#### **ORIGINAL**

# Estimation of heart age in 139.634 spanish workers: influence of sociodemographic variables and healthy habits and determination of cut-off points.

Estimación de la edad cardiaca en 139.634 trabajadores españoles: influencia de variables sociodemográficas y hábitos saludables y determinación de puntos de corte

Tomás Sastre Alzamora<sup>1</sup>, Pilar Tomás-Gil<sup>1</sup>, Pau Martí-Lliteras<sup>1</sup>, Lucio Pallarés Ferreres<sup>2</sup>, José Ignacio Ramírez-Manent<sup>1,3</sup>, Angel Arturo López-González<sup>1</sup>

Grupo ADEMA-Salud del IUNICS. Universitat de les Illes Balears. Spain
Hospital Son Espases. Balearic Islands Health Service. Spain
Familiy Medicine. Balearic Islands Health Service. Spain

#### Corresponding author

José Ignacio Ramírez-Manent E-mail: jignacioramirez@telefonica.net **Received:** 11 - X - 2022 **Accepted:** 24 - XI- 2022

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## **Abstract**

**Aim:** To assess the relationship of sociodemographic variables and healthy habits with heart age values. To establish cut-off points for moderate and high cardiac age.

**Methods:** Heart age was determined in 139.634 workers and its relationship with sociodemographic variables (age, sex, social class and educational level) and healthy habits (tobacco and alcohol consumption, physical activity and adherence to the Mediterranean diet) was assessed. The cut-off points for moderate and high cardiac age were determined by applying ROC curves.

**Results:** The mean values and prevalence of high heart age values are influenced by all the sociodemographic variables and healthy habits analyzed, especially by age and tobacco consumption. The cut-off points established for moderate and high heart age are set at +11 and +17 years respectively.

**Conclusions:** All sociodemographic variables, especially age, and healthy habits, mainly smoking, influence heart age values. Heart age values 11 and 17 years higher than chronological age are considered moderate and high respectively.

Key words: Heart age, cardiovascular risk, smoking, adherence to Mediterranean diet, physical activity, social class.

#### Resumen

**Objetivo:** Valorar la relación de variables sociodemográficas y hábitos saludables con los valores de edad del corazón. Establecer puntos de corte para edad cardiaca moderada y alta.

**Metodología:** Se determina la edad del corazón en 139.634 trabajadores y se valora su relación con variables sociodemográficas (edad, sexo, clase social y nivel de estudios) y hábitos saludables (consumo de tabaco y alcohol, actividad física y adherencia a la dieta mediterránea). Se determinan los puntos de corte de la edad cardiaca moderada y alta aplicando curvas ROC. **Resultados:** Los valores medios y la prevalencia de valores elevados de edad del corazón se ven influidos por todas las variables sociodemográficas y hábitos saludables analizados, especialmente por la edad y el consumo de tabaco. Los puntos de corte establecidos para edad cardiaca moderada y alta se establecen en +11 y +17 años respectivamente.

**Conclusiones:** Todas las variables sociodemográficas, especialmente la edad, y los hábitos saludables, principalmente el tabaco, influyen en los valores de edad del corazón. Valores de edad cardiaca superiores en 11 y 17 años a la edad cronológica se consideran moderados y alto respectivamente.

Palabras clave: Edad del corazón, riesgo cardiovascular, tabaco, adherencia a la dieta mediterránea, actividad física, clase social.

## Introduction

Cardiovascular diseases continue to be the leading cause of morbidity and mortality in all countries of the world, although their prevalence is particularly high in the most developed countries, and is continuously increasing<sup>1</sup>. Many scales have been developed to determine the level of risk of presenting a cardiovascular event, generally over a given period of time, which has mostly been estimated to be 10 years. The oldest scale is the Framingham scale developed on the basis of a cohort of people from this North American population<sup>3</sup>. Subsequently, this scale was adapted to the characteristics of different countries4. Years later, country-specific scales that were not based on Framingham began to be developed<sup>5,6</sup>. However, despite their undoubted usefulness, all these scales suffer from a common defect, which is the relativization of risk, for example, if we apply the REGICOR scale<sup>7</sup> (adaptation of the Framingham scale to the Spanish population) to a 60-year-old male smoker, with a systolic blood pressure of 145 mmHg and diastolic of 95 mmHg, total cholesterol of 250 mg/dL and HDL of 38 mg/dL, the probability of suffering a cardiovascular event in the next 10 years is 16%, or in other words, he has an 84% probability of not suffering it.

For this reason, in recent years tools have been developed to assess cardiovascular risk not as a percentage but as an absolute number. Based on this, the heart age tool was created<sup>8</sup> which, if applied to the same individual as above, will give us a value of 77 years, that is, 17 years older than his biological age. This value has been, according to a study by our group, more useful for modifying healthy habits and thereby reducing cardiovascular risk than the use of traditional risk scales.

The aim of this study is to determine, on the one hand, the cut-off points for heart age that are considered moderate and high and, on the other, to assess the influence of sociodemographic variables (age, sex, social class and level of education) and healthy habits (physical exercise, Mediterranean diet, tobacco and alcohol consumption) on heart age values.

# **Methods**

A descriptive, cross-sectional study was carried out using data from occupational medical examinations performed between January 2019 and June 2020 on 139,634 Spanish workers (83,282 men and 56,352 women) in the primary, secondary and tertiary sectors.

## Inclusion criteria were:

- Age between 18 and 69 years.
- Working in one of the companies included in the study.
- Agreeing to participate in the study.

The flow chart is presented in **figure 1**.

#### Determination of variables

The health professionals of the different companies were responsible for obtaining all the clinical, analytical and anthropometric variables necessary for the calculation of heart age. Interobserver bias was minimized by standardizing the measurements.

Waist circumference was measured with a tape measure placed at the level of the last rib, with the person in bipedestation and the abdomen relaxed.

Blood pressure was obtained with an OMRON M3 sphygmomanometer, while the patient was seated and after a 10-minute rest. Three measurements were taken and the mean was obtained.

The analysis was performed after a 12-hour fasting period using enzymatic techniques for glucose and using enzymatic techniques for blood glucose, triglycerides and cholesterol and precipitation techniques for HDL-cholesterol. LDL-cholesterol was obtained indirectly using the Friedewald formula (valid only for triglyceride values below 400). All analytical parameters were expressed in mg/dL.

Figure 1: Flow chart.

Workers start the study n= 142.296 (79.860 men and 57.256 women) Workers excluded n= 2.662 - 159 did not agree to participate in the study - 298 were under 20 years old or over 69 years old - 2.205 did not have any variable to calculate the differentet scales 139.634 finally entered the study (83.282 men

It is a tool based on the classic Framingham cardiovascular risk scale that allows calculation of a patient's probability of developing cardiovascular disease in the next ten years<sup>9</sup>. To calculate the age of the heart, the following are required: age, sex, height (in centimeters), weight (in kilograms), waist circumference

and 56.352 women)

(in centimeters), family history (parents) of cardiovascular disease and age when they first suffered it, presence or absence of diabetes, tobacco use (if not currently smoking, we ask whether smoking has been stopped in the last year), total cholesterol and HDL cholesterol values, systolic blood pressure values, and whether the patient is currently under antihypertensive treatment.

For the calculation, the "Heart age calculator" tool is used, which, in its Spanish version, is available on the web page: http://www.heartage.me. The scale is applicable between the ages of 18 and 80 years. The range of years gained or lost is 20, with a minimum age of 18 years and a maximum of 80 years.

An interesting concept is avoidable lost life years ALLY<sup>10</sup> which we can define as the difference between chronological age and heart age.

The baseline blood glucose results were classified based on the recommendations of the American Diabetes Association  $^{11}$ , whereby the individual was considered to have diabetes if the values were >125 mg/dl in two different determinations, if he/she also had HbA1c  $\geq$  6.5% or if the individual was receiving hypoglycemic treatment.

Any person who had consumed one or more cigarettes per day, or the equivalent in other consumption modalities, during the last 30 days or who had guit smoking less than one year before was considered a smoker. The heart-healthy diet was assessed with the "Mediterranean diet adherence questionnaire" of the PREDIMED study<sup>12</sup>. It consists of 14 questions that are scored with 0 and 1 point. Values of 9 or more indicate good adherence and that the diet is heart-healthy. Physical activity is assessed using the International Physical Activity Questionnaire IPAQ (International Physical Activity Questionnaire)<sup>13</sup>, which assesses physical activity in the last week. Alcohol consumption is assessed using the units of alcohol (UA). In Spain, one UA is equal to 10 grams of pure ethanol. High consumption was considered as from 14 UA in women and 21 in men per week<sup>14</sup>.

Based on the 2011 National Classification of Occupations (CNO-11) and applying the criteria of the Spanish Society of Epidemiology<sup>15</sup>, the workers were classified into three social classes: I. Managers, university professionals. II. Intermediate occupations and skilled self-employed workers. III. Unskilled workers.

#### Ethical considerations and aspects

The ethical standards of the institutional research committee and the 2013 Declaration of Helsinki were respected in the study. Anonymity and confidentiality of the data collected could be guaranteed at all times. The study had the approval of the Research Ethics Committee of the Balearic Islands (CEI-IB): IB 4383/20. The data of

each of the workers included in the study were coded and only the person responsible for the study was able to know the identity of each person. The research team undertook to strictly comply with the Organic Law 3/2018, of December 5, on the protection of personal data and guarantee of digital rights, guaranteeing the participant in this study the exercise of the rights of access, rectification, cancellation and opposition of the data collected.

## Statistical analysis

For quantitative variables, the Student's t-test was used to determine the mean and standard deviation. For qualitative variables, the chi-square test was applied and prevalences were determined. The cut-off points to determine the cardiac age considered moderate and high were obtained using ROC curves. The area under the curve (AUC), the cut-off points with their sensitivity, specificity and Youden index were calculated. Multivariate analysis was performed by multinomial logistic regression. SPSS 28.0 was used for the statistical analysis. The accepted level of statistical significance was p<0.05.

# **Results**

**Table I** shows the anthropometric and clinical characteristics of the individuals included in the study. A total of 139.634 (83.282 men 59.6% and 56.352 women 40.4%) were included in the analyses. The mean age of the sample was slightly over 40 years, the majority group being between 30 and 49 years of age. Anthropometric, clinical and analytical values were more unfavorable in men. Most of the workers were of social class III and with primary education. In men, most of them did not perform regular physical activity and did not have a healthy diet (in women the situation was better). Almost one in three workers were smokers.

**Table II** shows the mean values of ALLY heart age according to different sociodemographic variables and healthy habits in men and women. The mean values of ALLY heart age are higher in men, increase with age and as one descends in social class or level of education. The values are also higher in smokers, sedentary people, people with low adherence to the Mediterranean diet or those who consume a lot of alcohol. In all cases these increases in mean ALLY values are greater in men.

**Table III**, which shows the prevalence of ALLY vascular age values according to different sociodemographic variables and healthy habits in men and women, shows a trend similar to that observed with the mean values, ie, higher prevalence of high ALLY vascular age values as age increases, social class or level of education decreases, and the person has unhealthy habits

(smoking or alcohol consumption, little or no physical activity, and low adherence to the Mediterranean diet). **Table IV** shows the results of the multivariate analysis using multinomial logistic regression. The risk with this analysis of presenting moderate-high or high values of

ALLY vascular age is also affected by sex, age, social class, level of education, adherence to the Mediterranean diet, physical activity, tobacco and alcohol consumption. Of these, those with the highest ORs were age and tobacco consumption.

Table I: Characteristics of the population.

	Men n=83,282 Women n=56,352			
	Mean (SD)	Mean (SD)	p-value	
Age (years)	41.4 (10.7)	40.1 (10.4)	<0.0001	
Height (cm)	173.8 (7.1)	161.2 (6.5)	<0.0001	
Weight (kg)	83.2 (14.6)	66.3 (13.9)	<0.0001	
Body mass index (kg/m²)	27.5 (4.5)	25.5 (5.3)	<0.0001	
Waist circumference (cm)	90.2 (10.3)	76.3 (10.5)	<0.0001	
Waist to height ratio	0.52 (0.06)	0.47 (0.07)	<0.0001	
Systolic blood pressure (mmHg)	126.2 (15.9)	115.6 (15.7)	<0.0001	
Diastolic blood pressure (mmHg)	76.6 (10.9)	71.1 (10.7)	<0.0001	
Total cholesterol (mg/dl)	199.6 (38.6)	194.6 (36.9)	<0.0001	
HDL-cholesterol (mg/dl)	50.0 (7.7)	54.7 (9.2)	<0.0001	
LDL-cholesterol (mg/dl)	122.6 (37.4)	121.5 (37.1)	<0.0001	
Triglycerides (mg/dl)	133.8 (95.6)	90.8 (49.7)	<0.0001	
Glycaemia (mg/dl)	93.0 (25.4)	86.8 (18.1)	<0.0001	
	n (%)	n (%)	p-value	
18-29 years	12558 (15.1)	10110 (18.0)	<0.0001	
30-39 years	24648 (29.6)	17460 (31.0)		
40-49 years	25178 (30.2)	17094 (30.3)		
50-59 years	17370 (20.9)	9984 (17.7)		
60-70 years	3528 (4.2)	1704 (3.0)		
Social class I	6234 (7.5)	7632 (13.6)	<0.0001	
Social class II	19856 (23.8)	18112 (32.1)		
Social class III	57192 (68.7)	30608 (54.3)		
Primary school	55306 (66.4)	27086 (48.1)		
Secondary school	22408 (26.9)	22574 (40.0)		
University	5568 (6.7)	6692 (11.9)		
Non-smokers	55618 (66.8)	38252 (67.9)	<0.0001	
Smokers	27664 (33.2)	18100 (32.1)		
Non physical activity	51984 (62.4)	28962 (51.4)	<0.0001	
Yes physical activity	31298 (37.6)	27390 (48.6)		
Non healthy food	54792 (65.8)	29764 (52.8)	<0.0001	
Yes healthy food	28490 (34.2)	26588 (47.2)		
Non alcohol consumption	56022 (67.3)	47536 (84.4)	<0.0001	
Yes alcohol consumption	27260 (32.7)	8816 (15.6)		

HDL -cholesterolHigh density lipoprotein cholesterol. LDL -cholesterol Low density lipoprotein cholesterol.

Table II: Mean values of ALLY heart age according sociodemographic variables and healthy habits by sex.

	Men			Women			
ALLY heart age	n	Mean (SD)	p-value	n	Mean (SD)	p-value	
18-29 years 30-39 years 40-49 years 50-59 years 60-70 years	12558 24648 25178 17370 3528	1.3 (4.9) 4.2 (6.7) 7.9 (8.1) 11.7 (7.9) 11.8 (7.4)	<0.0001	10110 17460 17094 9984 1704	-2.0 (5.0) -1.8 (7.7) 2.8 (10.2) 8.4 (10.6) 8.6 (9.9)	<0.0001	
Social class I Social class II Social class III	6234 19856 57192	4.9 (7.5) 6.3 (8.1) 7.1 (8.1)	<0.0001	7632 18112 30608	-2.0 (7.7) 0.5 (9.3) 3.3 (9.9)	<0.0001	
Primary school Secondary school University	55306 22408 5568	6.7 (7.9) 7.3 (8.5) 5.2 (7.6)	<0.0001	27086 22574 6692	3.4 (10.0) 0.7 (9.4) -2.1 (7.7)	<0.0001	
Non-smokers Smokers	55618 27664	4.2 (7.3) 11.8 (7.2)	<0.0001	38252 18100	-0.6 (9.2) 6.5 (8.9)	<0.0001	
Non physical activity Yes physical activity	51984 31298	8.9 (7.9) 3.2 (7.0)	<0.0001	28962 27390	5.5 (9.8) -2.3 (7.7)	<0.0001	
Non healthy food Yes healthy food	54792 28490	8.7 (8.0) 3.0 (7.0)	<0.0001	29764 26588	5.1 (9.9) -2.2 (7.8)	<0.0001	
Non alcohol consumption Yes alcohol consumption	56022 27260	5.8 (7.8) (8.8 (8.2)	<0.0001	47536 8816	0.1 (8.9) 10.0 (9.5)	<0.0001	

ALLY Avoidable lost life years

Table III: Prevalence of values of ALLY heart age according sociodemographic variables and healthy habits by sex.

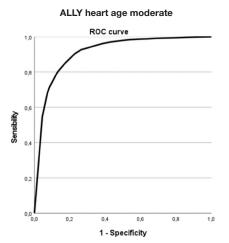
ALLY heart age		Normal	Moderate	High			Normal	Moderate	High	
	n	%	%	%	p-value	n	%	%	%	p-value
18-29 years	12558	96.8	2.5	0.7	<0.0001	10110	98.1	1.6	0.3	<0.0001
30-39 years	24648	85.2	9.2	5.6		17460	93.8	3.3	2.9	
40-49 years	25178	66.0	12.9	21.1		17094	77.2	8.5	14.3	
50-59 years	17370	45.2	15.8	39.0		9984	54.5	11.8	33.7	
60-70 years	3528	41.6	21.9	36.5		1704	49.3	20.4	30.3	
Social class I	6234	80.4	8.3	11.4	<0.0001	7632	92.8	3.4	3.7	<0.0001
Social class II	19856	73.0	10.7	16.3		18112	85.1	6.0	8.9	
Social class III	57192	69.2	11.7	19.1		30608	76.0	7.7	16.2	
Primary school	55306	71.6	11.6	16.8	<0.0001	27086	75.6	8.0	16.4	<0.0001
Secondary school	22408	67.5	10.9	21.6		22574	84.6	5.9	9.6	
University	5568	79.2	8.5	12.2		6692	92.9	3.3	3.7	
Non-smokers	55618	83.0	8.1	8.9	<0.0001	38252	87.1	4.8	8.1	<0.0001
Smokers	27664	46.7	17.5	35.8		18100	68.8	10.4	20.8	
Non physical activity	51984	61.6	13.5	24.8	<0.0001	28962	69.4	10.0	20.7	< 0.0001
Yes physical activity	31298	86.5	7.4	6.2		27390	93.8	3.0	3.2	
Non healthy food	54792	62.7	13.3	24.1	<0.0001	29764	70.3	9.6	20.0	<0.0001
Yes healthy food	28490	87.0	7.2	5.8		26588	93.4	3.2	3.4	
Non alcohol consumption	56022	75.4	11.0	13.6	<0.0001	47536	87.1	5.3	7.5	<0.0001
Yes alcohol consumption	27260	61.9	11.7	26.4		8816	49.5	13.3	37.2	

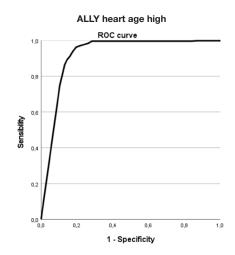
ALLY Avoidable lost life years

Table IV: Multinomial logistic regression.

	ALLY moderate		ALLY high	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Female	1		1	
Male	1.61 (1.56-1.67)	<0.0001	1.24 (1.19-1.29)	<0.0001
20-29 years	1		1	
30-39 years	1.41 (1.31-1.50)	<0.0001	1.98 (1.91-2.05)	0.528
40-49 years	4.41 (4.12-4.72)	< 0.0001	3.06 (2.84-3.30)	<0.0001
50-59 years	17.32 (16.07-18.67)	<0.0001	15.05 (13.81-16.40)	<0.0001
60-70 years	88.19 (79.11-98.30)	<0.0001	121.27 (99.96-147.11)	<0.0001
Social class I	1		1	
Social class II	1.69 (1.61-1.77)	<0.0001	1.93 (1.82-2.03)	< 0.0001
Social class III	2.38 (1.98-2.85)	<0.0001	3.02 (2.39-3.82)	< 0.0001
Primary school	1		1	
Secondary school	1.15 (1.05-1.24)	0.08	1.18 (1.13-1.24)	0.03
University	1.49 (1.23-1.80)	<0.0001	1.91 (1.50-2.44)	<0.0001
Non-smokers	1		1	
Smokers	15.89 (15.26-16.53)	<0.0001	14.66 (14.02-15.33)	<0.0001
Yes physical activity	1		1	
Non physical activity	2.51 (2.34-2.69)	<0.0001	2.55 (2.34-2.78)	<0.0001
Yes healthy food	1		1	
Non healthy food	1.82 (1.70-1.96)	<0.0001	1.94 (1.78-2.12)	<0.0001
Non alcohol consumption	1		1	
Yes alcohol consumption	1.85 (1.78-1.92)	<0.0001	2.37 (2.27-2.48)	<0.0001

Figure 2: ROC curve ALLY heart age moderate-high.





**Figure 2** shows the ROC curves for predicting moderate ALLY and high ALLY. The areas under the curve are very high, namely 0.911 (95% CI 0.908-0.913) for moderate ALLY and 0.919 (95% CI 0.915-0.923) for high ALLY. The established cut-off points are 11 (sensitivity 0.844 specificity 0.832 and Youden index 0.676) for moderate ALLY and 17 (sensitivity 0.878 specificity 0.862 and Youden index 0.740) for high ALLY.

## **Discussion**

In our study, the cut-off points for assessing heartage ALLY were set as moderate if they exceeded the biological age by 11 years and as high if they exceeded it by 17 years.

The mean value and prevalence of high heart age ALLY values increase with increasing age, decreasing social class and educational level. Worse values are also observed in people with unhealthy habits (smokers, high alcohol consumption, low adherence to the Mediterranean diet and low physical activity). The most influential variables are age and tobacco use.

Unfortunately, we have not found any article that assesses the influence of sociodemographic variables and healthy habits on heart age values. Nor have we found any article that establishes cut-off points for cardiac age. Due to this situation, we cannot compare our results with those obtained by other authors. To resolve this situation, we will assess the effect of sociodemographic variables and healthy habits on other cardiovascular risk scales.

Many studies have related age to an increase in cardiovascular risk and in the prevalence of cardiovascular disease<sup>16-17</sup>. There is unanimous agreement that cardiovascular risk is higher in women than in men<sup>18-19</sup>, although this gap decreases as the menopause approaches<sup>20-21</sup>.

Data from a study by Psaltopoulou et al<sup>22</sup> show the existence of a gradient in the incidence, morbidity and mortality of cardiovascular disease across the spectrum of socioeconomic status, defined by educational level, occupation or income. A study by Panagiotakos et al<sup>23</sup> in a Greek population showed that educational level appears to be an important determinant of disease incidence, concluding that low educational level was associated with an increased risk of CVD. This was

mainly explained by the association of low educational level with unhealthy choices.

Tobacco consumption is an important cardiovascular risk factor that has been known for decades, with many mechanisms being involved<sup>24-25</sup>. A negative effect of alcohol consumption and cardiovascular risk has also been found26 as we have found.

A systematic review by Ciumărnean et al<sup>27</sup> showed the positive effect of physical activity on cardiovascular risk. A study by Lavie et al<sup>28</sup> assessing the effect of physical activity of different intensities also found a beneficial effect on cardiovascular risk levels. Members of the EXPERT (EXercise Prescription in Everyday practice & Rehabilitative Training)<sup>29</sup> working group systematically reviewed the literature for meta-analyses, systematic reviews and/or clinical studies addressing exercise prescription in cardiovascular disease risk factors and concluded that physical activity had a significant beneficial effect on cardiovascular risk.

# **Strengths and limitations**

As strong points we can highlight the large sample size (almost 140,000 people) and the large number of sociodemographic variables and healthy habits used. A second strong point is that it is the first study to establish cut-off points for classifying heart age values.

The main limitation is that diet and physical activity were determined by questionnaire and survey, respectively, and not by objective methods.

#### **Conclusions**

Although all the variables, both sociodemographic and healthy habits, influence the ALLY heart age values, we should emphasize that those that show the greatest influence are age and tobacco consumption.

The cut-off points for ALLY moderate heart age are set at 11 and for ALLY high heart age at 17.

# **Conflict of interest**

None

### **Financing**

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