Calibrating the SCORE Cardiovascular Risk Chart for Use in Spain

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Introduction and objectives. The Third Joint European Task Force on cardiovascular prevention recommended the SCORE function for predicting 10-year cardiovascular mortality should be used to guide decision-making on clinical interventions. The objective of the present study was to calibrate the function for use in Spain.

Methods. A model was developed to apply the hazard ratios for cardiovascular mortality at 10 years in SCORE study cohorts to the mean age- and sex-specific risk factors found in the third survey of the MONICA-Catalonia study (1994-96) and to 10-year cardiovascular survival function for the Spanish population based on mortality rates for the year 2002.

Results. The estimated risks derived using the calibrated SCORE function were 13% higher than those estimated using the low-risk algorithm. However, the differences between the two varied with age, sex, and, in particular, smoking history. The calibrated SCORE risk chart identified 32 high-risk situations that were not identified in the original low-risk SCORE chart. However, 50% of these situations had a low or zero prevalence. The maximum percentage of subjects who were newly identified as being at a high risk using the calibrated chart was 22%. Most differences were observed in men aged over 55 years.

Conclusions. While risk estimates based on sufficiently large Spanish population cohorts are still not available, application of the original cardiovascular risk function calibrated for use in Spain should enable the appropriate clinical and public health decisions to be taken.


INTRODUCTION

Current guidelines in disease prevention stress the need for multifactorial risk assessment in order to be able to provide integrated preventive advice. Estimating an
ABREVIATIONS
CVD: cardiovascular disease
HR: hazard ratio
MONICA: MONItoring CArdiovascular Diseases
SCORE: Systematic COronary Risk Evaluation
CHD: coronary heart disease

individual’s risk of cardiovascular disease (CVD) or heart disease (CHD) is essential in clinical decision-making to control risk factors.

The first and second European Joint Task Forces on cardiovascular prevention\(^1,2\) estimated coronary risk using a risk chart which was based on a 12-year follow-up of individuals from the original Framingham cohort\(^3\) and their children, which included a total of 5573 individuals. This risk chart overestimates the risk of CHD in several European populations.\(^4-7\) The third Joint Task Force on cardiovascular prevention in clinical practice\(^8\) recommended using the SCORE\(^9\) (Systematic Coronary Risk Evaluation) model instead. This risk chart estimates the 10-year risk of fatal CVD by age, gender, systolic blood pressure, total cholesterol, and current smoking using data from 12 European cohorts which included a total of 205 178 individuals (43% female) aged 24 to 75 years. Given the geographic variability in CV risk in Europe,\(^10\) two SCORE charts were developed, for countries with high and low risk, respectively.\(^1\) The most novel aspect of the SCORE risk chart compared with the Framingham model is that it estimates risk for all atherothrombotic cardiovascular manifestations, including stroke, heart failure, peripheral arterial insufficiency or certain aneurysms, and not just CHD. The change was introduced as the same risk factors differ.\(^12\) The third MONICA-CoE survey (MONItoring Trends and Determinants in CArdiovascular Disease) was selected. This study was performed in 1994-1996\(^13-15\) (Table 1), following the World Health Organization protocol.\(^16\) In Table 2, it is compared with other selected studies\(^17-21\), although it should be borne in mind that the sampling methods and measurement of risk factors differ.

The aim of this article is to present the SCORE risk chart calibrated for Spain.

METHODS

Calibrating the SCORE function required making the following assumptions:

1. The SCORE hazard ratios (HR) for CVD mortality associated with CVD risk factors (total cholesterol, systolic blood pressure, and smoking) are universal and can be applied in the Spanish population.
2. There are no differences in HR by age and sex.
3. Mean risk factor levels used in the calibration can be extrapolated to the whole country.

4. The survival function for a given group defined by age and sex approximates survival associated with the mean level of risk in that group. A person with risk factors above the mean will be at greater risk than someone at the mean. This risk can be calculated if we know the size of the difference of probability of death at 10 years, resulting from the difference with the mean level of risk.

Risk is calculated using a function based on 3 parameters\(^12\):

1. The mean level of sex-specific risk by 5-year age groups. The third MONICA-Catalunya survey (MONItoring Trends and Determinants in CArdiovascular Disease) was selected. This study was performed in 1994-1996\(^13-15\) (Table 1), following the World Health Organization protocol.\(^16\) In Table 2, it is compared with other selected studies\(^17-21\), although it should be borne in mind that the sampling methods and measurement of risk factors differ.

2. Aggregate coefficients of all SCORE cohorts to determine the association of individual risk factors with CVD mortality.

3. CVD mortality rates for the Spanish population by sex and 5-year age groups obtained from the National Institute of Statistics.\(^22\) The year 2002 was chosen to simulate time between exposure to risk factors and death. CVD mortality was defined using the same International Classification of Diseases codes as those used in SCORE (I10-13, I20-25, I44-45, I47-51, I46.1, I60-73, R96.0-96.1 with the exception of I45.6, I60, I62.0, I67.1 and I67.7), though version 10 was used instead of version 9.

The following steps were followed in the calculations: sex-specific CVD mortality rates for each 5-year age group were calculated from the annual mortality rate and the Spanish population from mid-2002.\(^2\) A Poisson


<table>
<thead>
<tr>
<th>Sex and Age Group</th>
<th>N</th>
<th>Smokers, %</th>
<th>Systolic Blood Pressure, mm Hg, Mean (SD)</th>
<th>Total Cholesterol, mg/dL, Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40-44</td>
<td>215</td>
<td>50.2</td>
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<td>220 (42)</td>
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<td>45-49</td>
<td>249</td>
<td>39.0</td>
<td>121 (15)</td>
<td>220 (42)</td>
</tr>
<tr>
<td>50-54</td>
<td>222</td>
<td>36.0</td>
<td>123 (17)</td>
<td>218 (39)</td>
</tr>
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<td>55-59</td>
<td>229</td>
<td>37.6</td>
<td>127 (18)</td>
<td>222 (46)</td>
</tr>
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<td>60-64</td>
<td>252</td>
<td>26.6</td>
<td>128 (18)</td>
<td>218 (40)</td>
</tr>
<tr>
<td>≥65</td>
<td>24</td>
<td>20.8</td>
<td>130 (18)</td>
<td>220 (39)</td>
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<td><strong>Females</strong></td>
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<td>40-44</td>
<td>197</td>
<td>19.8</td>
<td>113 (14)</td>
<td>199 (36)</td>
</tr>
<tr>
<td>45-49</td>
<td>236</td>
<td>9.7</td>
<td>118 (17)</td>
<td>213 (42)</td>
</tr>
<tr>
<td>50-54</td>
<td>183</td>
<td>8.7</td>
<td>121 (16)</td>
<td>224 (37)</td>
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<td>55-59</td>
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<td>4.9</td>
<td>126 (18)</td>
<td>236 (37)</td>
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<td>60-64</td>
<td>201</td>
<td>1.5</td>
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<td>26</td>
<td>3.8</td>
<td>134 (18)</td>
<td>228 (37)</td>
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## TABLE 2. Mean and Standard Deviation for Cardiovascular Risk Factors in Selected Spanish Studies

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<thead>
<tr>
<th>Risk Factor</th>
<th>N</th>
<th>35-44, Mean (SD)</th>
<th>45-54, Mean (SD)</th>
<th>55-64, Mean (SD)</th>
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<tr>
<td>Total cholesterol, mg/dL</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iriarte 1986/87, Basque Country</td>
<td>2899</td>
<td>207.5 (40.5)</td>
<td>205.5 (44.0)</td>
<td>205.5 (43.0)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Banegas 1989, Spain</td>
<td>2021</td>
<td>207.9 (43.4)</td>
<td>209.5 (42.5)</td>
<td>212.3 (45.6)</td>
<td>196.2 (36.8)</td>
<td>214.3 (42.1)</td>
<td>224.2 (42.6)</td>
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<tr>
<td>Tormo 1992, Murcia</td>
<td>1762</td>
<td>197.2 (47.7)</td>
<td>210.9 (47.4)</td>
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<td>193.1 (42.6)</td>
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<tr>
<td>Segura 1994/96, Castilla-La Mancha</td>
<td>706</td>
<td>214.7 (38.3)</td>
<td>219.8 (39.6)</td>
<td>219.7 (41.6)</td>
<td>197.4 (34.1)</td>
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<td>230.3 (44.9)</td>
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<td>2609</td>
<td>212.5 (42.2)</td>
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<td>220.6 (42.9)</td>
<td>197.0 (34.4)</td>
<td>219.4 (40.6)</td>
<td>234.1 (37.2)</td>
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<tr>
<td>SBP, mm Hg</td>
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<td></td>
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<td>140 (18.5)</td>
<td>149 (21.5)</td>
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<td>–</td>
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<tr>
<td>Banegas 1989, Spain</td>
<td>2021</td>
<td>126 (16.9)</td>
<td>131 (17.2)</td>
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<td>2317</td>
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<td>139 (21.7)</td>
</tr>
<tr>
<td>Segura 1994/96, Castilla-La Mancha</td>
<td>722</td>
<td>128 (12.6)</td>
<td>134 (17.5)</td>
<td>144 (20)</td>
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<tr>
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<td>1119</td>
<td>122 (12.3)</td>
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<td>117 (12.5)</td>
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<tr>
<td>DBP, mm Hg</td>
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<td></td>
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<td>81 (10.4)</td>
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<td>73 (10.4)</td>
<td>79 (10.9)</td>
<td>83(12.4)</td>
</tr>
<tr>
<td>Segura 1994/96, Castilla-La Mancha</td>
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<td>79 (10.0)</td>
<td>83 (11.5)</td>
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<td>81 (11.8)</td>
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<td>76 (10.0)</td>
<td>70 (9.6)</td>
<td>74 (9.6)</td>
<td>76 (10.1)</td>
</tr>
<tr>
<td>Smokers, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Iriarte 1986/87, Basque Country</td>
<td>2932</td>
<td>43.0</td>
<td>37.5</td>
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<td>–</td>
</tr>
<tr>
<td>Banegas 1989, Spain</td>
<td>2021</td>
<td>56.3</td>
<td>47.7</td>
<td>43.3</td>
<td>32.2</td>
<td>11.4</td>
<td>4.7</td>
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<td>Tormo 1992, Murcia</td>
<td>2317</td>
<td>59.9</td>
<td>52.3</td>
<td>44.0</td>
<td>42.9</td>
<td>17.3</td>
<td>4.0</td>
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<tr>
<td>Segura 1994/96, Castilla-La Mancha</td>
<td>720</td>
<td>46.9</td>
<td>41.8</td>
<td>34.4</td>
<td>27.0</td>
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<td>0.6</td>
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<td>50.8</td>
<td>37.6</td>
<td>31.8</td>
<td>28.3</td>
<td>9.3</td>
<td>3.1</td>
</tr>
</tbody>
</table>

SD indicates standard deviation; DBP, diastolic blood pressure; SBP, systolic blood pressure.

†Venous blood. 12 hour fasting. Enzymatic method.

‡Non-fasting capillary blood. Reflotron method.

§Venous blood. 14 hour fasting. Analysis performed in samples frozen to –80°C 3-4 months after extraction.

¶Random zero sphygmomanometers.

IIStandard mercury sphygmomanometer.

#Different age groups: 30-39, 40-49, 50-65 years.
regression for those rates was performed with age as a linear function joining the midway point in each 5-year age interval. Ten-year mortality rates were then estimated for each age group and the CVD accumulated survival rate was calculated.

A quadratic regression model was used for blood pressure and total cholesterol and age. A logistic regression model was used for smoking prevalence. The regression function obtained allowed us to estimate the mean level of each risk factor for a given age group (Table 1). Finally, risk coefficients from all SCORE cohorts were applied to obtain the 10-year CVD mortality risk for smokers and non-smokers given specific blood pressure and cholesterol values. All statistical analysis and models were stratified by sex.

Using the SCORE function, the Third Task Force defined high risk as being a 5% risk of 10-year CVD mortality in asymptomatic individuals and recommended intensifying preventive interventions beyond that cutpoint. To compare the calibrated table with the low-risk SCORE chart, this cutpoint was used and agreement between rates in the 0%, 1%-2%, 3%-4%, 5%-9% and ≥10% risk categories was tested using the kappa statistic. In the calibrated table, an extra category (systolic blood pressure of 100-120 mm Hg) was added which was not included in the SCORE chart, to adapt the chart to the distribution of blood pressure in the Spanish population, particularly in females. To compare the two charts, individuals in this category were grouped with those in the category above.

The prevalence of different combinations of risk factors in the third health MONICA survey was calculated, for each age group and sex, using the same definitions and cut-points as in the SCORE chart and adding the extra blood pressure category described above.

Two sensitivity analyses were performed. The first explored the effect of using the risk functions from the low-risk cohort, instead of all of the SCORE cohorts, as small differences in HR had been observed (HR=1.07, 1.02-1.13) for cholesterol compared with all cohorts (HR=1.19, 1.17-1.21) and for smoking (HR=1.54, 1.34-1.77; HR=2.06, 1.96-2.16), although not for systolic blood pressure. In the second sensitivity analysis, the effect of applying risk factors from another study which had almost nation-wide coverage was examined, instead of using those from the MONICA-Catalonia study.

In order to estimate the number of people aged 40 to 74 years at high risk in Spain, the age and sex specific proportional distribution was extrapolated for each combination of factors leading to high risk (≥5%) to the demographic structure of each of the 17 autonomous communities. Finally, in order to comprehend the size of the CVD problem, these data were presented, together with total deaths and hospital admissions for the same age ranges published by the National Institute of Statistics.

The statistical analysis was carried out using Stata®, version 8.2, SPSS® version 9 (SPSS Inc. Chicago, IL, USA) and Microsoft Excel®.

**RESULTS**

In 2002, there were 25 875 atherosclerotic CVD deaths in Spain in the population aged 40 to 74 years (90 and 228 deaths per 100 000 women and men, respectively). Mortality rates increased with age, particularly in men over 60 and women over 65. CVD mortality rates in women are similar to those in men aged a decade younger. In the population under 65 years, the risk of CVD death is under 50% of the high risk threshold (≥5%) (Figure 1). Coronary mortality rates are 62% of atherosclerotic CVD mortality in men, but only 36% in women in the age range studied.
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Table. The calibrated Table identifies 32 such situations (41% in women). Nevertheless, the prevalence of half of the new situations was virtually nil in this population. The new high risk situations increase with age and smoking, and in males aged 55 years or over. There are practically no high risk situations under 50 years of age in either of the Tables, except where there is a very high risk isolated factor or diagnosed CVD disease. Of the 201 women aged 60–64 years, 29% (95% confidence interval [CI], 22–35) were at high risk. Among men aged 55, 57% (47–68) of smokers but only 5% (1–9) of non-smokers were at high risk. These percentages increase to 92% (85–99) and 37% (30–44) for smokers and non-smokers aged 60 years and to 100% and 90% (95–100), respectively, at 65 years.

Figure 2 shows the 10-year CVD mortality risk tables calibrated for Spain. Figure 3 shows the mean calibrated CVD risk by sex, smoking habit, and age group. CVD risk increases with age and smoking and is higher in men. CVD risk in a woman who smokes is similar to that of a non-smoking man, except in the 65 year age group.

Figure 4 has the same format as Figure 2 but instead shows the prevalence of different combinations of risk factors in the MONICA-Catalonia study. Summing the percentages in the red and purple cells provides the prevalence of the high risk population by age group, sex, and smoking habit. The color purple is used to indicate high risk categories in the calibrated Table which were not classified as such in the original SCORE

![Figure 2](http://www.revespcardiol.org)  Estimated 10-year risk of atherosclerotic cardiovascular mortality for specific systolic blood pressure values and total cholesterol, according to smoking history, sex, and age. SCORE chart calibrated for Spain.

![Figure 3](http://www.revespcardiol.org)
The overall level of agreement between both tables (Table 3) was good (kappa=0.65; \( P < .0001 \), males 0.56 and females 0.72).

**Sensitivity Analysis**

In the first sensitivity analysis, the calibration was repeated using the HR from low-risk SCORE cohorts. The probabilities obtained in this way were higher than those in the low-risk SCORE chart. Agreement with the low-risk SCORE chart was good (kappa=0.73; \( P < .0001 \)). Fifteen situations with a risk of \( \geq 5\% \) were identified which had not been identified in the low-risk SCORE chart, particularly in men (12). These are not necessarily the same situations as in the calibrated chart (Figure 4).

In the second sensitivity analysis, the risk factors from another study and the HR from all SCORE cohorts were used. Agreement with the low-risk SCORE charts (kappa=0.86; \( P < .0001 \)) and with the calibrated charts (kappa=0.67; \( P < .0001 \)) was good, and the differences with them were minimal except in the case of males aged 60 years. In the latter group, the calibrated risk was 38% lower.

Table 4 shows the estimated number of people between the ages of 40 and 74 years in the Spanish population who are at high risk according to the calibrated function. Andalusia and Catalonia had the highest numbers of individuals at high risk.

**DISCUSSION**

Risk estimation should be based on follow-up from large cohorts. However, in many countries, particularly in Southern Europe, there are no sufficiently large

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**TABLE 3.** Comparison of the Frequency of Cardiovascular Risk Categories in Both Sexes According to the Low Risk SCORE Charts and the Calibrated Risk Chart for Spain

<table>
<thead>
<tr>
<th>Cardiovascular Risk</th>
<th>Low Risk SCORE Chart</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Calibrated risk chart for Spain</td>
<td>46</td>
</tr>
</tbody>
</table>

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population-based cohorts to provide accurate estimates of risk by age and sex. The low-risk SCORE chart was based on HR which are common to all of the SCORE cohorts, and survival in the low-risk cohorts.\(^9\) The Third Task Force recommended adapting the charts while taking into account each country’s level of risk and mortality rates. Calibrating the charts to take into account the situation in any given country means using statistical models which are subject to a series of assumptions.

The first and second assumptions concern the external validity of the SCORE HRs for CVD mortality. Although some studies\(^{26-28}\) have found differences in the HR for heart disease between European regions, these differences were not observed in other studies, except for smoking. There were no significant, large differences between cohorts or genders for CVD mortality using SCORE, although differences were found when low-risk cohorts were aggregated. Given the reduced accuracy of the HR in these groups and the possibility of wrongly classifying individuals, it was considered appropriate to use the HR from all of the SCORE cohorts to carry out the calibration.

The third assumption implies that the mean for risk factors in the MONICA-Catalonia study is valid for the whole of Spain. The calibrated chart was calculated using Spanish mortality data together with risk factors from the third MONICA survey.\(^{11,15}\) The latter was adopted because of the exhaustive international controls which ensured their high quality\(^9\) and because no other study of risk factors has included cholesterol determination using standardized methods across the whole country. Furthermore, 50% of the individuals in the MONICA sample were born in other autonomous communities, similar the composition of the Catalan population. The study therefore incorporates the diversity of Spanish population.

Cholesterol levels and smoking habits in the MONICA-Catalonia study were similar to those in other MONICA centers in the Mediterranean region\(^{31}\) and other regions in Spain.\(^{19,21,32}\) Blood pressure values were similar to those in international studies,\(^{33,34}\) though they differ slightly from those in other Spanish studies. This is likely to be due to the fact that, in the other studies, blood pressure was measured with standard mercury sphygmomanometers, which do not avoid digit preference and lead to slightly higher blood pressure readings than the random zero sphygmomanometers used in the MONICA study.\(^{35}\) The second sensitivity analysis used risk factors from another study\(^{17}\) and led to similar risks. The use of the MONICA-Catalonia data to calibrate the SCORE model therefore seemed reasonable.

The fourth assumption is that expected survival times in a particular sex and age group approximately reflects survival, given mean levels of risk factors in that group. There has been some discussion as to whether the risks obtained in the analysis of individual cohorts might overestimate individual risk,\(^36\) but modeling indicates that the overestimation is not large.

The Framingham coronary function was calibrated for Spain using REGICOR data, but this study provided total cholesterol values which were higher than the mean for Spain (Table 2) and it has been shown that the Framingham algorithm overestimates risk in many European populations.\(^{4,7}\) The number of people at high risk who are candidates for cholesterol treatment in primary care was lower for Spain when using the SCORE function as compared to the Framingham model (ATP-III version [Adult Treatment Panel III]).\(^{38}\)

The SCORE model calibrated for Spain produces risks which are 13% higher than the low-risk SCORE function, principally due to smoking. However, the calibrated chart leads to some risk situations which were not identified in the original SCORE chart, and which are clinically evident; for example, non-smoking women aged 60 with blood pressure of 180 mm Hg and total cholesterol of 8 mmol/L. In both charts, very few women are at high risk before the age of 55 years, over 50% of smokers, but only a minority of non-smokers, will require prevention. These percentages increase considerably over the age of 60. Several studies\(^{9,40}\) have shown that 18% of patients with confirmed CVD continued to smoke 6 months after an acute episode, even though the proportion decreased between 2000 and 2005. If high risk smokers gave up smoking, their risk would decrease almost immediately and, accordingly, the proportion of the population at high risk. The stringent application of the recent Anti-Smoking
Law might help to lower CVD risk and the risk of other chronic disease across society as a whole.

It is estimated that over three million people aged 40 to 74 years in Spain are asymptomatic but have a risk of ≥25%. These people would be candidates for intensive preventive advice. This figure does not include individuals at high risk because they have one very high risk factor (blood pressure ≥180/110 mm Hg, total cholesterol ≥8 mmol/L, low-density lipoprotein cholesterol ≥6 mmol/L). If these are included, the number of candidates for individualized intervention in 2002 would increase to 4,646,896 (3,029,913 men, 1,616,983 women). Patients with manifest CVD should also be added to these numbers. Furthermore, CVD risk is a continuum. Clinicians will frequently see patients who warrant an intensive intervention when there is a 4% risk, but the patient also has a family history of premature CVD. The best clinical judgment will be need in patients aged 55 to 65 years, as this is where predictions are most unsure. Decisions above and below this age range are generally clearer.

High numbers of individuals are, therefore, candidates for intensive intervention, as in other countries. This should come as no surprise, however, as CVD is the leading cause of death, hospitalization (Figure 5), primary care consultations, and health care spending. Updating and adopting organized preventive measures therefore becomes of vital importance if we are to control a health problem which affects the whole of Spanish society.

**CONCLUSIONS**

A simple and practical means of evaluating risk of CVD death in the Spanish population using calibrated charts is presented. The challenge for the future is to introduce efficient public health policies which combine a reduction in population risk with the detection and appropriate treatment of individuals with a high risk of mortality or avoidable incapacity.
REFERENCES


