Predicting someone’s chances of experiencing a cardiovascular event is a medical challenge that has yet to be resolved.¹ Large-scale epidemiologic observation studies enable us to identify variables associated with greater probability of presenting cardiovascular disease. The INTERHEART study has recently corroborated these, comparing the circumstances that differentiated patients with myocardial infarction from those in a healthy control group.² The results facilitated the definition of 9 variables to which we can attribute 90% of the risk of presenting infarction. Smoking, dyslipidemia, diabetes, hypertension, obesity, and stress were, once again, the decisive factors, whereas consumption of fruit and vegetables, physical activity, and the consumption of alcohol protected patients from the process. These were the variables independently of age, gender, or geographical location. The tables and formulae used to calculate patient cardiovascular risk include most, but not all, of these factors as variables. Thus, conditions with an apparently clear association with vascular risk, like obesity, do not generate additional information. In the last decade, newly-defined, clinical and biochemical parameters have been associated with inflammation or thrombogenesis and are related with vascular risk. However, when used to improve the sensitivity and specificity of parameters based on classical factors, they do not contribute to significant improvement. In a recent study, the incorporation of as many as 10 biochemical parameters into classical risk factors to calculate cardiovascular risk did not improve the sensitivity or specificity of the classical formulae.³ The Reynolds Score,⁴ a new coefficient to calculate vascular risk for women, has recently been published. It incorporates ultrasensitive CRP data and family history of early cardiovascular disease, and clearly improved the predictive value of the Framingham algorithm.

The consistency of these conclusions and of the many previous studies seems to indicate that, bearing in mind the presence or absence of these variables, it is easy to identify the patients at greatest risk. However, the transfer of epidemiologic results to clinical practice is accompanied by low sensitivity and specificity. In recent years, many organisms and scientific societies have supported the idea that cardiovascular prevention should be tackled by evaluating the overall risk of an individual experiencing an event, instead of focusing on individual factors. The concept is logical and scrupulously rational. Making decisions on therapy for a young woman with 280 mg/dL cholesterol is not the same as dealing with a man with diabetes and the same level of cholesterol. Knowing the associated factors is fundamental when making therapeutic decisions. However, the grave problem is that the tools to measure overall cardiovascular risk are imperfect.

This issue of Revista Española de Cardiología compares the Framingham, REGICOR, and SCORE³ formulae to calculate overall cardiovascular risk: REGICOR takes account of the epidemiologic reality of Spain and SCORE caters for the situation in parts of Europe where prevalence of cardiovascular disease is low, like Spain.⁶,⁷ The article is based on a retrospective study to evaluate the capacity of these formulae to predict events at 5 years. The conclusions seem to support the superiority of REGICOR over the others. However, if we analyze the results carefully we find that the algorithms’ performance, including that of REGICOR, is less than satisfactory, to say the least. Firstly, we must remember that the study evaluates the predictive capacity at 5 years of tools designed to predict 10-year risk, which guarantees a shortfall in precision. The indices obtained should improve if real events were evaluated at 10 years. Sensitivity to detect 20% 10-year risk of experiencing a cardiovascular event in the case of Framingham and REGICOR, or 5% risk of cardiovascular death in the case of SCORE, at age 34-64 (the only age-group all 3 indices comparable) is 53.4%, 3.6%, and 32.7%, respectively. REGICOR improves slightly when calculating 10% 10-year risk as does SCORE when extrapolated to age <60 for the same age-group (29.4% and 48.6%, respectively). Specificity is 84.5%-99.3% for the different formulae, and positive predictive value 9.5%-17.1%; at 11.7%, it is identical for REGICOR at 10 years and SCORE. The differences are of minor relevance and, we believe, do not always point in the
same direction as the article’s conclusions. The use of REGICOR can entail not detecting high risk in 90% of patients studied although, obviously, those identified will not generally be false positives. The use of SCORE increases detection at the expense of more false positives. The positive predictive value obtained with the different formulae is not in itself so unusual.

When, after evaluation, we decide on a therapeutic intervention to prevent an event, we will be right in >10% of cases, although these values would improve slightly if we had data on real events at 10 years instead of 5.

As the authors indicate, the inexactitude of these methods would not be tolerable in other diagnostic systems; however, when we play with the probabilities of something happening or not, it may be an adequate orientation as to the patient’s situation. Therefore, we must remember how we intend to use these indices. National cardiovascular prevention policy cannot be solely based on calculating overall cardiovascular risk using inexact tools. This value is simply one more diagnostic weapon we can gather under the umbrella of our patients’ clinical data, based on which we apply therapeutic or preventative measures vouchsafed by more scrupulous scientific evidence.

Which therapeutic interventions depend on calculating overall cardiovascular risk? We have sufficient epidemiologic evidence to know that patients with previous myocardial infarction are at a very high risk of further events so our most intensive therapeutic interventions should be directed at this collective. In primary prevention, we are in no doubt as to what we should do about smoking. In patients with high blood pressure, the consequences for other organs and for arterial territory obliges us to adapt therapeutic interventions to other parameters, depending on the degree of hypertension and the effect on target organs. Therefore, it seems that calculating cardiovascular risk is only of interest in primary prevention in order to make decisions on therapeutic treatment of hypercholesterolemia. We start out from this hypothesis. In Spain, most scientific societies, even the Ministry of Health recommendations, coincide in indicating that in primary prevention for patients with high cardiovascular risk, low-density lipoprotein cholesterol (LDL-C) should be <130 mg/dL. Other countries, in the same situation, recommended LDL-C <100 mg/dL. Cardiovascular risk is defined as high when it is >20% at 10 years (5% for SCORE). Clinicians who use the REGICOR tables find that women without diabetes are never considered high-risk patients and that among women with diabetes, only those aged 65-74, smokers, with very high cholesterol and blood pressure figures are likely to be classified as such even though we know their life expectancy is <20 years and some 40% will die from cardiovascular disease. Something similar occurs with men non-smokers. We are convinced that these are the results of an epidemiologic study conducted to high standards of scientific rigor. However, they cause concern among clinicians who receive the message that cardiovascular disease is of little importance in Spain, when in fact it is the principle cause of death in men and women. If, instead of concentrating on absolute values we focus on individual patients’ relative risk within their age group and gender, all the tables and indices coincide in pointing to exactly the same patients occupying the highest percentiles. This data might perhaps be valid for physicians having to make decisions on therapy.

What does the scientific evidence say? In fact, it sends us a very different message. Firstly, no studies, clinical trials, or whatever, show that deciding on preventive therapy on the basis of overall cardiovascular risk is efficient; nor do they indicate that overall risk should be reduced instead of attending to individual factors. If this were the case, in a patient with multiple risk factors we could, for example, much reduce cholesterol without treating for high blood pressure, and we would achieve similar preventative effects to a combined treatment of risk factors. In the presence of various risk factors, the scientific evidence has shown that if we treat LDL-C, relative risk of presenting an event can fall by as much as 50%; that if we treat hypertension to achieve optimal values our prognosis improves; and that in patients with diabetes, the lower the LDL-C the better. We have clear scientific proof of these affirmations from internationally based studies that have often included Spanish patients, so we cannot argue against extrapolating their results to our population.

What can we do to improve our diagnostic capacity to detect individual patients with high cardiovascular risk? The use of risk tables will probably help us if we always consider them as just another tool and not as the only element in the decision-making process. However, it is clear we must seek out new, more precise tools with greater sensitivity, specificity, and positive and negative predictive value. We have already mentioned how little the incorporation of new biochemical parameters contributes to the classical indices and we could say the same of the genetic variables. In the immediate future, we will use diagnostic methods that indicate arterial status precisely and preventive action will be based on diagnosis of preclinical arterial lesion via functional imaging techniques. The ankle-arm index to detect peripheral vascular lesions will be calculated in these patients. Endothelial function tests, some of them easily reproducible, could be of help, but above all the echographic study of the carotid intimal-medial thickness (IMT) seems an especially useful tool. This exploration should be within the scope of all cardiovascular risk units, given that it points to the presence of arterial disease and not just vascular risk. The IMT correlates with coronary risk and is modified by different therapeutic interventions including treatment with lipid-lowering drugs. We would certainly prefer our patients had normal IMT, in spite of the intermediate-high risk value given in the tables, than...
the opposite: ie, high IMT, with atheroma plaque despite the intermediate-low value in the tables. Other techniques, like determining coronary calcium by computerized tomography, also enable us to treat this group of patients with precision. In this case, not only do we evaluate arterial status but we also visualize directly the presence of advanced coronary arteriosclerosis, and its high negative predictive value has been shown. The use of ever more accessible techniques based on positron emission tomography will facilitate the definition of their role in treating cardiovascular risk. Some international scientific groups (SHAPE) support the development of diagnostic algorithms based on imaging tests.12 Patients who should undergo this level of diagnosis will probably be those classified as at intermediate risk by using the tables or on analyzing the combined classical risk factors. One of the virtues we perceive in the comparative study published in this issue of Revista is that REGICOR classifies fewer subjects as high-risk. While this may lead to fewer therapeutic interventions (given that it means increasing the group of patients classified as at intermediate risk) it would mean, in the near future, having a greater subsidiary population to be studied with clarifying imaging techniques.

The tables calculating overall cardiovascular risk are very inexact and it would be a mistake to consider the values of absolute risk they produce as the axis of therapeutic decision-making. The tables should be used as one more element. In this context, both REGICOR and SCORE show us the relative risk situation of an individual by comparison with their age and gender and this information can be of use to us in deciding our attitude to therapy based on the scientific tests we have available. Access to an evaluation of arterial status by functional and vascular imaging techniques has permitted greater precision in detecting vulnerable patients.

REFERENCES