ORIGINAL ARTICLE

The REGICOR-Calibrated Function Provides a Better Classification of High-Risk Patients on Statin Treatment in the Spanish Population Than the Framingham or SCORE Classifications

José M. Baena-Díez,[a,b,c] María Grau,[c] Ricard Sánchez-Pérez,[a] Eva Altes-Vaques,[a] Luis H. Salas-Gaetjens,[a] and María R. Hernández-Ibáñez[a]

[a]Centro de Salud La Marina, Institut Català de la Salut, Barcelona, Spain
[b]IDIAP/Fundación Jordi Gol i Gurina, Institut Català de la Salut, Barcelona, Spain
[c]Grupo de Epidemiología y Genética Cardiovascular (ULEC-EGEC), Programa de Investigación en Procesos Inflamatorios y Cardiovasculares, Instituto Municipal de Investigación Médica, IMIM-Hospital del Mar, Barcelona, Spain

Introduction and objectives. To determine which cardiovascular risk function is best for classifying high-risk individuals on statins.

Methods. Descriptive cross-sectional study of 804 randomly selected patients aged 35-74 years. Variables studied included statin treatment, high cardiovascular risk according to Framingham-REGICOR (10-year risk ≥10%), Framingham-Wilson (10-year risk ≥20%) and SCORE (10-year risk ≥5%) functions, age, sex, cardiovascular risk factors, and total and high-density lipoprotein (HDL) cholesterol.

Results. Overall, 83 patients (10.3%) were taking statins. The prevalence of hypercholesterolemia was 25.6%. When high-risk patients were compared with low- and medium-risk patients, the SCORE function only found a significant difference in HDL-cholesterol level (difference, 5.1 mg/dl; *P*<.001), whereas the Framingham-REGICOR and Framingham-Wilson functions showed that hypercholesterolemia was more prevalent (at 41% and 37.8%, respectively), the total cholesterol level was higher (difference, 15 mg/dL and 12.5 mg/dL, respectively), and the HDL-cholesterol level was lower (difference, 11.9 mg/dL and 12 mg/dL, respectively; all *P*<.001). The percentage of patients on statins classified as high-risk by each function was 16% for Framingham-REGICOR (odds ratio [OR]=1.81; 95% confidence interval [CI], 1.01-3.27), 13.4% for Framingham-Wilson (OR=1.47; 95% CI, 0.87-2.47), and 10.6% for SCORE (OR=1.09; 95% CI, 0.50-2.37). Statin use was also significantly associated with hypertension (OR=1.89; 95% CI, 1.20-2.99) and hypercholesterolemia (OR=11.01; 95% CI, 6.55-18.53), and inversely associated with age in patients <65 years (OR=0.51; 95% CI, 0.32-0.81).

Conclusions. The Framingham-REGICOR function was better at classifying high-risk patients on statins than the Framingham-Wilson or SCORE functions. Statin use was associated with hypercholesterolemia and hypertension and inversely with age in patients <65 years.

Correspondence: Dr. J.M. Baena Díez.
Instituto Municipal de Investigación Médica (IMIM).
Dr. Aiguader 88. 08003 Barcelona. España.
E-mail: jbaena@imim.es

Received February 3, 2009.
Accepted for publication June 17, 2009.

Key words: *Statins. Primary prevention. Cardiovascular risk factors. Coronary heart disease risk functions.*

La función calibrada REGICOR mejora la clasificación de los pacientes de alto riesgo tratados con estatinas respecto a Framingham y SCORE en la población española

Introducción y objetivos. Estudiar qué función de riesgo cardiovascular clasifica mejor a los pacientes con riesgo cardiovascular alto que toman estatinas.

Métodos. Estudio descriptivo, transversal que incluye a 804 pacientes de 35-74 años, seleccionados aleatoriamente. Se estudiaron las variables tratamiento con estatinas, riesgo cardiovascular alto con las ecuaciones de Framingham-REGICOR (≥ 10% a 10 años), Framingham-Wilson (≥ 20% a 10 años) y SCORE (≥ 5% a 10 años), edad, sexo, colesterol total, colesterol de las lipoproteínas de alta densidad (cHDL) y factores de riesgo cardiovascular.

Resultados. Tomaban estatinas 83 (10,3%) pacientes. La prevalencia de hipercolesterolemia fue del 25,6%. Comparando a los pacientes de bajo y medio riesgo con los de alto riesgo, SCORE sólo halló diferencias significativas en el cHDL más bajo (diferencia: 5,1 mg/dl; p < 0,001), mientras que Framingham-REGICOR y Framingham-Wilson mostraron (p < 0,001) mayor prevalencia de hipercolesterolemia (el 41 y el 37,8%, respectivamente), colesterol total más elevado (diferencia, 15 y 12,5 mg/dl, respectivamente) y cHDL más bajo (diferencia, 11,9 y 12 mg/dl, respectivamente). Tomaba estatinas el 16% de pacientes de alto riesgo con Framingham-REGICOR (*odds ratio* [OR] = 1,81; intervalo de confianza [IC] del 95%, 1,01-3,27), el 13,4% con Framingham-Wilson (OR = 1,47; IC del 95%, 0,87-2,47) y el 10,6% con SCORE (OR = 1,09; IC del 95%, 0,50-2,37). Se asociaron significativamente al uso de estatinas la hipertensión (OR = 1,89; IC del 95%, 1,20-2,99) y la hipercolesterolemia (OR = 11,01; IC del 95%, 6,55-18,53), con una relación inversa con la edad < 65 años (OR = 0,51; IC del 95%, 0,32-0,81).

Conclusiones. La función Framingham-REGICOR clasifica mejor que Framingham-Wilson y SCORE a los pacientes de riesgo alto que reciben tratamiento con estatinas. La prescripción se asoció al diagnóstico de hipercolesterolemia y HTA y fue menor en pacientes < 65 años.

Palabras clave: *Estatinas. Prevención primaria. Factores de riesgo cardiovascular. Ecuaciones de riesgo cardiovascular.*

ABBREVIATIONS

CVR: cardiovascular risk
CVRF: cardiovascular risk factors
DM: diabetes mellitus
HDL-C: high-density lipoprotein cholesterol

INTRODUCTION

Cardiovascular disease is still the leading cause of death in Spain.[1] Primary prevention, by means of detection and treatment of cardiovascular risk factors (CVRF), is one of the most important preventive strategies.[2]

Hypercholesterolemia is one of the main modifiable CVRF,[2] together with smoking, diabetes mellitus (DM), and hypertension. Drugs, mainly statins, are available that efficiently reduce plasma cholesterol concentrations and cardiovascular events.[3] Their efficacy in secondary prevention is unquestioned and their use in these patients is a priority.[3] This efficacy is less in primary prevention, especially relating to the absolute reduction in risk,[3] and it has not yet been clearly demonstrated in women[4,5] or older persons.[4,6,7]

The prevalence of hypercholesterolemia is high, with 23% of the Spanish population having figures above 250 mg/dL,[8] and the prescription of statins has experienced an important increase over recent years.[9] This high prevalence, coupled with the low absolute reduction in risk with statins in primary prevention, has led to their use being encouraged[4,10] in patients with hypercholesterolemia and a high cardiovascular risk (CVR), mainly as a result of estimations from functions based on prospective studies.[4] Another argument favoring prioritizing the use of statins is that the risk:benefit ratio of lipid-lowering therapy in primary prevention has only been shown in patients with a 10-year coronary risk ≥13%.[11]

Currently in Spain there exist 3 functions to estimate a high CVR: the Framingham-Wilson function,[12] the Framingham-REGICOR calibrated function (Registre Gironí del COR),[13] and the SCORE function (Systematic COronary Risk Evaluation).[14] The Framingham-REGICOR and the Framingham-Wilson functions are better than SCORE at selecting patients with a high CVR who are candidates for treatment with statins, as they select a higher proportion of patients with hypercholesterolemia,[15,16] although other studies[17-19] have failed to detect clear differences in this respect. Additionally, no studies have evaluated whether the prescription of statins to patients with hypercholesterolemia and a high CVR estimated according to the above mentioned functions differs from what is done in patients with hypercholesterolemia but no high CVR.

The aim of this study was to determine which of the CVR functions (Framingham-Wilson, Framingham-REGICOR, and SCORE) best classifies patients with a high CVR and hypercholesterolemia who receive treatment with statins and to study the factors related with the prescription of these drugs in primary care.

METHODS

Type of Study

We undertook a descriptive, cross-sectional study within the framework of a study on the prevalence of CVRF.[20] This study was carried out in 2 urban health centers in the city of Barcelona, covering a population of 35 275 patients with a medium-low socioeconomic level.

Participant Selection

Participants were selected by simple random sampling among the catchment population. All the participants were aged 35-74 years and had no previous cardiovascular disease (ischemic heart disease, cerebrovascular disease, or peripheral arterial disease in the lower limbs).

Measurements

The data were collected during the first half of 1998, although the results of this study refer to the cross-section taken after 5 years during the first half of 2003, before the generalized use of cardiovascular risk functions.

The study variables included the following:

1. Age and sex.

2. Prescription of statins if the clinical history recorded the chronic prescription (a minimum of 6 months during the last 12 months) of any of the drugs coded as C10AA in the World Health Organization Anatomical Therapeutic Chemical Clasification.[21] Cardiovascular risk was calculated using the last available value of total cholesterol before the start of statin therapy.

3. A high CVR, measured with the following functions:

– Framingham-REGICOR. The patient was considered to have a high CVR if the 10-year risk was ≥10%.
– Framingham-Wilson. A cut-off point of ≥20% at 10 years.
– SCORE. The patient was considered to have a high CVR if the 10-year risk was ≥5%. The SCORE model for low risk countries was used.

4. CVRF. The definition criteria have been given previously,[20] and the following were considered: smoking (considering as smokers those persons who smoked any number of cigarettes daily and ex smokers those who had quit within the previous year[22]); hypertension (classifying the patients as hypertensive if they were taking antihypertensive medication or had 3 consecutive blood pressure measurements ≥140/90 mm Hg,[22] and recording the systolic and diastolic blood pressure figures[22]); confirmed hypercholesterolemia if the patient had 2 measurements ≥250 mg/dL on at least 2 occasions, and recording the values of total cholesterol and high-density lipoprotein cholesterol (HDL-C)[22]; DM according to the criteria of the American Diabetes Association and the World Health Organization, adopted by the Spanish Society of Family and Community Medicine,[23] ie, clinical symptoms together with a random glucose measurement >200 mg/dL, 2 baseline plasma glucose measurements ≥126 mg/dL or a 2-hour oral glucose tolerance test ≥200 mg/dL. Patients already diagnosed with DM or who were receiving treatment with insulin or oral antidiabetic agents were also included.

Statistical Analysis

This analysis was done with SPSS, version 12.0. The proportions were compared using the χ^2 test and the means with the Student *t* test or the corresponding tests if the application conditions were not fulfilled. Study of the factors related to statin prescription was done by calculating the odds ratio (OR), accompanied by its 95% confidence interval (CI), considering such factors to be a high CVR with Framingham-REGICOR, Framingham-Wilson and SCORE, age (classified in 2 groups: <65 and ≥65 years), sex, smoking (smokers and non smokers), hypertension, hypercholesterolemia, and DM, also categorized dichotomously. The sample size was calculated using the GRANMO program,[24] accepting an alpha error of .05 and a beta error of .75 in a bilateral contrast. At least 204 persons with hypercholesterolemia were required in order to detect a difference of ≥0.13 and assuming an expected proportion of hypercholesterolemia of 0.40.[15] The level of rejection of a null hypothesis was alpha <.05 in all cases.

RESULTS

The mean age of the 804 patients included was 56 years, with 59.2% women. Table 1 shows the other main characteristics. Confirmed hypercholesterolemia was diagnosed in 25.6% (95% CI, 22.7-28.8) of the patients, with a greater proportion of women (28.2%) than men (22%), as can be seen in Figure 1 (χ^2, *P*=.048). A high CVR was present in 12.4% of the patients according to Framingham-REGICOR, 20.4% with Framingham-Wilson and 20.1% with SCORE (Table 2).

Statins had been prescribed to 83 patients (10.3%; 95% CI, 8.4-12.6). The proportion of patients with hypercholesterolemia treated with statins was therefore 40.3% (95% CI, 33.8-47.1), with no significant differences between sexes (Figure 1).

Table 2 shows that the proportion of patients with definite hypercholesterolemia was greater in the patients with a high CVR according to the Framingham-REGICOR (41%) and Framingham-Wilson (37.8%) functions than in the patients without a high CVR (χ^2, *P*<.001). However, with SCORE (31.8%) no differences were found (χ^2, *P*=.201). Similar findings (Table 2) can be seen concerning the mean concentrations of total cholesterol: higher figures in the patients with a high CVR with Framingham-REGICOR and Framingham-Wilson (Student *t* test, *P*<.001), but no significant differences with SCORE (Student *t* test, *P*=.555). As regards HDL-C, all 3 functions selected patients with significantly lower values (Table 2), although Framingham-REGICOR and Framingham-Wilson selected a population with lower HDL-C concentrations (about 12 mg/dL) than SCORE (5 mg/dL).

TABLE 1. **Characteristics of the Study Patients**

Age	55.6 (11.1)
Women	476 (59.2)
Smokers	297 (36.9)
Hypertension	295 (36.7)
Systolic blood pressure, mmHg	130.8 (17.9)
Diastolic blood pressure, mmHg	80 (10.3)
Hypercholesterolemia	206 (25.6)
Total cholesterol, mg/dL	217.8 (37.9)
HDL cholesterol, mg/dL	52.4 (14.3)
Diabetes mellitus	112 (13.9)

HDL-C indicates high-density lipoprotein cholesterol.
Variables expressed as n (%) and mean (standard deviation).

TABLE 2. **Proportion of Patients With Hypercholesterolemia and Mean Figures of Total Cholesterol and HDL-C With the Risk Functions Studied**

	Framingham-REGICOR		Framingham-Wilson		STORE	
	<10% n=704	≥10% n=100	<20% n=640	≥20% n=164	<5% n=337	≥5% n=85
Hypercholesterolemia[a]	165 (23.4)[b]	41 (41)[b]	144 (22.5)[b]	62 (37.8)[b]	84 (24.9)	26 (30.6)
Total cholesterol, mg/dL	215.9 (36.9)[b]	230.9 (42.4)[b]	215.3 (36.9)[b]	227.8 (40.4)[b]	219 (38.3)	221.8 (38.1)
HDL-C, mg/dL	53.9 (14.2)[b]	42 (10)[b]	54.9 (14.2)[b]	42.9 (10.2)[b]	54.4 (15.4)[b]	49.3 (13.8)[b]

HHDL-C indicates high-density lipoprotein cholesterol.
[a]Cut-off point, 250 mg/dL.
[b]χ^2/Student *t* test, *P*<.001.
Values expressed as n (%) and mean (standard deviation).

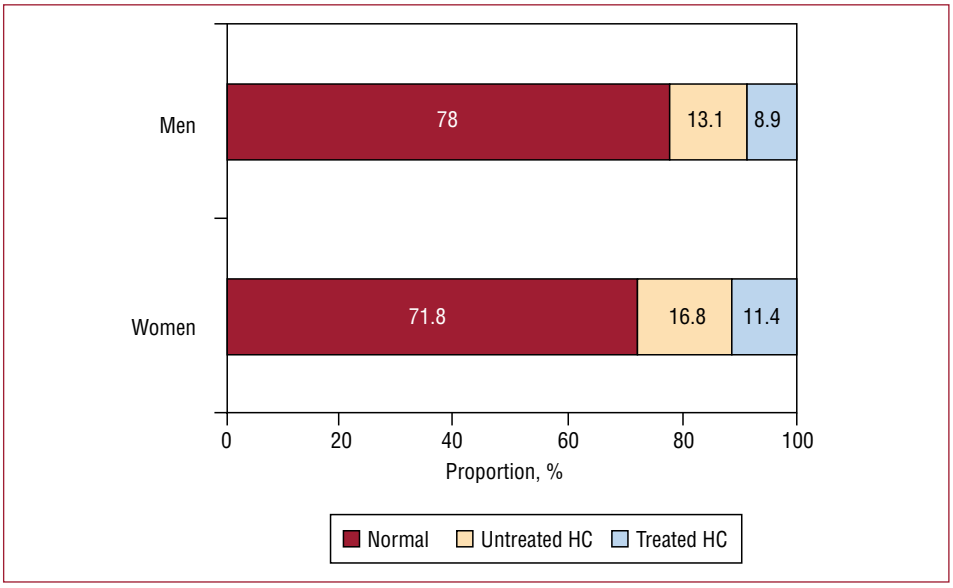

Figure 1. Proportion of patients with treated and untreated hypercholesterolemia (HC) according to sex. Significant differences in the proportion of patients with a diagnosis of HC, treated or untreated (χ^2, *P*=.048).

Table 3 shows the raw OR of the variables associated with the prescription of statins. Prescription was lower in those younger than 65 years of age (OR=0.51; 95% CI, 0.32-0.81). It was also lower in men and in smokers, although the differences were not statistically significant. It was significantly higher in the patients with hypertension (OR=1.89; 95% CI, 1.20-2.99) and hypercholesterolemia (OR=11.01; 95% CI, 6.55-18.53), but not significantly higher in the patients with DM. In the analysis adjusted for the other variables (age <65 years, sex, smoking, hypertension, DM, and hypercholesterolemia), only hypercholesterolemia retained its significance (OR=9.10; 95% CI, 5.48-15.01). Statins were being taken by 16% of the patients with a high CVR according to Framingham-REGICOR, a proportion that was 9.5% in the patients without a high CVR, a significant difference (χ^2, *P*=.046; OR=1.81; 95% CI, 1.01-3.27). However, no significant differences were found with the Framingham-Wilson (OR=1.47; 95% CI, 0.87-2.47) and SCORE (OR=1.09; 95% CI, 0.50-2.37) functions.

DISCUSSION

The results of this study confirm that the proportion of patients with hypercholesterolemia and the mean levels of total cholesterol are higher in patients classified as having a high CVR using the Framingham-REGICOR and Framingham-Wilson functions, but not the SCORE function. The prescription of statins was greater in the patients with a high CVR using Framingham-REGICOR as compared with Framingham-Wilson and SCORE. Considering that cardiovascular risk functions are used to prioritize the use of statins[4,10] in primary prevention patients, the Framingham-REGICOR function would be more useful to rationalize the use of these drugs.

The proportion of patients with confirmed hypercholesterolemia (cut-off point, 250 mg/

TABLE 3. **Variables Associated With the Prescription of Statins in Primary Prevention**

Variable	Patients, n (%)	Raw OR (95% CI)	Adjusted OR (95% CI)
Age <65 years			
Yes	49 (8.4)	0.51 (0.32-0.81)	0.73 (0.42-1.26)
No	34 (15.3)		
Men			
Yes	29 (8.8)	0.76 (0.47-1.21)	0.96 (0.53-1.76)
No	54 (11.3)		
Smokers			
Yes	25 (8.4)	0.71 (0.43-1.16)	1.00 (0.55-1.85)
No	58 (11.4)		
Hypertension			
Yes	42 (14.2)	1.89 (1.20-2.99)	1.31 (0.77-2.23)
No	41 (8.1)		
Hypercholesterolemia			
Yes	61 (29.6)	11.01 (6.55-19.53)	9.10 (5.48-15.01)
No	22 (3.7)		
Diabetes mellitus			
Yes	16 (14.3)	1.56 (0.86-2.79)	1.05 (0.49-2.24)
No	67 (9.7)		
High CVR Framingham-REGICOR			
Yes	16 (16)	1.81 (1.01-3.27)	ND
No	67 (9.5)		
High CVR Framingham-Wilson			
Yes	22 (13.4)	1.47 (0.87-2.47)	ND
No	61 (9.5)		
High CVR SCORE[a]			
Yes	9 (10.6)	1.09 (0.50-2.37)	ND
No	33 (9.8)		

CVR indicates cardiovascular risk; ND, calculation not done in order to avoid overadjusting the model; OR, odds ratio.
[a]In the patients aged 35 to 64 years.

dL) was similar to that reported in the review by Medrano et al,[8] and it also coincides in the distribution by sex.[8] Fewer than half the patients with hypercholesterolemia were receiving statin therapy, a slightly higher proportion of treated patients than in the study by Ramos et al.[25] We found no differences between the sexes regarding statin therapy (Figure 1) in the patients with definite hypercholesterolemia, which agrees with the study by Bonet et al,[26] although another study did find that the women received more lipid lowering drugs.[27] Notwithstanding this, analysis according to sex of statin prescription in all the patients in primary prevention, given that statins can be used with lower levels of cholesterol if there exists a high CVR or more intensive recommendations are followed,[4] showed that the prescription was lower (Table 3) in the men than the women, though the difference was not statistically significant. Interestingly in this respect, the efficacy of statins in primary prevention in women has not in fact been demonstrated, despite carrying out meta-analysis techniques.[5]

Framingham-REGICOR, and to a lesser extent Framingham-Wilson (as expected, since they are very similar functions), were better than SCORE at selecting the population with a high CVR susceptible to statin therapy (Table 2), given that they both included a greater proportion of patients with hypercholesterolemia, with higher concentrations of total cholesterol and lower concentrations of HDL-C. An earlier study[15] found that the proportion of patients with hypercholesterolemia was lower with SCORE (24.7%) than with Framingham-REGICOR (40%) and Framingham-Wilson (38.4%), although the values of total cholesterol and HDL-C were not analyzed. The study by Gil-Guillén et al[16] analyzed the cases of discrepancy in the high-risk patients between SCORE and Framingham-REGICOR; these authors also found important differences in the above mentioned lipid values. Although the patients with a high CVR according to SCORE had a significantly (Table 2) lower level of HDL cholesterol (similar to Framingham-REGICOR and Framingham-Wilson, but with a much smaller

difference), it is important to recall that the SCORE function does not include HDL-C because it fails to improve the predictive capacity of the function.[14] Using SCORE instead of Framingham-REGICOR would result in fewer statins being given to the patients who, paradoxically, most need them.

Surprisingly (Table 3), statins were prescribed less in those younger than 65 years of age, which is precisely the age for which most evidence is available.[3,4] A similar phenomenon was seen in the men and the smokers, about which similar observations can be made,[3,4] though the differences were not statistically significant. The explanation of this paradox might be that the most determining factor in the prescription is the diagnosis of hypercholesterolemia (OR=11.1), with a greater prevalence in women. More coherent are the results in the case of hypertension and DM, although only the former reached statistical significance. After adjusting the effect for the other variables (Table 3), only a diagnosis of confirmed hypercholesterolemia was significantly associated with the prescription of statins.

The patients with a high CVR as estimated with the Framingham-REGICOR function received (Table 3) more statins than those with a high CVR estimated using the other 2 functions. Table 3 does not include the adjusted OR, as the functions studied already included the rest of the risk factors in Table 3, in order to avoid overadjustment. Previous studies using the Framingham function coincide with these results.[27,28] With SCORE, however, the proportion of patients treated with statins was very similar for the patients with a high CVR (10.6%) and those without (9.8%).

Study Limitations

The proportion of women was higher than men, which is usual in other population-based studies in our setting.[29] The inclusion of patients who were being attended should not be considered a bias, as the center has been in operation for over 10 years and 83.8% of the population were seen during the last year.[30] The assigned population and the attended population are methods that are preferable to the censored population in primary care, after a study carried out by the Fundación Jordi Gol y Gurina.[31] The calculation of cardiovascular risk with Framingham-REGICOR and SCORE was generalized in 2003,[13,14] and it is not therefore likely that the prescription of statins has been influential, as the cross-section cut of the study was done beforehand. Nevertheless, the extrapolation of these results to other populations should be made with caution, as this was not a strict multicenter study, and it may be interesting to carry out similar studies in other populations with different prevalences of CVRF and cardiovascular disorders.

Clinical Implications

Several different autonomous communities in Spain (Catalonia, Basque Country, Balearic Isles, Navarre) have officially adopted the use of the Framingham-REGICOR function. However, the debate still exists as far as the scientific societies are concerned.[4] The Program for Preventive Activities and Health Promotion support[2] the use of SCORE in spite of the fact that the validation of REGICOR had already been published.[32] The Spanish Interdisciplinary Committee for Cardiovascular Prevention,[33] whilst they were in favor of SCORE in 2004, made it clear that decisions should be made according to the local adaptations and validations until such time as their own functions were available.[4]

CONCLUSIONS

In summary, the Framingham-REGICOR calibrated function is better than the Framingham-Wilson and SCORE functions in patients with a high CVR who receive treatment with statins, for 2 reasons: it categorizes a higher proportion of patients with hypercholesterolemia (in whom statin treatment has been shown to be effective) and of patients who receive treatment in clinical practice. This fact contributes making the case for adopting the Framingham-REGICOR function, wich is also the only function that has been validated in Spain.[32]

REFERENCES

1. Instituto Nacional de Estadística. Available from: http://www.ine.es/
2. Maiques Galán A, Villar Álvarez F, Brotons Cuixart C, Torcal Laguna J, Orozco-Beltrán D, Navarro Pérez J, et al. Recomendaciones preventivas cardiovasculares. Aten Primaria. 2007;39 Suppl:15-26.
3. Thavendiranathan P, Bagai A, Brookhart MA, Choudhry NK. Primary prevention of cardiovascular disease with statin therapy. Arch Intern Med. 2006;166:2307-13.
4. Miguel García F, García Ortiz A, Montero Alonso MJ. Prevención primaria con estatinas, consensos y tablas de riesgo. Aten Primaria. 2005;36:31-8.
5. Walsh JME, Pignone M. Drug treatment of hyperlipidemia in women. JAMA. 2004;291:2243-52.
6. The ALLHAT officers and coordinators for the ALLHAT collaborative research group. Major outcomes in moderately hypercholesterolemic, hypertensive patients randomized to pravastatin vs usual care. The antihypertensive and lipid-lowering treatment to prevent heart attack trial (ALLHAT-LLT). JAMA. 2002;288:2998-3007.
7. Shepherd J, Blauw GJ, Murphy MB, Bollen EL, Buckley BM, Cobbe SM, et al. PROspective Study of Pravastatin in the Elderly at Risk. Pravastatin in elderly individuals at risk of

vascular disease (PROSPER): a randomised controlled trial. Lancet. 2002;360:1623-30.
8. Medrano MJ, Cerrato C, Boix R, Delgado-Rodríguez M. Factores de riesgo cardiovascular en la población española: metaanálisis de estudios transversales. Med Clin (Barc). 2005;124:606-12.
9. Walley T, Folino-Gallo P, Schwabe U, van Ganse E. Variations and increase in use statins across Europe: data from administrative databases. BMJ. 2004;328:385-6.
10. Cooper A, O'Flynn N. Risk assesment and lipid modification for primary and secondary prevention of cardiovascular disease: summary of NICE guidance. BMJ. 2008;336:1246-8.
11. Jackson PR, Wallis EJ, Haq IU, Ramsay LE. Statins for primary prevention: at what coronary risk is safety assured? Br J Clin Pharmacol. 2001;52:439-46.
12. 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.
13. Marrugat J, Solanas P, D'Agostino R, Sullivan L, Ordovas J, Cordón F, et al. Estimación del riesgo coronario en España mediante la función de Framingham calibrada. Rev Esp Cardiol. 2003;56:253-61.
14. 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.
15. Baena Díez JM, del Val García JL, Salas Gaetgens LH, Sanchez Pérez R, Altes Vaques E, Deixens Martínez B, et al. Comparación de los modelos SCORE y REGICOR para el cálculo del riesgo cardiovascular en sujetos sin enfermedad cardiovascular atendidos en un centro de salud de Barcelona. Rev Esp Salud Pública. 2005;79:453-64.
16. Gil-Guillén V, Orozco-Beltrán D, Maiqués-Galán A, Aznar-Vicente J, Navarro J, Cea-Calvo L, et al. Concordancia de las escalas REGICOR y SCORE para la identificación del riesgo cardiovascular alto en la población española. Rev Esp Cardiol. 2007;60:1042-50.
17. Maiques Galán A, Antón García F, Franch Taix M, Albert Ros X, Aleixandre Martí E, Collado Gil A. Riesgo cardiovascular del SCORE comparado con el de Framingham. Consecuencias del cambio propuesto por las Sociedades Europeas. Med Clin (Barc). 2004;123:681-5.
18. Buitrago F, Cañón-Barroso L, Díaz-Herrera N, Cruces-Muro E, Escobar-Fernández M, Serrano-Arias JM. Comparación de las tablas REGICOR y SCORE para la clasificación del riesgo cardiovascular y la identificación de pacientes candidatos a tratamiento hipolipemiante o antihipertensivo. Rev Esp Cardiol. 2007;60:139-47.
19. Comin E, Solanas P, Cabezas C, Subirana I, Ramos R, Gené-Badía J, et al. Rendimiento de la estimación del riesgo cardiovascular en España mediante la utilización de distintas funciones. Rev Esp Cardiol. 2007;60:693-702.
20. Baena Díez JM, del Val García JL, Tomàs Peregrina J, Martínez Martínez JL, Martín Peñacoba R, González Tejón I, et al. Epidemiología de las enfermedades cardiovasculares y factores de riesgo en atención primaria. Rev Esp Cardiol. 2005;58:367-73.
21. Anathomical Therapeutic Chemical (ATC) Classification Index. Oslo: World Health Organization; 1998.
22. Córdoba García R, Ortega Sanchez-Pinilla R, Cabezas Peña C, Forés García D, Nebot Adell M. Recomendaciones sobre el estilo de vida. Aten Primaria. 1999;24 Supl:118-32.
23. Programas básicos de salud. Diabetes mellitus. Sociedad Española de Medicina Familiar y Comunitaria. Madrid: Doyma; 1998.
24. Marrugat J, Vila J, Pavesi P, Sanz F. Estimación del tamaño de la muestra en la investigación clínica y epidemiológica. Med Clin (Barc). 1998;111:267-76.
25. 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.
26. Bonet S, García Villena I, Tomás Santos P, Tapia Mayor I, Gussinyé Canabal P, Mundet Tuduri X. ¿Cúando y cómo tratamos a nuestros pacientes hipercolesterolémicos? Aten Primaria. 1999;24:397-403.
27. Vilaseca Canals J, Buxeda Mestres C, Cámara Contreras C, Flor Serra F, Pérez Guinaldo R, Sanchez Viñas M. ¿Tienen riesgo coronario los pacientes que tratamos con fármacos hipolipemiantes? Aten Primaria. 1997;20:49-53.
28. Bonné Moreno MV, González Löwenberg O, Charques Velasco E, Alonso Martínez MM. Riesgo coronario y prescripción en pacientes con hipercolesterolemia en atención primaria. Aten Primaria. 2000;25:209-13.
29. Marín A, Medrano MJ, González J, Pintado H, Compaired V, Bárcena M, et al. Risk of ischaemic heart disease and acute myocardial infarction in a Spanish population: observational prospective study in a primary-care setting. BMC Public Health. 2006;6:38.
30. Encuesta Nacional de Salud de España 2006. Madrid: Ministerio de Sanidad y Consumo; 2006. Disponible en: http://www.msc.es/estadEstudios/estadisticas/encuestaNacional/encuesta2006.htm
31. Taxes d'Incidència i prevalença a l'Atenció Primària. Mètodes per a la seva obtenció. Barcelona: Fundació Jordi Gol i Gurina; 2002.
32. Brotons C, Royo-Bordonada MA, Álvarez-Sala L, Armario P, Artigao R, Conthe P, et al. Adaptación española de la Guía Europea de Prevención Cardiovascular. Aten Primaria. 2004;34:427-32.
33. Marrugat J, Subirana I, Comín E, Cabezas C, Vila J, Elosua R, et al. Validity of an adaptation of the Framingham cardiovascular risk function: the VERIFICA Study. J Epidemiol Community Health. 2007;61:40-7.