

Adaptation of the Framingham-Wilson Coronary Risk Equation for the Population of Navarra (RICORNA)

Paulino González-Diego,^{a,b} Conchi Moreno-Iribas,^c María Jesús Guembe,^a José Javier Viñes,^a and Joan Vila^d

^aServicio de Docencia e Investigación, Departamento de Salud, Gobierno de Navarra, Pamplona, Navarra, Spain

^bHospital García Orcoyen, Servicio Navarro de Salud, Estella, Navarra, Spain

^cInstituto de Salud Pública de Navarra, Departamento de Salud, Gobierno de Navarra, Pamplona, Navarra, Spain

^dUnidad de Lípidos y Epidemiología Cardiovascular, Instituto Municipal de Investigación Médica (IMIM), Barcelona, Spain

Introduction and objectives. The Framingham equations overestimate the risk of coronary disease in populations with a low disease incidence. It is more appropriate to take the local population's characteristics into account when estimating coronary risk. Accordingly, the Framingham-Wilson equation has been adapted for the population of Navarra, Spain. This article presents 10-year overall coronary risk charts.

Methods. The Framingham-Wilson equation was adapted using data on the prevalence of cardiovascular risk factors and the coronary event rate in the population of Navarra. The version of the Framingham-Wilson equation used included high-density lipoprotein cholesterol (HDL-C). The probability of an event at 10 years for different combinations of risk factors, with an HDL-C concentration of 35-59 mg/dL, are illustrated.

Results. Using the Framingham equation adapted for Navarra (ie, the RICORNA or Riesgo Coronario Navarra), the proportion with an estimated probability of a coronary event in the next 10 years greater than 9% is approximately half that in the original Framingham population, and the proportion with a high or very high probability (ie, 20%) is one-third. An HDL-C level <35 mg/dL increases the risk by 50% and a level ≥ 60 mg/dL reduces it by 50%, approximately. The average HDL-C level observed in the population was 63.9 mg/dL overall, and 70.1 mg/dL in women.

Conclusions. The RICORNA equation can provide a more precise estimate of overall coronary risk and could be useful in primary disease prevention in Navarra. The high HDL-C concentration observed in Navarra might contribute to the associated low coronary morbidity and mortality.

Key words: *Cardiovascular risk equations. Coronary disease. Coronary disease risk. Primary prevention.*

Adaptación de la función de riesgo coronario de Framingham-Wilson para la población de Navarra (RICORNA)

Introducción y objetivos. Las funciones de Framingham sobrestiman el riesgo de enfermedad coronaria en poblaciones con baja incidencia. Es más apropiado estimar el riesgo coronario considerando las características poblacionales locales. En este sentido, se ha adaptado la ecuación de Framingham-Wilson para la población de Navarra. Se presentan las tablas de riesgo coronario global a 10 años.

Métodos. Se ha adaptado la ecuación de Framingham-Wilson mediante los datos de prevalencia de los factores de riesgo cardiovascular y la tasa de acontecimientos coronarios de Navarra. Se ha utilizado la ecuación de Framingham-Wilson que incluye el colesterol unido a lipoproteínas de alta densidad (cHDL). Se muestran las probabilidades de acontecimientos a 10 años correspondientes a las distintas combinaciones de los factores de riesgo, para una concentración de cHDL de 35-59 mg/dl.

Resultados. En la función adaptada Framingham-Navarra (RICORNA), la proporción de estimaciones de probabilidad de acontecimiento coronario a 10 años superior al 9% es aproximadamente 2 veces menor, y la de riesgo alto o muy alto ($\geq 20\%$) es 3 veces menor que en las originales de Framingham. Los valores de cHDL < 35 mg/dl incrementan el riesgo un 50% y los valores ≥ 60 mg/dl lo reducen un 50%, aproximadamente. El cHDL observado tuvo un valor medio poblacional de 63,9 mg/dl y de 70,1 mg/dl en las mujeres.

Conclusiones. La función RICORNA es una herramienta que puede ser utilizada para estimar con más precisión el riesgo coronario global en la prevención primaria de esta enfermedad en Navarra. La elevada concentración de cHDL observada en Navarra puede contribuir a su baja morbimortalidad coronaria.

Palabras clave: *Ecuaciones de riesgo cardiovascular. Enfermedad coronaria. Riesgo de enfermedad coronaria. Prevención primaria.*

Correspondence: Dr. P. González Diego.
Servicio de Medicina Preventiva y Gestión de Calidad.
Santa Soria, 22. 31200 Estella. Navarra. España.
E-mail: paulino.gonzalez.diego@cfnavarra.es

Received February 6, 2009.

Accepted for publication May 11, 2009.

ABBREVIATIONS

AMI: acute myocardial infarction
HDL-C: high-density lipoprotein cholesterol
REGICOR: Registre Gironí del Cor (Gerona Heart Registry)
RICORNA: Riesgo Coronario Navarra (Navarra Coronary Risk)
SCORE: Systematic Coronary Risk Evaluation
VERIFICA: Validación de la Ecuación de Riesgo Individual de Framingham de Incidente Coronario Adaptada (Validation of the Framingham individual risk equation for coronary events – Adapted)

INTRODUCTION

Coronary heart disease is one of the main public health problems in Navarra, Spain.¹⁻³ Acute myocardial infarction (AMI) is the second leading cause of death in men and the third in women. One quarter of all deaths before patients reach hospital care occur during the first 28 days after onset of symptoms.³

Some of these deaths could be avoided with effective primary prevention to improve the detection and appropriate management of risk factors for coronary heart disease. It is necessary to promote the primary prevention of cardiovascular disease, balancing activities dealing with prevention with those involving the care of persons who already have coronary heart disease.⁴

Arteriosclerosis, the main etiopathological cause of ischemic heart disease, is a multiple factor entity. As far as is known, no particular factor is required for its development, but rather it depends on the coexistence and severity of different component factors and the synergistic or antagonistic effect of each factor. Its preventive approach should therefore be multi-factorial as well.⁵ Evaluation of the risk by means of multiple risk factor models predicts the overall individual risk more precisely and enables primary prevention priorities to be established, adjusting the intensity of the intervention aimed at avoiding the onset of a first cardiovascular episode in asymptomatic but vulnerable persons.

Cardiovascular risk equations are the best tool to establish priorities in primary prevention. These equations estimate the excess risk that a person has of experiencing an event over a certain period of time, usually 5 or 10 years, in relation to the average risk of the population to which that individual belongs. Several different equations or scales exist to calculate the coronary risk, all based on the findings of the North American Framingham cohort. Various epidemiological studies have identified that the use

of these equations in Anglo-Saxon populations provides an adequate estimate of the future risk of an event, but their use in low-risk countries such as Spain systematically overestimates this risk.⁶⁻¹⁰

The most used risk tables in Spain are REGICOR (REGistre GIRONÍ del COR)^{6,7} and SCORE (Systematic Coronary Risk Evaluation).¹¹ The REGICOR equation has proven to have a good prediction capacity for coronary events in Spanish persons aged 35-74 years—Validación de la Ecuación de Riesgo Individual de Framingham de Incidente Coronario Adaptada (Validation of the Framingham individual risk equation for coronary events Adapted) (VERIFICA)—.¹² The SCORE equation, in its version adapted for use in low-risk countries, for the calculation of the risk of cardiovascular death in persons aged 40 to 65 years, has recently been adapted to Spain.¹³

The estimation of the coronary risk should be based on the follow-up of large cross-sectional cohorts. Navarra currently has a population cohort, though the follow-up period is still not long enough to provide risk estimates according to age and sex that possess the required precision. This, therefore, demands that we use charts that have been generated in other populations or else adapt these charts. The aim of this study was to adapt the Framingham-Wilson equation by calibrating it using the rates of coronary events and the prevalence of cardiovascular risk factors found in Navarra.

METHODS

The estimation of the coronary risk was based on the original equation of the Framingham study in the version published by Wilson et al¹⁴ in 1998. This equation includes high-density lipoprotein cholesterol (HDL-C), and estimates the 10-year risk of having a myocardial infarction, whether fatal or not, symptomatic or silent, and angina.

The method used to adapt the Framingham equation is known and has been evaluated in our setting.^{6,7,12} The calibration was done by substituting the comparison elements of the Framingham population with those of the Navarra population. Estimates are available of the prevalence of cardiovascular risk factors and the rates of major coronary events (fatal or non-fatal symptomatic AMI) of Navarra. Additionally, the original coefficients of the Framingham-Wilson equation were used.¹⁴ The calculation of the calibrated equation is described in the appendix.

Adaptation Process

The population data concerning cardiovascular risk factors were obtained from the Riesgo Vascular

en Navarra (Vascular risk in Navarra) (RIVANA) study, for the population aged 35 to 74 years in 2003.^{15,16} The sampling strategy recruited 5197 persons. The final rate of participation was 74.6%. The variables studied were sex, age, total cholesterol, HDL-C, systolic blood pressure (SBP), diastolic blood pressure (DBP), smoking, and a diagnosis of diabetes mellitus. The prevalence of the various risk factors was calculated for each group according to age and sex, using the definitions and cut-off points of the Framingham-Wilson cohort.¹⁴

The blood pressure was measured 3 times, with an interval of at least 5 min between each measurement. At the first measurement the blood pressure was measured in both arms, and the value for the arm showing the highest SBP or DBP was used. The measurement was made with an automatic blood pressure monitor (OMRON® M4-1).

Laboratory Measurements

All the analyses were centralized at the laboratory of the Hospital de Navarra (Pamplona). All the analytical procedures were calibrated and standardized in order to guarantee the quality of the biochemical determinations. Internal and external controls were made systematically. The internal quality control consisted of a daily control and weekly calibration. The internal controls were made with Precinorm U and Precipath U for the measurements of total cholesterol and glucose, and Precipath lipids for the HDL-C (Roche Diagnostics). Concurrent external quality controls were made with Unity (BioRad Laboratories). The total cholesterol was measured with the CHOD-PAP enzymatic-colorimetric method and the HDL-C with the second generation direct HDL plus method (without pretreatment). The glucose was measured by the hexokinase method.

The study used the data from the Navarra population registry of AMI, which records all patients with an AMI, both fatal and non-fatal. The registry covers the years 1997-1998 and 2003-2004.^{3,17} A simple weighting of the observed rate was made for each point in the series (1997, 1998, 2003, and 2004); each year had an equal contribution (weighting $K = 2.5$) to the estimated rate of coronary events at 10 years.

The calculation of the rates included all cases of myocardial infarction in Navarra, classified according to the algorithm of the MONICA project (MONItoring of trends and determinants in Cardiovascular diseases).¹⁸ Each case studied was classified as: definite AMI, fatal or not; possible AMI, or AMI with insufficient data. The 4 categories compose definition 1 of the MONICA study, which is that used to calculate the rate. Given that the Wilson

equation, besides symptomatic AMI, also includes cases of angina and silent AMI, data that are not known in Navarra, the proportion was assumed to be similar to that of Framingham. The following ratio was used for the estimate:

$$Ho(t)/FramAll/Ho(t)/FramMajor$$

where t is the follow-up time, in our case 10 years; $Ho(t)/FramAll$, the rate of coronary events including angina and silent myocardial infarction in Framingham, and $Ho(t)/FramMajor$, the rate of fatal or non-fatal symptomatic infarction. The value of this quotient was 1.4 for men and 1.91 for women.⁷ Thus, as the rate of major events in Navarra in men according to the registry was 3.6%, this was multiplied by 1.4 to obtain the estimated rate of all coronary events (5.1%). This, in turn, enabled us to calculate the population rate free of coronary events at 10 years: $100\% - 5.1\% = 94.9\%$. For women, the rate of major events was 0.9%, which multiplied by 1.91 gives an estimated rate of all coronary events of 1.8%. The female population rate free of events was therefore $100\% - 1.8\% = 98.2\%$.

Charts were constructed to show the absolute risks, calculated with the adapted equation, rounded to the next nearest whole figure, for each box of the combination of the risk factor categories. The absolute risks were calculated for an HDL-C concentration of 35-59 mg/dL. The risk was classified in 5 levels: low (<5%), mild (5%-9%), moderate (10%-19%), high (20%-39%), and very high (>39%). A color code was used for the intensity of the risk for the various risk factor combinations, for men and women, diabetic and non-diabetic, individually.

RESULTS

Table 1 shows the frequency distribution by sex of the risk factors of the population of Navarra, as well as the values for the Framingham population.

Comparison of the 2 distributions shows that they differ in several categories in a few factors, in both men and women. The most relevant finding here was the high concentration of HDL-C in the population of Navarra. The HDL-C had a mean population value of 63.9 mg/dL (95% confidence interval [CI], 63.4-64.4); 56.7 mg/dL (95% CI, 56.1-57.3) in men and 70.1 mg/dL (95% CI, 69.4-70.8) in women. Likewise, the prevalence of smoking was much lower in Navarra, in both men and women. The data for hypertension, however, showed a higher prevalence in the Navarra men but not the women.

Concerning the incidence rate of coronary events, the rate in both sexes was significantly lower in Navarra (Table 1).

TABLE 1. Coefficients of Regression of the Cox Proportional Hazards Model of the Framingham Equation for the Incidence of Coronary Events at 10 Years and the Prevalence of Each Category of the Risk Factors in Framingham (USA) and Navarra (Spain)

	Men			Women		
	Cox	Framingham	Navarra	Cox	Framingham	Navarra
Age, mean, y	0.04826	48.3	52.7	0.33766	49.6	52.4
Age squared				-0.00268	2.604.5	2.870
Total cholesterol						
<160 mg/dL	-0.65945	7.5%	7.7%	-0.26138	7.9%	6.4%
160-199 mg/dL	0	31.3%	30.3%	0	30.3%	31.3%
200-239 mg/dL	0.17692	39%	39%	0.20771	32.7%	39.8%
240-279 mg/dL	0.50539	16.5%	18.1%	0.24385	20%	19%
≥280 mg/dL	0.65713	5.7%	4.9%	0.53513	9.1%	3.4%
HDL-C						
<35 mg/dL	0.49744	19.2%	2.4%	0.84312	4.3%	0.5%
35-44 mg/dL	0.24310	35.7%	15.6%	0.37796	14.9%	3.7%
45-49 mg/dL	0	15.5%	14.1%	0.19785	12.4%	4%
50-59 mg/dL	-0.05107	19%	31.6%	0	27.7%	18.4%
≥60 mg/dL	-0.48660	10.6%	36.3%	-0.42951	40.7%	73.3%
Blood pressure						
Optimal (SBP<120/DBP<80 mm Hg)	-0.00226	20.2%	12.4%	-0.53363	34.8%	37.1%
Normal (SBP 120-129/DBP 80-84 mm Hg)	0	24.3%	19.2%	0	21.6%	20.4%
High normal (SBP 130-139/DBP 85-89 mm Hg)	0.28320	20.2%	24.1%	-0.06773	15%	16.2%
Grade I (SBP 140-159/DBP 90-99 mm Hg)	0.52168	22.5%	32.6%	0.26288	18.6%	18.4%
Grades II-IV (SBP≥160/DBP≥100 mm Hg)	0.61859	12.8%	11.7%	0.46573	10%	7.8%
Diabetes	0.42839	5%	7.5%	0.59626	3.8%	3.3%
Smoking	0.52337	40.3%	28%	0.29246	37.8%	19.7%
10-year incidence of coronary heart disease		10% ^a	5.1% ^b		3.8% ^a	1.8% ^b

DBP indicates diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; SBP, systolic blood pressure.

^aFatal or non-fatal myocardial infarction, with or without symptoms and angina. Estimated from true data on the incidence of symptomatic myocardial infarction, fatal or non-fatal, and the proportion of angina and silent myocardial infarction in the population of Framingham.

^bEstimated in the population of Navarra.

Figure 1 shows the risk table for AMI, fatal or non-fatal, with or without symptoms, and angina for men, with different combinations of risk factors. Figure 2 shows the same for the diabetic men. Figure 3 shows the risk table for women and Figure 4 for the diabetic women.

The proportion of combinations of risk factors determining a high or very high risk of coronary heart disease (≥20% risk at 10 years) in the whole set of calibrated tables was 3.3 times lower in Navarra than in the original tables for the Framingham population (Table 2). The proportion of combinations of factors leading to a moderate to very high risk was 1.82 times lower (Table 2). At this level of risk, the reduction was very notable in the non-diabetic women.

The tables show the corresponding likelihood at the various different combinations of risk factors, for an HDL-C concentration of 35-59 mg/dL. The risk, calculated using the adapted Framingham-Navarra equation (RICORNA) corresponding to HDL-C values <35 mg/dL was approximately 50% greater than that seen in the tables, and that for an HDL-C

concentration of 60 mg/dL was approximately 50% lower. Those persons with concentrations between 35 and 59 mg/dL had the risk indicated by the box for the combination of risk factors, though those nearer 35 mg/dL were slightly higher (about 3 percentage points) and those nearer 59 mg/dL slightly lower (again, about 3 percentage points). This correction is proposed in order to simplify the use of the tables. The fact of including the effect of HDL-C in the risk estimate in our setting is definitely important, as 73% of the women and 36% of the men aged 35 to 74 years in Navarra had an HDL-C level ≥60 mg/dL.

DISCUSSION

We present proposed tables for overall 10-year coronary risk for use in the population of Navarra, based on the Framingham-Wilson equation, calibrated according to the prevalence of risk factors and rate of events recorded for Navarra.

Generally speaking, the risk calculated from the RICORNA (Framingham-Navarra) equation for the various combinations of risk factors is significantly

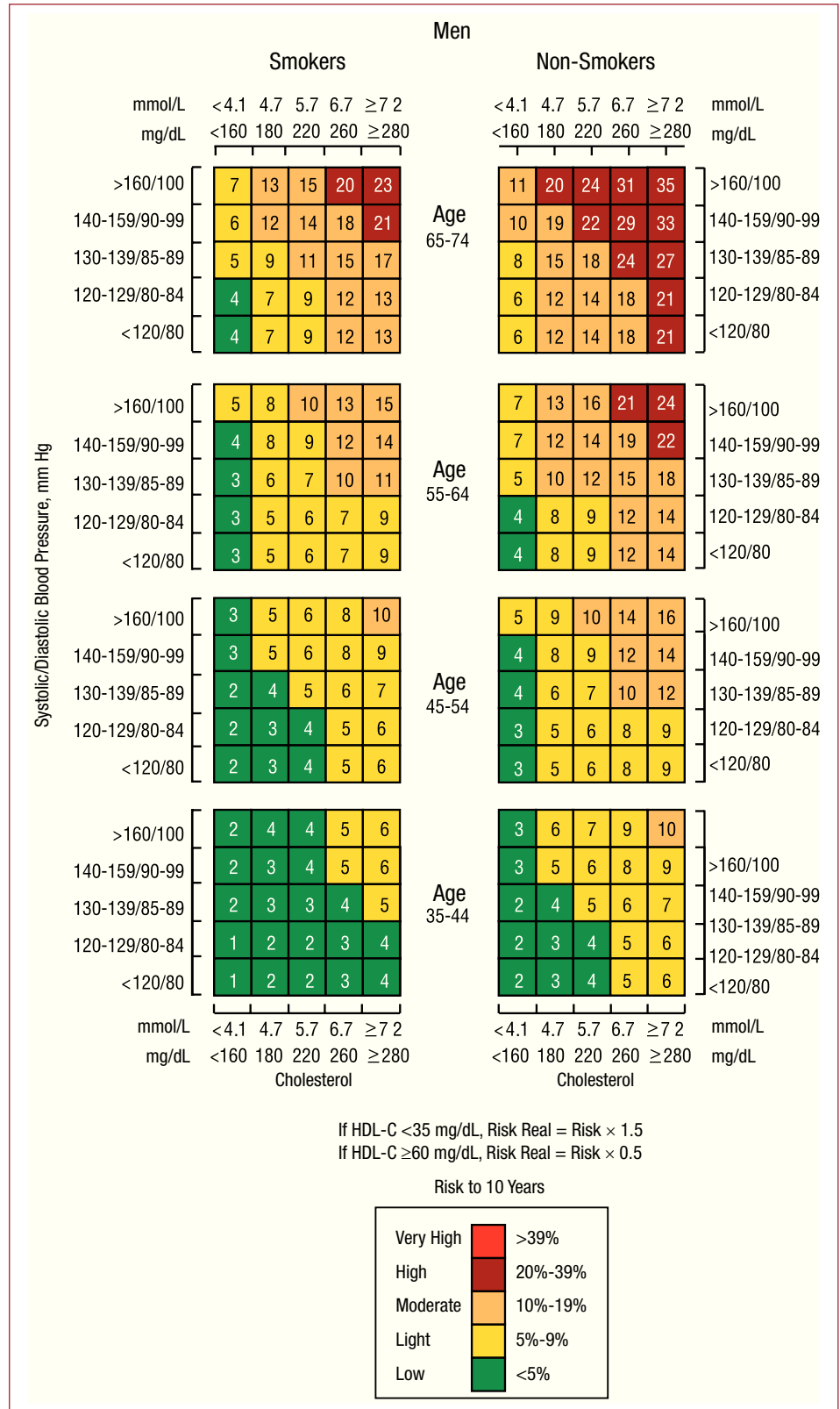


Figure 1. Risk of myocardial infarction, fatal or non-fatal, with or without symptoms, or angina in non-diabetic men with high-density lipoprotein cholesterol (HDL-C) concentrations of 35-59 mg/dL.

lower than in the original Framingham study. The proportion of coronary risk estimations that were moderate to very high was 1.82 times lower in the adapted tables than in the original tables.

Several different epidemiological studies have shown that mathematical functions based on the original data of the Framingham cohort overestimate the absolute coronary risk in populations with a

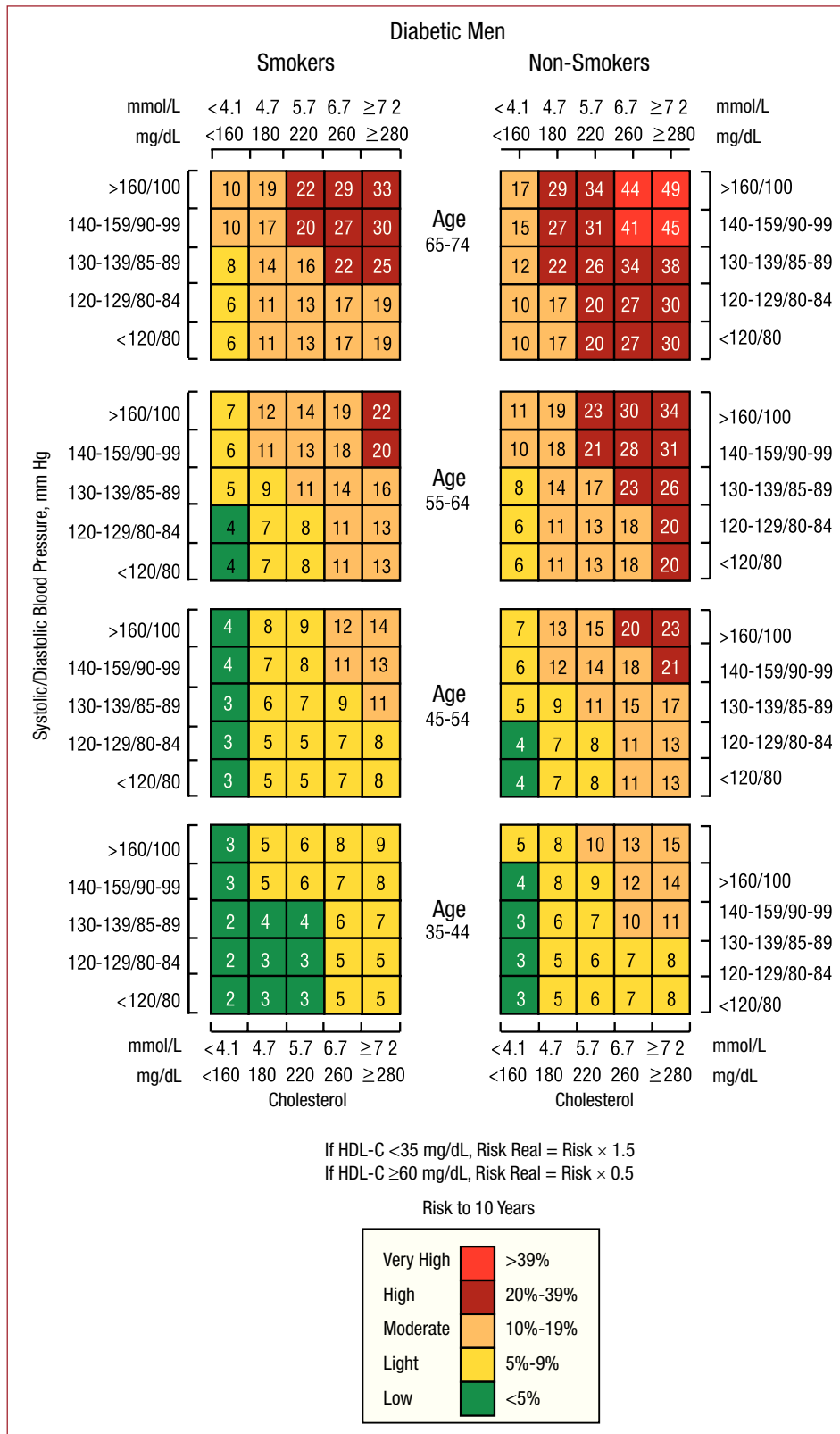


Figure 2. Risk of myocardial infarction, fatal or non-fatal, with or without symptoms, or angina in diabetic men with HDL-C concentrations of 35-59 mg/dL.

low incidence of coronary disease and associated mortality rate.⁶⁻¹⁰ Navarra is among the regions of the developed world with the lowest mortality rates, both for overall mortality due to cardiovascular

disease and for mortality due to coronary heart disease, as well as for cerebrovascular disease.^{1-3,19,20} The results of our study are in accordance with these data and corroborate the starting hypothesis

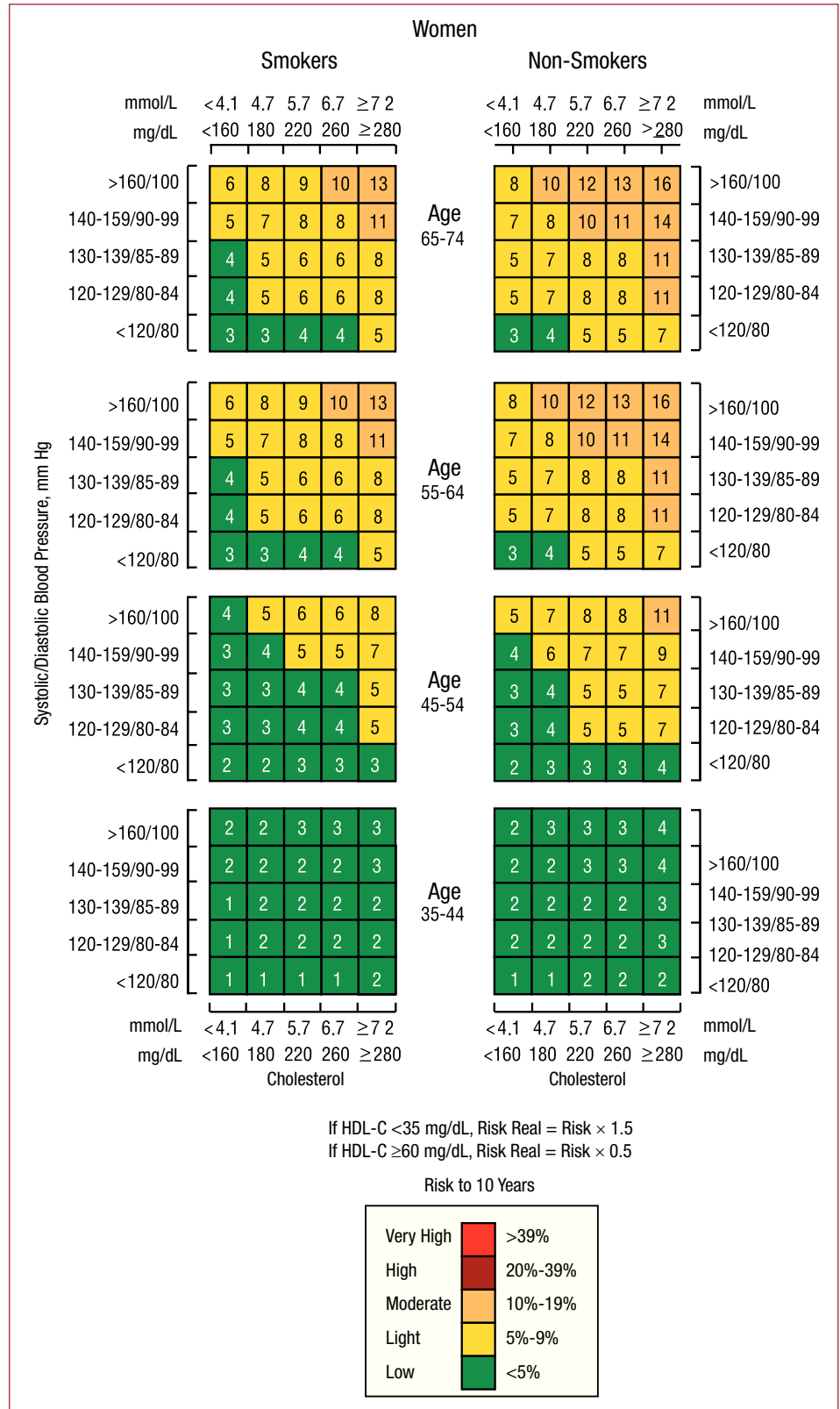


Figure 3. Risk of myocardial infarction, fatal or non-fatal, with or without symptoms, or angina in non-diabetic women in non-diabetic women with HDL-C of 35-59 mg/dL.

that the coronary risk is overestimated in our population.
The guidelines of the national and international scientific societies are aimed at promoting the

adaptation of the recommendations concerning cardiovascular prevention to the particular characteristics and circumstances of the end-user population.^{21,22} In accordance with these

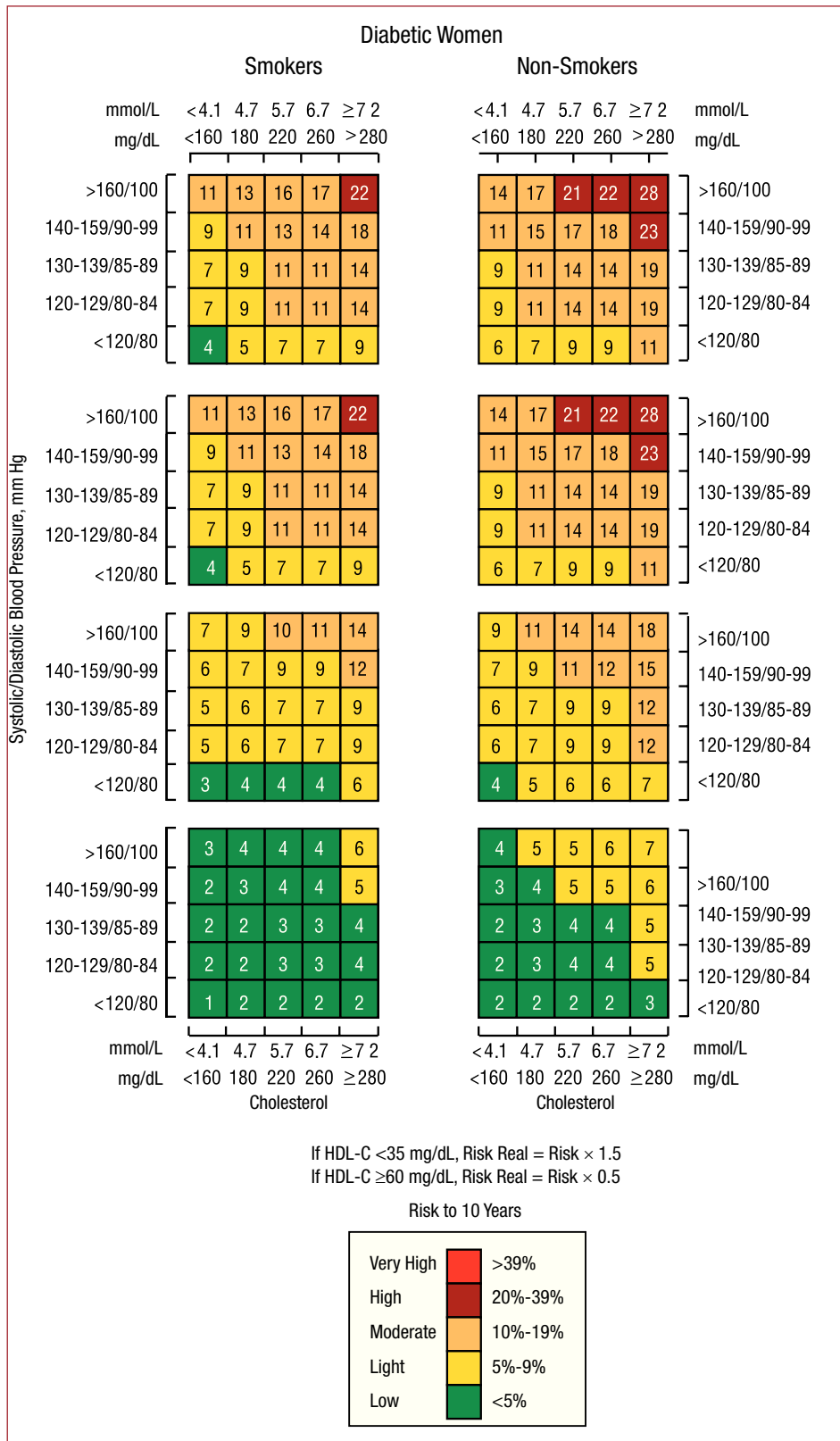


Figure 4. Risk of myocardial infarction, fatal or non-fatal, with or without symptoms, or angina in diabetic women with HDL-C concentrations of 35-59 mg/dL.

recommendations, various Spanish research groups over recent years have undertaken notable efforts to obtain precise, reliable prediction models, adapted to the characteristics of the Spanish population.

For instance, the 1998 version of the Framingham equation has been calibrated according to the data for the population of Gerona, and the REGICOR equation obtained. With the same method as that

TABLE 2. Proportion of Combinations of Risk Factors With a Low-Mild, Moderate and High/Very High Risk in the Tables based on the Framingham-Wilson Equation, Which Includes HDL-C, and the Table Calibrated for the Population of Navarra (RICORNA)

	Original			Calibrated		
	Framingham-Wilson			RICORNA		
	Low/Mild, %	Moderate, %	High/Very High, %	Low/Mild, %	Moderate, %	High/Very High, %
Non-diabetic						
Men						
Non-smokers	47	35	18	77	20	3
Smokers	23	36	41	54	32	14
Women						
Non-smokers	65	33	2	95	5	0
Smokers	51	41	8	81	19	0
Diabetic						
Men						
Non-smokers	29	37	34	58	32	10
Smokers	10	29	61	31	38	31
Women						
Non-smokers	33	45	22	66	32	2
Smokers	23	35	42	53	39	8

HDL-C indicates high-density lipoprotein cholesterol.

used for the REGICOR study, but based on a different population, the DORICA (Dislipemia, Obesidad y Riesgo Cardiovascular–Dyslipidemia, Obesity, and Cardiovascular Risk) tables were obtained.²³ Finally, the European SCORE project, in which Spain participated with 3 cohorts, gave rise to the SCORE scale in its version adapted to low-risk countries to calculate the risk of cardiovascular death in persons aged 40 to 65 years. The low-risk SCORE model has been calibrated for Spain.¹³

The researchers involved in the REGICOR study recently analyzed the validity of the equation calibrated from the VERIFICA study.¹² The VERIFICA study (Validación de la Ecuación de Riesgo Individual de Framingham de Incidente Coronario Adaptada) has proved to have a good 5-year predictive capacity of coronary events for the Spanish population aged between 35 and 74 years, both in men and women, and also in diabetic patients. This is the first, and only, risk equation validated for the Spanish population.

At the present time, the REGICOR and SCORE tables are the most used in general practice for the stratification of cardiovascular risk in our health care setting.

Ideally, the estimation of coronary risk in Navarra should be based on the follow-up of a cohort of our population, with a sufficient sample size to estimate the probabilities precisely. Additionally, it should include those persons aged up to 74 years, and more especially the estimation of coronary risk in women, whose life expectancy is greater. Currently, Navarra

has a population cohort of 4168 persons aged between 35 and 84 years, though the follow-up period is still short (4 years). This therefore explains the need for the time being to use equations generated in other populations or else to adapt these equations.

Spain is a country with a wide geographic variability in the pattern of the incidence and mortality from coronary heart disease,²⁴⁻²⁶ as well as marked geographic differences in the burden and distribution of risk factors that could contribute to the explanation of these differences.^{27,28} In this study we characterized a representative sample of the population of Navarra with an HDL-C concentration of 63.9 mg/dL (56.7 mg/dL in men and 70.1 mg/dL in women). These figures are higher than those of other regions in our setting, especially those found for women.^{27,28} Numerous studies have shown that HDL is one of the most important independent protectors against the arteriosclerosis that underlies coronary heart disease.²⁹⁻³¹ The high concentration of HDL-C found in the population of Navarra may well contribute to the low coronary morbidity and mortality.

Comparison of the risk tables adapted for Navarra with those of REGICOR⁷ shows that the risk of a coronary event is slightly higher in the population of Navarra, reflecting the different pattern of prevalence of risk factors included in the model, in spite of the fact that the 2 populations have similar rates of heart disease. In this context, it seems justified to have risk tables adjusted to the particular characteristics of our population. The present study

was designed to respond to this need using a well-established method.

The study reported here has certain limitations that should be taken into account. One limitation is that the tables shown have not been validated in a prospective, population-based study. Nevertheless, the method used to adapt the tables has been used before and has a reasonable guarantee of validity.

Population data are not available that would enable us to confirm that the proportion of silent AMI and angina with respect to the total number of coronary events in Navarra is similar to that found in the Framingham study. This option, chosen as a measure of safety, endows the tables with a conservative character, as is it very unlikely that the true values in Navarra are greater than those of the American city.

Finally, the cardiovascular risk equations, despite their limitations, are the best screening tool that we currently have for the selection of patients in whom to apply the various different primary prevention strategies, as well as to determine their intensity. Any equation nowadays is far from being an ideal tool, and it should simply be considered as useful in primary prevention and is no substitute for the correct clinical judgment, and any specific conditions must be taken into account when the tool is applied.

CONCLUSIONS

We believe that the tables proposed here may be useful instruments for the more precise estimation of the overall coronary risk of the population of Navarra. The RICORNA equation answers the need for tables to calculate the coronary risk adapted to the characteristics of the population of Navarra.

Use of the original Framingham equation should be avoided as it overestimates excessively the true risk of coronary heart disease in the population of Navarra.

The population-based cohort in the RIVANA Study could provide information that will soon enable the RICORNA equation to be validated.

REFERENCES

- Moreno-Iribas C, Floristan Y, Egüés N. Tendencias recientes de las principales causas de muerte en Navarra. 1995-2004. *An Sist Sanit Navar*. 2006;29:399-414.
- Mortalidad en Navarra, 1996-2005. Instituto de Salud Pública de Navarra. *Boletín de Salud Pública* 44: May 2007 [cited Feb 15, 2008]. Available from: <http://www.cfnavarra.es/ISP/documentacion/BOL44-07.pdf>
- Incidencia, letalidad y tratamiento del infarto agudo de miocardio en Navarra, 2003-2004, 1996-2005. Instituto de Salud Pública de Navarra. *Boletín de Salud Pública* 45: Agosto 2007 [cited Feb 15, 2008]. Available from: <http://www.cfnavarra.es/ISP/documentacion/BOL45-07.pdf>
- Banegas JR, Villar F, Graciani A, Rodríguez-Artalejo F. Epidemiología de las enfermedades cardiovasculares en España. *Rev Esp Cardiol*. 2007;6:3-12.
- Grundy SM, Pasternak R, Greenland P, Smith S, Fuster V. Assessment of cardiovascular risk by use of multiple-risk-factor assessment equations: a statement for healthcare professionals from the American Heart Association and the American College of Cardiology. *Circulation*. 1999;100:1481-92.
- Marrugat J, d'Agostino R, Sullivan L, Elosua R, Wilson P, Ordoñas J, et al. An adaptation of the Framingham coronary risk function to Southern Europe Mediterranean areas. *J Epidemiol Comm Health*. 2003;57:634-8.
- Marrugat J, Solanas P, d'Agostino R, Sullivan L, Ordoñas J, Cordón F, et al. Estimación del riesgo coronario en España mediante la ecuación de Framingham calibrada. *Rev Esp Cardiol*. 2003;56:253-61.
- Menotti A, Puddu PE, Lanti M. Comparison of the Framingham risk function-based coronary chart risk function from an Italian population study. *Eur Heart J*. 2000;21:365-70.
- Ramos R, Solanas P, Cordón F, Rohlfs I, Elosua R, Sala J, et al. Comparación de la función de Framingham original y la calibrada del REGICOR en la predicción del riesgo coronario poblacional. *Med Clin (Barc)*. 2003;121:521-6.
- d'Agostino RB, Grundy S, Sullivan LM, Wilson P. Validation of the Framingham Coronary Heart Disease Prediction Scores: Results of a Multiple Ethnic Groups Investigation. *JAMA*. 2001;286:180-7.
- 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.
- Marrugat J, Subirana I, Comín E, Cabezas C, Vila J, Elosua R, et al, for the VERIFICA Investigators. Validity of an adaptation of the Framingham cardiovascular risk function: the VERIFICA study. *J Epidemiol Community Health*. 2007;61:40-7.
- Sans S, Fitzgerald AP, Royo D, Conroy R, Graham I. Calibración de la tabla SCORE de riesgo cardiovascular para España. *Rev Esp Cardiol*. 2007;60:476-85.
- Wilson PWF, 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.
- Viñes JJ, Diez J, Guembe MJ, González P, Amézqueta C, Barba J, et al. Estudio de riesgo vascular en Navarra: objetivos y diseño. Prevalencia del síndrome metabólico y de los factores mayores de riesgo vascular. *An Sist Sanit Navar*. 2007;30:113-24.
- Viñes JJ, Guembe MJ, González-Diego P, Amézqueta C, Sobejano I, Grijalba A, et al. Riesgo Vascular en Navarra (RVN). *An Sist Sanit Navar*. 2008; Monografía n.º 4 [cited Jan 15, 2008]. Available from: <http://www.cfnavarra.es/salud/docencia/investigacion/monografias.htm>
- Moreno C, Turumbay J, García V, Ezpeleta I, de los Arcos E, Manrique A. El infarto de miocardio en la población de 25-74 años de Navarra. Incidencia, letalidad y tratamiento en el periodo 1997-1998. Estudio IBERICA. *An Sist Sanit Navar*. 2002;25:155-66.
- Manual of The MONICA Project [Manual en Internet]. Ginebra: World Health Organization; 2000 [cited Nov 15, 2007]. Available from: <http://www.ktl.fi/publications/monica/manual/index.htm>
- Causes of death —Standardised death rate (per 100 000 inhabitants) (Annual Data)— [cited Feb 15, 2008]. Available from: <http://epp.eurostat.ec.europa.eu>
- Thom T, Haase N, Rosamond W, Howard VJ, Rumsfeld J, Manolio T, et al. Heart disease and stroke statistics—2006 update: a report from the American Heart Association Statistics

- Committee and Stroke Statistics Subcommittee. *Circulation*. 2006;113:85-151.
21. Prevention of coronary heart disease in clinical practice. Recommendations of the Second Joint Task Force of European and other societies on coronary prevention. *Eur Heart J*. 1998;19:1434-503.
 22. de Backer G, Ambrosini E, Borch-Johnsen K, Brotons C, Cifkova R, Dallongeville J, et al. European guidelines on cardiovascular disease prevention in clinical practice. Third Joint Task Force of European and Other Societies on Cardiovascular Disease Prevention in Clinical Practice. *Eur Heart J*. 2003;24:1601-10.
 23. Aranceta J, Pérez Rodrigo C, Foz Sala M, Mantilla T, Serra Majem L, Moreno B, et al. Tablas de evaluación del riesgo coronario adaptadas a la población española. Estudio DORICA. *Med Clin (Barc)*. 2004;123:686-91.
 24. Rodríguez Artalejo F, Banegas Banegas JR, Guallar-Castillón P, López García E, Puente Mendizábal M, del Rey Calero J. Distribución geográfica de las enfermedades cardiovasculares en España: la mortalidad es mayor en las regiones del sur y del mediterráneo. *Cardiovascular Risk Factors*. 2000;9:311-8.
 25. Elosua R, Fiol M, Tormo MJ, Segura A, Bregada J, Villegas M, et al; en nombre del grupo IBERICA. Letalidad poblacional del infarto agudo de miocardio en cuatro regiones españolas. Estudio IBERICA. *Rev Esp Cardiol*. 1999;52:91.
 26. Marrugat J, Fiol M, Sala J, Tormo MJ, Segura A, Muñoz J, et al. Variabilidad geográfica en España en las tasas de incidencia y mortalidad poblacionales por infarto agudo de miocardio en el Estudio IBERICA. *Rev Esp Cardiol*. 2000;53 Suppl 2:71.
 27. Gabriel R, Alonso M, Segura A, Tormo MJ, Artigao LM, Banegas JR, et al; en nombre del Grupo Cooperativo ERICE. Prevalence, Geographic Distribution and Geographic Variability of Major Cardiovascular Risk Factors in Spain. Pooled Analysis of Data From Population-Based Epidemiological Studies: The ERICE Study. *Rev Esp Cardiol*. 2008;61:1030-40.
 28. Medrano MJ, Cerrato E, Boix R, Delgado-Rodríguez M. Factores de riesgo cardiovascular en la población española: metaanálisis de estudios transversales. *Med Clin (Barc)*. 2005;124:606-12.
 29. Miller GJ, Miller NE. Plasma-high-density-lipoprotein concentration and development of ischaemic heart-disease. *Lancet*. 1975;1:16-9.
 30. Gordon T, Castelli WP, Hjortland MC, Kannel WB, Dawber TR. High density lipoprotein as a protective factor against coronary heart disease. The Framingham Study. *Am J Med*. 1977;62:707-14.
 31. Tomás M, Latorre G, Senti M, Marrugat J. Función antioxidante de las lipoproteínas de alta densidad: un nuevo paradigma en la arteriosclerosis. *Rev Esp Cardiol*. 2004;57:557-69.

APPENDIX

The predictive equation is based on the calculation of the likelihood of an event using the Cox proportional hazards model:

$$P_{x(t)} = 1 - S_{0(t)}^{e^{\sum(\beta_i x_i) - (\sum(\beta_i x_m))}}$$

where $P_{x(t)}$ is the probability of a coronary event in a time t (10 years) in a person with a group of risk factors x_i , $\sum(\beta_i x_m)$ is a linear equation of the average risk of the group of values x_m of each category for each factor in the population, and $\sum(\beta_i x_i)$ is the linear equation calculated for the group of values x_i that represents the value of each factor in a specific person. In both linear equations, β_i is the coefficient of the Cox proportional hazards equation for each category of each factor considered. $S_{0(t)}$ is the probability that no coronary event will occur in time t in the study population and e is the base of the natural logarithms. $\sum(\beta_i x_i)$ is obtained by multiplying the coefficients β_i of the model that appears in Table 1 by the value x_i of each one of that person's risk factors, using (1) when the factor degree is present and (0) for the remaining factor degrees. In the case of age, x_i is replaced by the age in years—and, additionally, in women by the age squared—, and diabetes and smoking by (0) or (1), depending on whether they are or are not present. $\sum(\beta_i x_m)$ is obtained by multiplying the same coefficients β_i by the prevalence of the risk factors in the study population. For a 54 year-old woman, with a total cholesterol of 246 mg/dL, HDL-C of 54 mg/dL, SBP of 143 mm Hg and DBP of 89 mm Hg, with diabetes and a non-smoker, the value would be calculated as follows:

$$\sum(\beta_i x_i) = 0.3377(54) + (-0.0027(54 \times 54)) + 0.2439(1) + 0(1) + 0.2629(1) + 0.5963(1) + (1) = 11.4$$

$$\sum(\beta_i x_m) = 9.8$$

$$S_{0(t)} = 1 - 0.018 = 0.98$$

$$P_{x(t)} = 1 - 0.98e^{(11.4 - 9.8)} = 0.089$$

The probability of a woman with the characteristics described above having a coronary event in our setting in the next 10 years is 8.9%, a very similar figure to that seen in the box corresponding to the risk tables presented (9%).