. Measurements: Suspected fatal and nonfatal CVD (both coronary heart disease and stroke) were investigated annually and confirmed using the WHO-MONICA criteria. All participants were followed-up on until occurrence of a first CVD event, until death, or until December 31, 2015.

Results. Age was the strongest predictor of CVD at 10 years in both men and women. In men, variables associated with CVD were high blood pressure treatment (HR: 1.35; 95% CI: 1.067–1.710), diabetes (HR: 1.359; 95% CI: 0.997–1.852), and smoking (HR: 1.207; 95% CI: 0.945–1.541) and in women, the variables were smoking (HR: 1.881; 95% CI: 1.356–2.609) and diabetes (HR: 1.285; 95% CI: 0.967–1.707). Total cholesterol did not increase the risk of CVD in men or women. However, total cholesterol levels >200 mg/dL were inversely associated with 10-year risk of CVD in men and women.

Conclusions. In elderly Spanish men, total CVD at 10 years is significantly increased by age, diabetes, and antihypertensive treatment and in elderly Spanish women by diabetes and smoking. Total cholesterol levels did not increase the risk of CVD, particularly in males.

Resumen

Antecedentes y objetivos. La estimación del riesgo cardiovascular en personas mayores de 70 años es problemática. La mayoría de las escalas se han creado basándose en cohortes de personas de mediana edad, con una representación insuficiente de los adultos de más edad. El poder predictivo de los factores de riesgo cardiovascular clásicos disminuye con la edad. El objetivo de este estudio es desarrollar una escala específica para estimar el riesgo cardiovascular de la población anciana española.

Métodos. Este estudio se realizó en una cohorte poblacional establecida en 1995. Marco: tres zonas geográficas de España (Madrid, Ávila y Lugo). Participantes: 3.729 personas mayores de 64 años sin enfermedades cardiovasculares (ECV) al inicio del seguimiento. Mediciones: Se investigaron anualmente las sospechas de ECV mortal y no mortal (cardiopatía coronaria e ictus) y se confirmaron usando los criterios del proyecto MONICA de la OMS. Se siguió a

todos los participantes hasta que apareció el primer episodio de ECV, hasta su muerte o hasta el 31 de diciembre de 2015.

Resultados. La edad fue el factor predictivo más potente de ECV a los 10 años en ambos sexos. Las variables asociadas con ECV en los varones fueron el tratamiento de la hipertensión arterial (HR: 1,35; IC al 95%: 1,067–1,710), la diabetes (HR: 1,359; IC al 95%: 0,997–1,852) y el tabaquismo (HR: 1,207; IC al 95%: 0,945–1,541) y en las mujeres, el tabaquismo (HR: 1,881; IC al 95%: 1,356–2,609) y la diabetes (HR: 1,285; IC al 95%: 0,967–1,707). El colesterol-total no aumentó el riesgo de ECV, ni en varones ni en mujeres. Sin embargo, las concentraciones de colesterol total > 200 mg/dL se asociaron inversamente al riesgo de ECV a los 10 años, tanto en varones como en mujeres.

Conclusiones. La ECV total a los 10 años aumenta significativamente en los varones españoles de edad avanzada con la edad, la diabetes y el tratamiento antihipertensivo y en las mujeres con la diabetes y el tabaquismo. Los niveles de colesterol total no aumentaron el riesgo de ECV, sobre todo en los varones.

Keywords

Cardiovascular risk score; Elderly; Spain

Palabras clave

Escalas de riesgo cardiovascular; Individuos de edad avanzada; España

Introduction

Several cardiovascular disease (CVD) risk charts are currently available, but the majority have been developed based on middle-aged populations with little representation of individuals older than 70 years of age^{1,2}. In addition, the existing scores have several limitations for their use in the elderly, as they usually do not consider the effect of treatment of cardiovascular risk factors (CVRF)³ or frailty, both of which are important determinants of CVD in older adults. Therefore, they can err when calculating the actual CVD risk in this population^{4,5}. For example, the European SCORE risk chart is mainly aimed at middle-aged individuals and its use is recommended for those who are 40–65 years of age¹.

Moreover, observational studies in the elderly have shown that risk estimation in people older than 70 years is problematic because the predictive power of CVRF declines with age. The Leiden 85-plus study showed that the Framingham score is not useful for people older than 70 because of its low power of discrimination⁶.

Several studies have reported that the association between hypertension and mortality is attenuated in older adults and thus, age might make hypertension a poor determinant of CVD risk in the elderly^{7,8,9,10}. However, measures of frailty and function may better identify older adults at risk of adverse consequences of hypertension. It has been reported that systolic blood pressure (SBP) is associated with an increased risk of mortality in elderly individuals with reduced walking speed¹¹. In addition, the effects of some classical CVRF such as total cholesterol (TC) on CVD risk become nebulous or even invert among elderly individuals¹². Therefore, a more adequate assessment of CVD risk in the old and very old is desirable in order to target and optimize prevention and treatment.

The aim of this study was to determine the major predictors of total CVD risk in the elderly population in Spain and to develop specific CVD risk charts for this age group.

Methods

The EPICARDIAN study is a multicenter, population-based, cohort study of people 65 years of age and older from three geographical areas of Spain: the city of Madrid, the municipality of Arévalo (Ávila province), and the municipality of Begonte (Lugo province). The study design and methods have previously been published elsewhere^{13,14}. In summary, a total of 3,729 individuals older than 64 years participated in the baseline examination. Two hundred fifty-five patients (6.8%) showed overt clinical CVD at baseline. Only individuals without CVD at baseline were included in the analyses. Therefore, the initial cohort comprised 3,474 individuals (1,462 men and 2,012 women). All participants were followed until occurrence of a first cardiovascular event, death, or for ten years.

Variables were measured at baseline and the risk formula included age; sex; SBP; smoking; TC; fasting blood glucose; and a medical diagnosis of hypertension, hypercholesterolemia, diabetes mellitus, or specific drug treatment for these conditions. Serum TC was determined by enzymatic methods¹⁵. LDL cholesterol was not measured in the cohort because only a small proportion of participants had HDL cholesterol values available. Blood glucose was determined by means of a glucose-oxidase assay¹⁶. For the Cox proportional hazards model, variables were grouped using the Framingham risk factor categories¹⁷: age was grouped in five-year categories starting from 65 to 69 years, SBP was classified into three categories, and TC was classified into four categories. Participants were categorized either as smokers (those who smoked at baseline or quit smoking within six months of baseline) or non-smokers/ex-smokers (Table 1). Hypertension was considered present if SBP \geq 140 mmHg, diastolic blood pressure (DBP) \geq 90 mmHg, or if the subject received antihypertensive treatment¹⁸. Hypercholesterolemia was considered present if TC \geq 5.1 mmol/L or if the subject received lipid-lowering treatment¹⁵. Diabetes was considered present if fasting plasma glucose \geq 7.0 mmol/L or if the subject received antidiabetic treatment¹⁹.

A search was conducted for data on CVD events in the initial cohort using primary care and hospital medical records, information from primary care physicians, postal mail, and telephone calls to the subject or relatives. The date and cause of death of deceased

individuals in the cohort were confirmed through the Spanish National Death Index and the death records of each healthcare district.

The International Classification of Diseases (ICD-9 and ICD-10) was used for recording coronary heart disease (ICD-9: 410–414, ICD-10: I20-I25) and other cardiovascular conditions (ICD-9: 797–799; ICD-10: I46, R96, R98, I50). Coronary events were confirmed using the WHO-MONICA algorithm²⁰. The CVD outcome was defined as a composite of first coronary event (fatal or non-fatal definite myocardial infarction (MI) and fatal possible MI).

In order to describe the selected data, the arithmetic mean with standard deviation (SD) was calculated for continuous variables and relative frequency distribution was calculated for categorical variables. In order to compare proportions, Pearson's chi-square (χ^2) test and Somers' D were calculated in the case of ordinal variables. To compare groups, Student's *t*-test was used in the case of independent binary measures and analysis of variance for variables with more than two categories.

The aforementioned independent variables were included in the multivariate models using the Enter method. We created separate models for men and women. In the first step, we treated SBP and TC as continuous variables in order to assess interactions between antihypertensive treatment and SBP values and between lipid-lowering drug and TC levels. In the second step, SBP and TC were categorized. In the third step, the interactions were removed. Finally, in order to simplify the model, the lipid-lowering treatment variable was eliminated because it was not statistically significant.

Bivariate and multivariate associations between each independent variable in the model and the outcome were assessed. The β -coefficient associated with each potential CVRF and the first recorded CVD event were estimated by means of Cox proportional hazards model separately for men and women. Ten-year Kaplan-Meier survival curves for the first fatal/non-fatal CVD event were determined in order to calculate the mean cumulative incidence. The estimate of survival function was calculated using a Cox model adjusted for competing 10-year mortality from non-CVD using the Fine-Gray model, and stratified according to sex. The omnibus test was used to validate the model ($p < .05$). Sex-specific risk scores for the prediction of fatal and non-fatal CVD using categorical variables were calculated from the β -coefficients of the Cox proportional hazards models. The observed total 10-year CVD risk was categorized as low risk

(<20%), mild risk (20%–29%), moderate risk (30%–39%), moderate high risk (40%–49%), high risk (50%–59%), or very high risk ($\geq 60\%$).

All statistical analyses were performed using R statistics software (<http://www.R-project.org>).

Additional statistical analyses—including the calculation of β -coefficients for different risk factors in the typical 10-year CVD risk model and afterwards using age as a time-scale variable—calibration, discrimination of the risk functions, and comparisons of mean ten-year cardiovascular risk according to the SCORE-OP charts and the EPICARDIAN score by sex are shown in the Appendix A supplementary material.

The study was conducted in compliance with the Declaration of Helsinki (<http://www.wma.net/e/policy/b3.htm>). Written informed consent was obtained from all participants during the baseline examination. The study protocol was approved by the Ethics Committee of La Princesa University Hospital, Madrid.

Results

A total of 3,474 participants were included, which yielded 27,749 person-years of follow-up. At baseline, 42.5% of the sample had hypertension, 28.4% had hypercholesterolemia, 11.5% had diabetes mellitus, 11.9% smoked, and 52% were on antihypertensive treatment. Follow-up information was obtained on 3,474 individuals (99.8%; 1,462 men and 2,012 women). There were a total of 1,340 deaths (38.6%) in the entire cohort during the follow-up period (702 deaths in men and 638 in women), of which 457 were fatal CVD deaths (222 in men and 235 in women). In total, 768 CVD events (457 fatal CVD events and 311 non-fatal CVD events) were observed. Table 1 shows the distribution of CVRF and CVD events by sex.

Table 2 shows the multivariate Cox proportional hazards model of mean 10-year first fatal or non-fatal CVD for men (panel A) and women (panel B). Age was the strongest predictor of CVD in both men and women. In men, the variables most strongly associated with CVD were high blood pressure treatment (HR: 1.35; 95% CI: 1.067–1.710), diabetes (HR: 1.359; 95% CI: 0.997–1.852), and smoking (HR: 1.207; 95% CI: 0.945–1.541). In women, the variables most strongly associated with CVD were smoking (HR: 1.881; 95% CI: 1.356–2.609) and diabetes (HR: 1.285; 95% CI: 0.967–

1.707). The model showed a discriminative power (C-statistic) of 0.656 (95% CI 0.601–0.701) in men, and 0.702 (95% CI 0.669–0.723) in women.

In a second stage of the analysis, we used age as a time-scale variable rather than a typical independent variable. The Cox proportional hazards model significantly improved for diabetes as a predictive variable. The HR of diabetes increased from 1.37 to 1.48 in men and from 1.28 to 1.34 in women (data shown in the Appendix A supplementary material). The HR of other variables included in the Cox proportional hazards model (serum TC, smoking, SBP, and antihypertensive treatment) did not increase when age was treated as a time-scale variable.

Table 3 shows the individual absolute 10-year cardiovascular risk specifically for men who do not smoke (panel A) and men who smoke (panel B). Table 4 shows the corresponding values for women who do not smoke (panel A) and women who smoke (panel B). This visual format facilitates the interpretation of individual absolute 10-year total cardiovascular risk (fatal and non-fatal CVD) for each individual's sex and smoking status while also taking into account his or her antihypertensive treatment, diabetes status, age, TC, and SBP.

Discussion

The EPICARDIAN score is based on a large cohort of 3,474 elderly Spanish citizens. Previous scores, such as the Framingham score and the European SCORE risk chart, are based on populations recruited before the 1980s, when the prevalence of risk factors in the population was lower. In contrast, the EPICARDIAN cohort was assembled more recently and provides a risk estimation for people who receive or do not receive antihypertensives or other cardiovascular drugs. The EPICARDIAN score also overcomes the problem of applying β -coefficients derived from studies on middle-aged populations to older adults, which may lead to an inadequate risk estimation in the elderly.

Age is the strongest predictor of cardiovascular risk in older men and women. When using age as a time-scale variable rather than as a standard variable, the performance of the Cox proportional hazards model improved, particularly for women. For example, diabetes emerged as an independent predictor in women (in the original model diabetes

was borderline). For example, diabetes emerged as an independent predictor in women (in the original model diabetes was borderline), though the finding was not statistically significant.

A different CVRF pattern was observed in men versus women. In men, diabetes was the strongest predictive factor and high blood pressure treatment had a greater impact than it did in women. Smoking also showed a significant association with CVD, which was stronger in women than in men. Similar to previous studies^{21,22}, the contribution of TC to CVD acts in an inverse manner in those older than 70 years compared to in those younger than 70 years. The absence of a positive predictive value of TC raises the question of whether risk estimation in the elderly may warrant a different approach than in middle-aged individuals and confirms that the predictive power of certain classic risk factors such as hypercholesterolemia diminish with age.

Current scores used to predict CVD in the elderly mainly rely on calibrated risk equations based on the original Framingham²³ and European SCORE risk charts²⁴. Important limitations of these scores include the small number of participants older than 70 years of age, the occupational origin of some cohorts, and the consideration of CVD mortality as the only main outcome in the predictive model. In contrast, the EPICARDIAN score includes a significant proportion of individuals older than 75 years of age and indicates total CVD risk, which is a more comprehensive estimate of individual total risk in a Mediterranean country such as Spain, which has low rates of coronary heart disease (CHD). Moreover, previous European scores for the elderly do not include diabetes or, as is the case in the Framingham study, the prediction is based on a sample with a small proportion of individuals with diabetes (4%) whose diagnoses were not made using the current international definition of diabetes. Finally, a unique feature of the EPICARDIAN score is that it accounts for the use of antihypertensive drugs—the most common treatment in older adults—which addresses a major gap in previous risk assessment tools²⁵.

Recently, a new European SCORE risk chart for elderly individuals, SCORE-OP, has been published²⁶. We applied the SCORE-OP to our population and found that mean 10-year CVD risk was significantly lower in men and women than what was obtained with the EPICARDIAN charts²⁷. This is most likely due to the fact that the mean age of the EPICARDIAN study population is older and the prevalence of diabetes and

smoking is higher than in the cohorts included in the SCORE-OP, which mainly came from Northern and Central Europe. Also, the two equations do not include exactly the same parameters. For instance, the EPICARDIAN equation includes hypertension treatment as a variable in the model whereas the SCORE-OP includes c-HDL values. We have also found that the SCORE-OP identifies fewer patients 65 years of age and older as being at high or very high risk than the original SCORE risk chart for low-risk countries, which includes Spain²⁷.

The EPICARDIAN charts consider only the major CVRF. Other factors such as family history of CVD, fibrinogen levels, physical activity, waist circumference, or C-reactive protein levels can theoretically modulate the CVD risk in the elderly. In contrast, as mentioned above, the predictive value of classic risk factors such as hypercholesterolemia or systolic hypertension weakens with age^{8,21}. Therefore, the absolute risk estimations in some boxes, particularly in groups of older adults with few individuals with very high levels of TC and SBP, could be less accurate as a result.

Our findings are in line with a recently published systematic review²⁸ showing the inconsistency of predictive values of traditional CVD risk factors such as cholesterol fractions, blood pressure, smoking, or BMI in elderly individuals. These findings justify the development of new risk models like the EPICARDIAN score, which consider competing causes of death.

Our study has several strengths. The sample included individuals recruited from urban and rural settings, from different geographical locations, from a wide age range within the segment of the population defined as elderly, and included a high proportion of individuals with diabetes. The availability of information on CVRF treatment, particularly antihypertensive treatment, is another strength of this study. It provides useful information for clinicians when it comes to adjusting estimated CVD risk in patients already receiving antihypertensive treatment. The EPICARDIAN cohort provides the first prospective association between total CVD and multiple CVRF for the elderly in Spain, a country with low incidence of CVD. The EPICARDIAN score allows for the direct estimation of total CVD risk based on the current background risk of the elderly population rather than based on foreign scores calibrated for low-risk European populations. Predictions based on these calibrations may not be accurate if a

long time has passed and a marked change in CVD mortality has occurred between when the risk score was designed and when it is applied to different populations.

Conclusions

Our results allow for adjusting the degree to which some specific CVRF, such as cholesterol levels, may affect the specific population they were drawn from. It is expected that this risk score will be validated in the future.

The EPICARDIAN score offers a novel estimation of total CVD risk by incorporating hypertensive treatment to the risk calculation. CVD risk is significantly higher in elderly men with diabetes, elderly men who receive antihypertensive treatment, and elderly women who smoke. The score is a practical tool that clinicians can use to estimate the total individual CVD risk in Spanish individuals older than 70 years of age.

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Conflicts of interests

The authors declare that they do not have any conflicts of interests.

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References

1. Conroy RM, Pyörälä K, Fitzgerald AP, Sans S, Menotti A, De Backer G, et al. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. *Eur Heart J*. 2003;24:987-1003.
2. Gabriel R, Brotons C, Tormo MJ, Segura A, Rigo F, Elosua R, et al. The ERICE-score: the new native cardiovascular score for the low-risk and aged Mediterranean population of Spain. *Rev Esp Cardiol (Engl Ed)*. 2015;68:205-15.
3. Liew SM, Doust J, Glasziou P. Cardiovascular risk scores do not account for the effect of treatment: a review. *Heart*. 2011;97:689-97.
4. Cooney MT, Dudina AL, Graham IM. Value and limitations of existing scores for the assessment of cardiovascular risk. A review for clinicians. *J Am Coll Cardiol*. 2009;54:1209-27.
5. Hoes AW, Grobbee DE, Valkenburg HA, Lubsen J, Hofman A. Cardiovascular risk and all cause mortality: a 12-year follow-up study in The Netherlands. *Eur J Epidemiol*. 1993;9:285-92.
6. De Ruijter W, Westendorp RG, Assendelft WJ, den Elzen WP, de Craen AJ, le Cessie S, et al. Use of Framingham risk score and new biomarkers to predict cardiovascular mortality in older people: population based observational cohort study. *BMJ*. 2009;338:a3083.
7. Satish S, Freeman DH Jr, Ray L, Goodwin JS. The relationship between blood pressure and mortality in the oldest old. *J Am Geriatr Soc*. 2001;49:367-74.
8. Bemmels T, Gussekloo J, Westendorp RG, Blauw GJ. In a population-based prospective study, no association between high blood pressure and mortality after age 85 years. *J Hypertens*. 2006;24:287-92.
9. Oates DJ, Berlowitz DR, Glickman ME, Silliman RA, Borzecki AM. Blood pressure and survival in the oldest old. *J Am Geriatr Soc*. 2007;55:383-8.
10. Rastas S, Pirttilä T, Viramo P, Verkkoniemi A, Halonen P, Juva K, et al. Association between blood pressure and survival over 9 years in a general population aged 85 and older. *J Am Geriatr Soc*. 2006;54:912-8.
11. Odden MC, Peralta CA, Haan MN, Covinsky KE. Rethinking the association of high blood pressure with mortality in elderly adults: the impact of frailty. *Arch Intern Med*. 2012;172:1162-8.
12. Weverling-Rijnsburger AW, Blauw GJ, Lagaay AM, Knook DL, Meinders AE, Westendorp RG. Total cholesterol and risk of mortality in the oldest old. *Lancet*. 1997;350:1119-23.

13. Novella B, Alonso M, Rodriguez-Salvanés F, Susi R, Reviriego B, Escalante L, et al. Ten-year incidence of fatal and non-fatal myocardial infarction in the elderly population of Madrid. *Rev Esp Cardiol*. 2008;61:1140-9.
14. Gabriel R, Alonso M, Reviriego B, Muñoz J, Vega S, López I, et al. Ten-year fatal and non-fatal myocardial infarction incidence in elderly populations in Spain: the EPICARDIAN cohort study. *BMC Public Health*. 2009;9:360-8.
15. Ray KK, Kastelein JJ, Boekholdt SM, Nicholls SJ, Khaw KT, Ballantyne CM, et al. The ACC/AHA 2013 guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular disease risk in adults: the good the bad and the uncertain: a comparison with ESC/EAS guidelines for the management of dyslipidaemias 2011. *Eur Heart J*. 2014;35:960-8.
16. Carstensen B, Lindström J, Sundvall J, Borch-Johnsen K, Tuomilehto J, DPS Study Group. Measurement of blood glucose: comparison between different types of specimens. *Ann Clin Biochem*. 2008;45:140-8.
17. Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. *Circulation*. 1998;97:1837-47.
18. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LS, Izzo JL Jr, et al. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. The JNC 7 report. *JAMA*. 2003;289:2560-72.
19. World Health Organization. Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia. Report of a WHO/IDF consultation. Geneva: WHO; 2006.
20. Tunstall-Pedoe H, Kuulasmaa K, Amouyel P, Arveiler D, Rajakangas AM, Pajak A. Myocardial infarction and coronary death in the World Health Organization MONICA Project. Registration procedures, event rates and case-fatality rates in 38 populations from 21 countries in four continents. *Circulation*. 1994;90:583-612.
21. Tuikkala P, Hartikainen S, Korhonen SM, Lavikainen P, Kettunen R, Sulkava R, et al. Serum total cholesterol levels and all-cause mortality in a home-dwelling elderly population: a six-year follow-up. *Scand J Prim Health Care*. 2010;28:121-7.
22. Tilvis R, Valvanne JN, Strandberg TE, Miettinen TA. Prognostic significance of serum cholesterol, lathosterol, and sitosterol in old age; a 17-year population study. *Ann Med*. 2011;43:292-301.
23. Kannel WB. Coronary heart disease risk factors in the elderly. *Am J Geriatr Cardiol*. 2002;11:101-7.
24. Sans S, Fitzgerald AP, Royo D, Conroy R, Graham I. Calibrating the SCORE cardiovascular risk chart for use in Spain. *Rev Esp Cardiol*. 2007;60:476-85.

25. McGovern PG, Pankow JS, Sharar E, Doliszny KM, Folsom AR, Blackburn H, et al. Recent trends in acute coronary heart disease-mortality, morbidity, medical care, and risk factors. *N Engl J Med.* 1996;334:884-90.
26. Cooney MT, Selmer R, Lindman A, Tverdal A, Menotti A, Thomsen T, et al. Cardiovascular risk estimation in older persons: SCORE OP. *Eur J Prev Cardiol.* 2016; 23:1093-103.
27. Brotons C, Moral I, Fernández D, Cuixart L, Soteras A, Puig M. Assessment of the new SCORE OP cardiovascular risk charts in patients older than 65 years. *Rev Esp Cardiol (Engl Ed).* 2016;69:981-3.
28. Van Bussel EF, Hoevenaar-Blom MP, Poortvliet RKE, Gussekloo J, van Dalen JW, van Gool WA, et al. Predictive value of traditional risk factors for cardiovascular disease in older people: a systematic review. *Prev Med.* 2020;132:105986, doi:10.1016/j.ypmed.2020.105986.

Table 1. Demographic characteristics and distribution of major cardiovascular risk factors in the EPICARDIAN study population at baseline.

Cardiovascular risk factors	Men n (%) n = 1,462	Women n (%) n = 2,012	All n (%) n = 3,474
Age groups (years)			
65–69	479 (32.8)	622 (30.9)	1,101 (31.7)
70–74	425 (29.1)	549 (27.3)	974 (28.0)
75–79	259 (17.7)	386 (19.2)	645 (18.6)
80–84	184 (12.6)	263 (13.1)	447 (12.9)
≥ 85	115 (7.9)	192 (9.5)	307 (8.8)
Hypertension ^a	465 (32.0)	1,003 (50.1)	1,468 (42.5)
Hypercholesterolemia ^{a,b}	337 (23.4)	634 (32.1)	971 (28.4)
Diabetes ^c	156 (10.7)	243 (12.1)	399 (11.5)
Obesity ^d	279 (19.1)	590 (29.3)	869 (25.0)
Smoker ^e	340 (23.3)	72 (3.6)	412 (11.9)
Ex-smoker	741 (50.8)	89 (4.4)	830 (23.9)
First cardiovascular event	356 (24.4)	412 (20.5)	768 (22.1)
Fatal cardiovascular event	222 (15.2)	235 (11.7)	457 (13.2)

Number of cases and their corresponding percentages (%).

^a Systolic Blood Pressure \geq 140 mmHg, Diastolic Blood Pressure \geq 90 mmHg, or antihypertensive treatment.

^b Total cholesterol \geq 5.1 mg/dL or lipid-lowering treatment.

^c Blood glucose \geq 126 mg/dL or antidiabetic treatment.

^d Body Mass Index (BMI) \geq 30 kg/m².

^e At least 1 cigarette per day or 5 cigarettes per week during the last year.

Table 2. Multivariate Cox proportional hazards model for the mean 10-year risk for a first fatal or non-fatal cardiovascular events.

Panel A. Men	β	SE	Wald	df	<i>p</i> value	exp. (β)	95% CI for exp (β)	
							Lower	Upper
Age (ref. 65–69 years-old)			76.291	4	0.000			
70–74 years	0.306	0.153	3.997	1	0.046	1.358	1.006	1.832
75–79 years	0.689	0.162	18.169	1	0.000	1.991	1.451	2.733
80–84 years	0.956	0.170	31.466	1	0.000	2.601	1.862	3.631
≥ 85 years	1.453	0.187	60.378	1	0.000	4.277	2.965	6.172
Diabetes	0.307	0.158	3.778	1	0.052	1.359	0.997	1.852
Smoking	0.188	0.125	2.275	1	0.131	1.207	0.945	1.541
Systolic blood pressure (ref. < 140 mmHg)			3.027	3	0.387			
140–149 mmHg	0.098	0.140	0.485	1	0.486	1.103	0.837	1.452
150–159 mmHg	0.092	0.162	0.325	1	0.569	1.096	0.799	1.505
≥ 160 mmHg	0.257	0.148	3.022	1	0.082	1.293	0.968	1.726
Total cholesterol (ref. < 160 mg/dL)			5.916	3	0.116			
160–199 mg/dL	0.175	0.179	0.956	1	0.328	1.191	0.839	1.692
200–239 mg/dL	0.119	0.176	0.455	1	0.500	1.126	0.797	1.590
≥ 240 mg/dL	−0.170	0.191	0.791	1	0.374	0.844	0.580	1.227
Antihypertensive treatment	0.301	0.120	6.259	1	0.012	1.351	1.067	1.710
Panel B. Women	β	SE	Wald	df	<i>p</i> value	exp. (β)	95% CI for exp (β)	
							Lower	Upper
Age (ref. 65–69 years-old)			168.745	4	0.000			
70–74 years	0.596	0.161	13.734	1	0.000	1.815	1.324	2.488
75–79 years	0.971	0.164	35.104	1	0.000	2.639	1.915	3.639
80–84 years	1.380	0.170	66.284	1	0.000	3.976	2.852	5.544
≥ 85 years	2.038	0.170	143.523	1	0.000	7.677	5.500	10.716
Diabetes	0.251	0.145	2.996	1	0.083	1.285	0.967	1.707
Smoking	0.632	0.167	14.317	1	0.000	1.881	1.356	2.609
Systolic blood pressure (ref. < 140 mmHg)			2.998	3	0.392			
140–149 mmHg	0.013	0.135	0.009	1	0.925	1.013	0.777	1.320

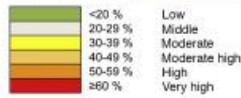
150–159 mmHg	0.141	0.145	0.944	1	0.331	0.868	0.653	1.154
≥ 160 mmHg	0.198	0.138	2.062	1	0.151	0.820	0.626	1.075
Total cholesterol (ref. < 160 mg/dL)			3.129	3	0.372			
160–199 mg/dL	0.229	0.213	1.160	1	0.282	0.795	0.524	1.207
200–239 mg/dL	0.319	0.205	2.414	1	0.120	0.727	0.486	1.087
≥ 240 mg/dL	0.339	0.207	2.677	1	0.102	0.712	0.475	1.069
Antihypertensive treatment	0.123	0.106	1.338	1	0.247	1.131	0.918	1.393

SE: standard error; df: degrees of freedom; 95% CI: 95% confidence interval; $\exp(\beta)$ used to obtain relative risk.

Table 3. Individual total 10-year absolute cardiovascular risk by age, diabetes status, antihypertensive treatment, total cholesterol, and systolic blood pressure levels for men who do not smoke (panel A) and men who smoke (panel B).

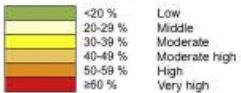
Panel A. Men who do not smoke.

Age, years	Total cholesterol, mg/dL	NON-SMOKER								NON-SMOKER								
		NON-DIABETIC				NON-DIABETIC				DIABETIC				DIABETIC				
		SBP NO HYPERTENSION TREATMENT, mmHg				SBP HYPERTENSION TREATMENT, mmHg				SBP NO HYPERTENSION TREATMENT, mmHg				SBP HYPERTENSION TREATMENT, mmHg				
		<160	160-199	200-239	≥240	<160	160-199	200-239	≥240	<160	160-199	200-239	≥240	<160	160-199	200-239	≥240	
≥85	SBP	≥160	35	40	41	34	44	51	52	44	42	48	49	41	52	59	60	52
		150-160	32	37	38	31	41	46	48	40	38	44	45	37	48	54	56	47
		140-150	33	38	39	33	42	48	50	42	40	46	47	39	50	56	58	49
80-84	SBP	<140	29	34	35	29	37	43	44	37	35	40	41	35	45	51	52	44
		≥160	29	34	34	28	37	43	44	37	35	40	41	34	44	50	56	44
		150-160	26	30	31	26	34	39	40	33	32	37	38	31	40	46	47	40
75-79	SBP	140-150	27	32	33	27	35	41	42	35	33	38	39	33	42	48	49	42
		<140	24	28	29	23	31	36	37	31	29	34	35	29	37	43	44	37
		≥160	24	28	29	24	32	37	38	31	30	34	35	29	38	44	45	37
70-74	SBP	150-160	22	26	26	22	29	33	34	28	27	31	32	26	35	40	41	34
		140-150	23	28	28	23	30	35	36	30	28	33	33	28	36	42	43	36
		<140	20	24	24	20	26	31	32	26	24	29	29	24	32	37	38	31
65-69	SBP	≥160	19	22	22	18	24	29	29	24	23	27	27	22	30	34	35	29
		150-160	17	20	20	16	22	26	26	22	20	24	25	20	27	31	32	26
		140-150	17	21	21	17	23	27	28	23	21	25	26	21	28	33	34	28
65-69	SBP	<140	15	18	18	15	20	24	24	20	19	22	23	18	24	29	29	24
		≥160	15	17	18	14	20	23	24	19	18	21	22	18	24	28	29	24
		150-160	13	16	16	13	18	21	21	17	16	19	20	16	22	25	26	21
65-69	SBP	140-150	14	16	17	14	18	22	22	18	17	20	21	17	23	27	27	22
		<140	12	14	15	12	16	19	19	16	15	18	18	15	20	23	24	19



Panel B. Men who smoke.

Age, years	Total cholesterol, mg/dL	SMOKER								SMOKER								
		NON-DIABETIC				NON-DIABETIC				DIABETIC				DIABETIC				
		SBP NO HYPERTENSION TREATMENT, mmHg				SBP HYPERTENSION TREATMENT, mmHg				SBP NO HYPERTENSION TREATMENT, mmHg				SBP HYPERTENSION TREATMENT, mmHg				
		<160	160-199	200-239	≥240	<160	160-199	200-239	≥240	<160	160-199	200-239	≥240	<160	160-199	200-239	≥240	
≥85	SBP	≥160	37	42	43	36	46	53	54	46	44	50	51	43	54	61	62	54
		150-160	33	38	39	33	42	48	50	42	40	46	47	39	50	56	58	49
		140-150	35	40	41	34	44	50	51	44	41	47	49	41	52	58	60	51
80-84	SBP	<140	30	35	36	30	39	45	46	39	37	42	43	36	46	53	54	46
		≥160	30	35	36	30	39	45	46	38	36	42	43	36	46	52	54	45
		150-160	27	32	33	27	35	41	42	35	33	38	39	33	42	48	49	42
75-79	SBP	140-150	29	33	34	28	37	43	44	36	35	40	41	34	44	50	51	43
		<140	25	29	30	25	33	38	39	32	30	35	36	30	39	45	46	38
		≥160	26	30	31	25	33	38	39	33	31	36	37	31	40	46	47	39
70-74	SBP	150-160	23	27	28	23	30	35	36	30	28	33	33	28	36	42	43	36
		140-150	24	28	29	24	31	37	37	31	29	34	35	29	38	43	45	37
		<140	21	25	25	21	28	32	33	27	26	30	31	25	33	39	40	33
65-69	SBP	≥160	19	23	24	19	26	30	31	25	24	28	29	23	31	36	37	31
		150-160	17	21	21	17	23	27	28	23	21	25	26	21	28	33	34	28
		140-150	18	22	22	18	24	28	29	24	23	26	27	22	29	34	35	29
65-69	SBP	<140	16	19	19	16	21	25	25	21	20	23	24	19	26	30	31	25
		≥160	16	18	19	15	21	24	25	20	18	22	23	19	25	29	30	25
		150-160	14	16	17	14	18	22	22	18	17	20	21	17	23	27	27	22
65-69	SBP	140-150	15	17	18	14	19	23	24	19	18	21	22	18	24	28	29	23
		<140	13	15	15	12	17	20	20	17	16	18	19	15	21	24	25	20



SBP: systolic blood pressure.

Table 4. Individual total 10-year absolute cardiovascular risk by age, diabetes status, antihypertensive treatment, total cholesterol, and systolic blood pressure levels for women who do not smoke (panel A) and women who smoke (panel B).

Panel A. Women who do not smoke.

Age, years	Total cholesterol, mg/dL	NON-SMOKER								NON-SMOKER								
		NON-DIABETIC				NON-DIABETIC				DIABETIC				DIABETIC				
		SBP NO HYPERTENSION TREATMENT, mmHg				SBP HYPERTENSION TREATMENT, mmHg				SBP NO HYPERTENSION TREATMENT, mmHg				SBP HYPERTENSION TREATMENT, mmHg				
		<160	160-199	200-239	≥240	<160	160-199	200-239	≥240	<160	160-199	200-239	≥240	<160	160-199	200-239	≥240	
≥85	SBP	≥160	41	37	36	35	47	42	41	40	48	43	42	41	53	49	48	47
		150-160	43	39	38	37	49	44	43	42	50	45	44	43	55	51	50	49
		140-150	49	45	44	43	55	50	49	48	56	52	50	49	62	57	56	55
		<140	48	44	43	42	50	48	47	46	55	51	50	49	57	55	55	55
80-84	SBP	≥160	26	23	23	22	30	27	26	26	31	28	27	26	35	32	31	30
		150-160	28	25	24	23	32	28	27	27	33	29	28	28	37	33	32	32
		140-150	32	29	28	27	37	33	32	31	38	34	33	32	43	39	38	37
		<140	32	28	27	27	36	32	32	31	37	33	32	32	42	38	37	36
75-79	SBP	≥160	21	18	18	17	24	21	21	20	25	22	21	21	28	25	25	24
		150-160	22	19	19	18	25	22	22	21	26	23	22	22	30	27	26	25
		140-150	26	23	22	22	29	26	26	25	30	27	26	26	35	31	30	30
		<140	25	22	22	21	29	26	25	24	30	27	26	25	34	30	30	29
70-74	SBP	≥160	15	14	13	13	18	16	15	15	18	16	16	15	21	19	18	18
		150-160	16	14	14	14	19	17	16	16	19	17	17	16	22	20	19	19
		140-150	19	17	16	16	22	20	19	19	23	20	20	19	26	23	23	22
		<140	19	17	16	16	22	19	19	18	22	20	19	19	26	23	22	22
65-69	SBP	≥160	9	8	8	8	11	9	9	9	11	10	9	9	13	11	11	11
		150-160	10	8	8	8	11	10	10	9	12	10	10	10	13	12	11	11
		140-150	11	10	10	9	13	12	11	11	14	12	12	11	16	14	14	13
		<140	11	10	9	9	13	11	11	11	13	12	11	11	16	14	13	13

	<20 %	Low
	20-29 %	Middle
	30-39 %	Moderate
	40-49 %	Moderate high
	50-59 %	High
	≥60 %	Very high

Panel B. Women who smoke.

Age, years	Total cholesterol, mg/dL	SMOKER								SMOKER								
		NON-DIABETIC				NON-DIABETIC				DIABETIC				DIABETIC				
		SBP NO HYPERTENSION TREATMENT, mmHg				SBP HYPERTENSION TREATMENT, mmHg				SBP NO HYPERTENSION TREATMENT, mmHg				SBP HYPERTENSION TREATMENT, mmHg				
		<160	160-199	200-239	≥240	<160	160-199	200-239	≥240	<160	160-199	200-239	≥240	<160	160-199	200-239	≥240	
≥85	SBP	≥160	82	57	56	55	88	63	62	61	69	64	63	62	78	70	69	68
		150-160	84	59	58	57	70	65	64	63	71	67	65	64	77	73	71	70
		140-150	71	66	65	64	77	72	71	70	78	73	72	71	83	79	78	77
		<140	70	65	64	63	76	71	70	69	77	72	71	70	82	78	77	76
80-84	SBP	≥160	43	38	37	37	48	44	42	42	49	45	44	43	55	50	49	48
		150-160	44	40	39	38	50	45	44	43	51	47	45	45	57	52	51	50
		140-150	51	46	45	44	57	52	51	50	58	53	52	51	64	59	58	57
		<140	50	45	44	43	56	51	50	49	57	52	51	50	63	58	57	56
75-79	SBP	≥160	34	31	30	29	39	35	34	34	40	36	35	35	45	41	40	39
		150-160	36	32	32	31	41	37	36	35	42	38	37	36	47	43	42	41
		140-150	42	38	37	36	47	43	42	41	48	44	43	42	54	49	48	47
		<140	41	37	36	35	46	42	41	40	47	43	42	41	53	48	47	46
70-74	SBP	≥160	26	23	23	22	30	27	26	25	31	28	27	26	35	32	31	30
		150-160	27	25	24	23	31	28	27	27	32	29	28	28	37	33	32	32
		140-150	32	29	28	27	37	33	32	31	38	34	33	32	43	38	37	37
		<140	31	28	27	27	36	32	31	31	37	33	32	32	42	38	37	36
65-69	SBP	≥160	16	14	14	13	18	16	16	15	19	17	16	16	22	19	19	18
		150-160	17	15	14	14	19	17	17	16	20	18	17	17	23	21	20	19
		140-150	20	18	17	17	23	20	20	19	24	21	20	20	27	24	23	23
		<140	19	17	17	16	22	20	19	19	23	20	20	19	26	24	23	22

	<20 %	Low
	20-29 %	Middle
	30-39 %	Moderate
	40-49 %	Moderate high
	50-59 %	High
	≥60 %	Very high

SBP: systolic blood pressure.