Consequences of using different methods to assess cardiovascular risk in primary care

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\textbf{Background.} There are two promising methods to assess cardiovascular risk: the Adult Treatment Panel III (ATPIII) and the Systematic Coronary Risk Evaluation (SCORE). The ATPIII calculates the 10-year risk of coronary events based on an adaptation of the original Framingham function. The SCORE chart is based on European studies and measures the absolute risk of cardiovascular mortality in the next 10 years.

\textbf{Objective.} To evaluate the clinical consequences of using different methods to calculate cardiovascular risk and different primary prevention guidelines.

\textbf{Methods.} A cross sectional study of 914 dyslipidemic patients from three primary health centres from Catalonia, Spain, was conducted. Outcome variables were the risk level according to the different equations (classical Framingham table by Anderson, ATPIII adapted Framingham table, and SCORE system), and candidates for lipid lowering treatment according to European and ATPIII guidelines.

\textbf{Results.} The proportion of high-risk patients according to the three equations and excluding diabetic patients was 13.5%, 11.4% and 7.1%, respectively, and 20.2%, 25.7% and 29.2%, respectively when including diabetic patients. The prevalence of candidates for lipid lowering treatment according to European guidelines and ATPIII guidelines were 28.8% and 39.3%, respectively. A 49% disagreement with a Kappa of –0.1, and a 37% disagreement with a Kappa of 0.08 were observed when comparing candidates identified for lipid lowering treatment and patients actually receiving that treatment, according to ATPIII and SCORE guidelines, respectively.

\textbf{Conclusion.} Our results suggest important clinical and economic consequences when comparing European guidelines or ATPIII guidelines for the treatment of dyslipidemic patients in general practice.

\textbf{Keywords.} Cardiovascular risk assessment, lipid lowering drugs, primary care.

\section*{Introduction}

Cardiovascular risk assessment is critical for primary prevention of cardiovascular disease through the prescription of lipid lowering drugs, blood pressure lowering drugs, antiaggregant agents or to give specific medical counseling regarding lifestyle habits.\textsuperscript{1–3} Risk assessment is based on the calculation of the absolute cardiovascular risk through the application of charts or equations included in different guidelines.\textsuperscript{2,3} Most charts/equations have been derived from the Framingham study\textsuperscript{4–6} including some local recalibrations of it.\textsuperscript{7,8} Thus, the most commonly used chart until now was the classical chart by Anderson\textsuperscript{4} because of its simplicity and wide dissemination. However that chart has some drawbacks such as the use of continuous variables (which makes data collection more difficult), the necessity to perform an electrocardiogram (ECG), the use of total coronary end points [angina, silent myocardial infarction (MI), MI, and coronary death] that sometimes are difficult to reproduce (such as angina), and the lack of an accompanying guideline.
Another limitation of this chart was identified when several studies found that this equation overestimated the risk for some European countries.\textsuperscript{9,10}

In order to overcome some of these limitations, Wilson \textit{et al.}\textsuperscript{5} developed a variant of the classical Framingham equation using categorical variables, eliminating the need for an ECG and measuring only hard endpoints (MI and coronary death).

In 2001, the Adult Treatment Panel III (ATPIII) published new recommendations and adopted this new version of the Framingham equation.\textsuperscript{5} Recently, the Systematic Coronary Risk Evaluation (SCORE) systems were launched,\textsuperscript{11} and for the first time the risk chart is based on European studies, looking at northern and southern European countries, and measuring as the end point the absolute risk of cardiovascular mortality in the next 10 years. New European guidelines recommend the SCORE as the new model for cardiovascular risk estimation.\textsuperscript{3}

When comparing some of the risk charts available important differences are found between them, such as different aspects of the studies from which they were developed, the equations themselves and the availability of guidelines (Table 1). The use of equations/charts has been complemented with the development of guidelines for the prevention of cardiovascular disease. Nonetheless, guidelines such as the European guidelines and the ATPIII guidelines are also heterogeneous in terms of identifying candidates for lipid lowering treatment, as is shown in Table 2.

Due to the great heterogeneity of charts and guidelines it is necessary to evaluate the consequences of using different methods of cardiovascular risk assessment in general practice. The objective of this study was to assess and compare the proportion of high-risk patients using the most widely used equations (classical Framingham, ATPIII and SCORE), and the candidates for lipid lowering treatment according to ATPIII and SCORE guidelines.

\section*{Methods}

A cross-sectional study was conducted in patients with a diagnosis of dyslipidemia from three primary health centers in Barcelona, Spain. Patients with incomplete data were invited to attend the center in order to complete the required information. Males and females 30 to 85 years old with a diagnosis of dyslipidemia were included. Exclusion criteria were: established cardiovascular disease and familial dyslipidemia. Independent variables were: age, sex, systolic blood pressure (SBP), smoking, total cholesterol, low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c), diabetes, left ventricular hypertrophy.

\begin{table}[h]
\centering
\caption{Comparison of methods to assess cardiovascular risk patients}
\begin{tabular}{|l|c|c|c|}
\hline
Variable & FRAMINGHAM ATP III & SCORE & FRAMINGHAM ANDERSON \\
\hline
Number of subjects & 5,345 & 205,178 & 5,573 \\
Proportion of females & 53\% & 43\% & 53\% \\
Age range & 20–79 & 40–65 & 30–74 \\
End points & Hard coronary events & Cardiovascular deaths & Hard and soft coronary events \\
Locations & Framingham & 12 studies in Europe & Framingham \\
Type of study & Cohort & Cohort & Cohort \\
Statistical analysis & Cox regression & Weibull & Cox regression \\
Number of variables & 7 & 5 & 9 \\
List of variables & Age & Age & Age \\
& SEX & Sex & Sex \\
& SBP & TC & SBP \\
&treated & SBP & TC \\
& untreated & Smoking & Smoking \\
& TC & HDL-c & Smoking \\
& HDL-c & Smoking & diabetes \\
Guidelines & YES & YES & NO \\
Validation & NO & NO & YES \\
\hline
\end{tabular}
\end{table}

ATP = Adult Treatment Panel; SCORE = Systematic Coronary Risk Evaluation; SBP = systolic blood pressure; HBP = high blood pressure; TC = total cholesterol; HDL-c = high-density lipoprotein cholesterol; LVH = left ventricular hypertrophy.
hypertrophy and antihypertensive treatment (AHT). In patients undergoing lipid lowering or antihypertensive treatment values used were those on treatment. Dependent variables were the risk level according to the following equations: (1) classical Framingham table by Anderson; (2) ATPIII adapted Framingham table; and (3) SCORE system, and candidates for lipid lowering treatment according to European guidelines and ATPIII guidelines. The Anderson and the SCORE equations were programmed in the SPSS software, whereas the calculations for the ATPIII adapted Framingham table were carried out on the website of the National Heart, Lung and Blood Institute. Patients were classified as high-risk patients when their ten-year risk of coronary heart disease was \( > 20\% \) according to Framingham equations (Anderson and ATPIII adaptation) or when their ten-year risk of cardiovascular mortality was \( > 5\% \) according to SCORE system.

Patients were also identified as candidates for lipid lowering treatment according to the new European guidelines or according to ATPIII guidelines.

**Analysis**

Percentages were calculated for categorical variables and means with their standard deviation were calculated for the continuous variables. In addition, the Kappa statistic and the proportion of agreement between ATPIII and SCORE were calculated. The software used for all analysis was SPSS for Windows 12.0.

**Results**

Complete data were obtained from 914 of 1016 subjects (90%). There were 565 women (61.8%). The mean age of subjects was 61.9 \( \pm \) 11.3 years, women being older than men (64.1 \( \pm \) 10.4 versus 58.3 \( \pm \) 11.8 respectively, \( P < 0.001 \)). The prevalence of cardiovascular risk factors was as follows: smoking 19.1\%, diabetes 20\%, hypertension 45.6\%, left ventricular hypertrophy 3.5\%, lipid lowering treatment 41.2\%, and hypertension treatment 39.5\%. The means with their respective standard deviations of cholesterol and its lipid fractions were: cholesterol 241.4 \( \pm \) 42.6 mg/dl, LDL-c 154.7 \( \pm \) 41.1 mg/dl, HDL-c 54.7 \( \pm \) 13.7 mg/dl, triglycerides 163.3 \( \pm \) 92.9. In addition, the mean value of glycaemia was 108.2 \( \pm \) 35.7 mg/dl and the mean value of body mass index (BMI) was 28.4 \( \pm \) 4.5.

Figure 1 shows the proportion of high-risk patients when applying the three equations (classical Framingham, ATPIII and SCORE) and excluding diabetic patients. The highest prevalence of high-risk patients was obtained with the classical Framingham equation (13.5\%), followed by the SCORE (11.4\%), and the ATPIII (7.1\%). However, the highest prevalence among women was obtained with SCORE (3.9\%).

When diabetic patients were included in the calculations as shown in Figure 2 (all diabetics were classified directly as high-risk patients when using both the ATPIII adapted Framingham equation and the

<table>
<thead>
<tr>
<th>European guidelines</th>
<th>ATPIII guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 Year Risk</td>
<td></td>
</tr>
<tr>
<td>( \geq 5% ) and either:</td>
<td>( \geq 20% ) and:</td>
</tr>
<tr>
<td>Cholesterol ( &gt; 190 ) mg/dl</td>
<td>LDL-c ( &gt; 100 ) mg/dl</td>
</tr>
<tr>
<td>LDL-c ( &gt; 115 ) mg/dl</td>
<td></td>
</tr>
<tr>
<td>10 Year Risk</td>
<td></td>
</tr>
<tr>
<td>10 Year Risk</td>
<td></td>
</tr>
<tr>
<td>Cholesterol ( &gt; 320 ) mg/dl</td>
<td></td>
</tr>
<tr>
<td>LDL-c ( &gt; 240 ) mg/dl</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
</tr>
<tr>
<td>Cholesterol ( &gt; 175 ) mg/dl</td>
<td>LDL-c ( &gt; 100 ) mg/dl</td>
</tr>
<tr>
<td>LDL-c ( &gt; 100 ) mg/dl</td>
<td></td>
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</tbody>
</table>

ATP = Adult Treatment Panel; LDL-c = low-density lipoprotein cholesterol.

**Table 2** Comparison of guidelines to assess candidates for lipid lowering treatment
SCORE system, since both guidelines consider diabetes as a risk equivalent of an MI), the highest prevalence of high-risk patients was obtained with SCORE (29.2%) and the lowest with the Framingham Anderson (20.2%). In this Figure again, the highest prevalence among women was observed with the SCORE equation (22.1%) whereas the lowest prevalence among women was obtained with the original Framingham equation (9.2%). The prevalence of candidates for lipid lowering treatment according to European Guidelines and ATPIII are presented in Figure 3. The overall prevalence of candidates for lipid lowering treatment is 39.3% for the ATPIII guideline, and 28.8% for the European guidelines. Table 3 shows the characteristics and mean values of candidates for lipid lowering treatment according to European guidelines and ATPIII guidelines. Candidates for lipid lowering treatment according to European guidelines are significantly older, with higher systolic blood pressure, triglycerides, BMI and fasting glycemia, and a higher proportion of smokers when compared with those identified by ATPIII guidelines.

When excluding diabetic patients, a disagreement of 22.9% was observed when comparing high-risk patients according to SCORE and ATPIII equations, with a corresponding Kappa value of 0.35. A 49% disagreement with a Kappa of –0.1, and a 37% disagreement with a Kappa of 0.08 were observed when comparing candidates for lipid lowering treatment and patients actually receiving that treatment, according to ATPIII and SCORE guidelines, respectively.

![Figure 2](https://example.com/figure2.png)  
**Figure 2** Proportion of high risk patients according to different risk equations (including diabetics)

![Figure 3](https://example.com/figure3.png)  
**Figure 3** Proportion of CLLT according to European Guidelines and ATPIII guidelines

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Comparison of percentages and mean values of the characteristics of patients candidates for lipid lowering treatment according to European guidelines and ATPIII guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>European guidelines n = 263/915</td>
</tr>
<tr>
<td>Age</td>
<td>61.3 ± 6.0</td>
</tr>
<tr>
<td>Females (%)</td>
<td>50.2</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>140.5 ± 17.2</td>
</tr>
<tr>
<td>Hypertension treatment (%)</td>
<td>55.9</td>
</tr>
<tr>
<td>Anti-aggregant (%)</td>
<td>24.3</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>26.2</td>
</tr>
<tr>
<td>Total cholesterol mg/dl</td>
<td>247.0 ± 47.9</td>
</tr>
<tr>
<td>LDL-c mg/dl</td>
<td>156.9 ± 44.3</td>
</tr>
<tr>
<td>HDL-c mg/dl</td>
<td>52.4 ± 12.4</td>
</tr>
<tr>
<td>Triglycerides mg/dl</td>
<td>186.1 ± 100.0</td>
</tr>
<tr>
<td>BMI</td>
<td>29.2 ± 4.6</td>
</tr>
<tr>
<td>Glycemia</td>
<td>134.2 ± 46.5</td>
</tr>
</tbody>
</table>

ATP = Adult Treatment Panel; LDL-c = low-density lipoprotein cholesterol; HDL-c = high-density lipoprotein cholesterol; BMI = body mass index.
Discussion

In this study we evaluated the clinical consequences of using different methods of cardiovascular risk assessment in patients diagnosed with dyslipidaemia in general practice. Guidelines have become important management tools in evidence-based health care and preventive medicine. Recommendations on how to prevent cardiovascular disease have been given by different expert committees in Europe and abroad.

The most important results of this study with clear implications in general practice are the ones when comparing ATPIII guidelines and European guidelines, because in practice we may use one or the other which include tables to assess cardiovascular risk but also consider other aspects of importance in the decision to treat dyslipidaemic patients with lipid lowering drugs. Specifically, we have observed that when using European guidelines 29% of our dyslipidaemic patients were candidates for lipid lowering drugs while when using ATPIII guidelines 39% of our dyslipidaemic patients were candidates for lipid lowering drugs. If we apply those results to our population (914 patients diagnosed with dyslipidaemia), it would mean treating 265 patients if European guidelines were used or treating 365 patients if ATPIII guidelines were used. If we translate this into costs, it would turn out that if we apply the European guidelines it would cost 105 385 euros per year, while if we apply the ATPIII guidelines it would cost 145 153 euros per year, an increase of 38% (based on the Spanish price of a generic statin, 40 mg a day).

Another important issue that we have observed in our results, also with clinical consequences in general practice, is the remarkable difference in the patient profile identified by both systems. While ATPIII identified more female, younger and with worse lipid profile patients (higher LDL-c and total cholesterol) the SCORE system identified patients with higher systolic blood pressure, triglycerides, BMI and fasting glycemia, and they were more often smokers. These differences are likely to be due to the different outcomes that the two systems measure. The ATPIII measures the risk of hard coronary events, whereas the SCORE measures the risk of cardiovascular death.

In addition to the large difference in the prevalence of candidates for lipid lowering treatment observed when applying the two systems, important disagreement between SCORE and ATPIII was observed (23%) with a corresponding Kappa value of 0.35. Even greater disagreement was observed when patients actually receiving lipid lowering drugs were compared with candidates for lipid lowering treatment according to ATPIII guidelines and European guidelines. It is interesting to notice that the actual prevalence of patients taking lipid-lowering drugs (41.2%) was greater than those potentially obtained with European guidelines (28.8%) or with ATPIII guidelines (39.3%). However, a limitation of this study was inherent to its own cross-sectional design; all patients were dyslipidaemic and 20% were diabetics (which could distort the use of these equations and guidelines in the general population) and many were already receiving lipid lowering treatment which could have modified their risk at the time their risk assessment was performed.

Other studies that had the intention to compare risk calculation tools in general practice\(^4\) did not achieve that because only a minority of patients’ records contained all the risk factors required for the formal calculation. In our study we actively searched for those patients for whom some data on risk factors was not available, therefore we obtained complete data on 90% of the subjects.

Other studies\(^5\) compared the accuracy of cardiovascular disease risk prediction methods but always based on equations derived from the Framingham heart study. To our knowledge this is the first study based in general practice where there is a formal comparison of classical tools for risk estimation such as the Framingham equation,\(^4\) and guidelines based on this equation\(^5\) and new tools such as the recently published SCORE system based on European populations.\(^1\) Our results are relevant to general practice where most primary prevention of CHD and management of people with risk factors takes place, in the sense that if we were to use ATPIII guidelines more people with dyslipidaemia would be treated than if we were to use European guidelines, a fact that has also clear economic consequences. Another clinical consequence in general practice of using one or the other recommendation is that the profile of patients identified as high risk is different.

Conclusion

Our results suggest important clinical and economic consequences when comparing European guidelines and ATPIII guidelines for the treatment of dyslipidaemic patients in general practice, both in terms of the absolute number of patients who are candidates for lipid lowering treatment and also in the different profiles of patients identified to be treated.

Acknowledgements

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Declaration

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Ethical approval: Ethical Committee of the University Clinic Hospital of Barcelona.
Conflicts of interest: none.
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