

# Cardiovascular risk calculation

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Cardiovascular disease remains a major cause of global mortality and morbidity. Atherosclerosis is the main underlying cause in the majority of cardiovascular disease events. Traditional independent risk factors for cardiovascular disease include age, abnormal lipid levels, elevated blood pressure, smoking and elevated blood sugar levels (diabetes mellitus). These risk factors are incorporated into a risk score, such as the Framingham Risk Score (FRS), that is used to predict an individual's absolute risk of a cardiovascular event, typically over the next 10 years, e.g. 15% risk over 10 years. These risk scores are useful in predicting risk in populations, but their ability to predict a cardiovascular event in an individual patient is not accurate and varies considerably across different populations. Currently, there are three methods of calculating cardiovascular risk. These are risk charts, e.g. FRS, a non-laboratory-based risk calculation, and lastly, screening for subclinical cardiac disease.

**Keywords:** calculation, cardiovascular disease, cardiovascular risk

## Introduction

Cardiovascular disease remains a major cause of global mortality and morbidity. Atherosclerosis is the main underlying cause in the majority of cardiovascular disease events. Traditional independent risk factors for cardiovascular disease include age, abnormal lipid levels, elevated blood pressure, smoking and elevated blood sugar levels (diabetes mellitus). These risk factors are incorporated into a risk score, such as the Framingham Risk Score (FRS), that is used to predict an individual's absolute risk of a cardiovascular event, typically over the next 10 years, e.g. 15% risk over 10 years.

These risk scores are useful in predicting risk in populations, but their ability to predict a cardiovascular event in an individual patient is not accurate and varies considerably across different populations.<sup>1</sup>

Currently, there are three methods of calculating cardiovascular risk. These are risk charts, e.g. FRS, a non-laboratory-based risk calculation, and lastly, screening for subclinical cardiac disease.

## Problems with cardiovascular risk prediction

The estimation of cardiovascular risk is not an exact science. One of the problems is that different combinations of risk factors in any given patient may interact in a complex way that is difficult to incorporate into a risk score.<sup>2</sup> Risk is the product of several factors. Risk estimation attempts to determine the combined effects of several risk factors.

Risk prediction models, e.g. FRS, systematic coronary risk evaluation (SCORE) score, QRESEARCH cardiovascular risk algorithms (QRISK1 and QRISK2) and Prospective Cardiovascular Münster (PROCAM) score, are risk estimates for populations. It is problematic to apply a risk estimate to an individual patient. On average, these risk scores provide fairly accurate risk estimates, but they have high intrinsic variance for the prediction of risk when applied to a given patient.<sup>1</sup>

There is low short-term risk (over 10 years) in a significant proportion of the population, but high lifetime risk. Age in all risk tables is a major driver of short-term risk of cardiovascular events in this regard. The result is that the risk scores become

misleading. Becoming older is by far the strongest predictor of a cardiovascular event. Typically, there is an increased lifetime risk of a young person developing an event, but a low short-time risk because of age.

## Framingham Risk Score

The Framingham Heart Study taught us the concept that a cumulative average of risk provided by cardiovascular risk factors could be more important than the peak of one cardiovascular risk factor.<sup>3</sup> The FRS is a well validated tool and has been tested in many populations. However, it has well established limitations in non-white, female and young cohorts.<sup>4</sup>

A systematic review of studies comparing FRS predicted risk of coronary artery disease to the observed incidence of such events over 10 years has demonstrated under-prediction in high-risk people (predicted to observed ratio of 0.43) and over-prediction in low-risk people (predicted to observed ratio of 2.87).<sup>5</sup> Typically, there is a *c*-statistic of 0.763 in men and 0.793 in women when using the FRS.<sup>6</sup> The *c*-statistic (area under the receiver operating characteristic curve) incorporates two measures of the accuracy of a screening or diagnostic test, namely sensitivity (the ability to detect disease when it is present), and specificity (the ability to exclude disease when it is absent). A *c*-statistic of 0.50 is uninformative with no discrimination. There is perfect discrimination with a *c*-statistic of 1. A *c*-statistic of 0.76 and 0.79 means that at least one in four to one in five cases of cardiovascular events will be missed using the FRS prediction. Various additions to the basic FRS, such as C-reactive protein and B-type natriuretic peptide, have not led to large improvements in the *c*-statistic. For example, including an observed carotid atherosclerotic plaque adds 0.01–0.05 to the FRS. There are too little data on whether or not various other emerging risk factors could improve the FRS. However, testing of emerging risk factors is underway as how to improve the accuracy of the FRS.

The FRS is also being tested on its ability to predict lifetime risk in the Framingham Offspring Study, to be followed over 30 years for hard cardiovascular end-points, such as coronary death, myocardial infarction and strokes. The *c*-statistic was 0.803.<sup>7</sup>

In addition, the updated FRS can be used to calculate the vascular age of a patient using the same cardiovascular risk factors, e.g. a patient may have a risk score of 10% over the next 10 years, and the vascular age could be 60 years when the patient is only 48 years old. The vascular age is useful in motivating patients to improve their vascular age by better adhering to therapy.<sup>6</sup>

### Non-laboratory-based risk calculation

At least five risk calculators that use age, smoking status, blood pressure level, hypertension treatment status, the presence of diabetes mellitus (or not) and body mass index (kg/m<sup>2</sup>), replace laboratory-measured serum cholesterol levels. Removing cholesterol from the risk chart has not led to a significant reduction in the *c*-statistic.<sup>8</sup> These non-laboratory-based risk scores can be used in low-income countries where the cost of a laboratory test can be prohibitive and a barrier to the use of cardiovascular risk prediction. Available models for non-laboratory-based risk scores were evaluated in a recent publication.<sup>9</sup>

### Screening for subclinical disease

Screening for, or the measurement of, the presence of subclinical disease (including target organ damage), represents a more definitive way of personalising preventative cardiovascular treatment.<sup>1</sup> Screening for disease also reduces uncertainty for the patient and may facilitate an improvement in personalised decision-making.

Coronary artery calcium (CAC) is a marker and direct measurement of the total burden of atherosclerosis in the coronary artery. CAC integrates the cumulative effect of measured and unmeasured risk factors on an individual's vascular bed. A CAC score of zero indicates little or no significant coronary artery disease, while increasing CAC scores are associated with increasing risk.<sup>10</sup>

Visualised carotid plaques improve the ability to predict future myocardial infarction significantly.<sup>11</sup> Both increased CAC scores and visualised carotid plaques, as evidence of disease in asymptomatic patients, may benefit the patient through plaque stabilisation and lipid-reducing statin therapy.

Left ventricular hypertrophy, reduced estimated glomerular filtration rate and microalbuminuria are indicative of organ damage, and are associated with increased cardiovascular risk. There is a cumulative impact if these are added to a risk score, especially in patients with an intermediate risk score.<sup>12</sup>

### Not included in the current risk charts

A family history of premature coronary heart disease or cardiovascular death is associated with an approximately 50% higher long-term risk of cardiovascular disease, even after adjustment for traditional risk factors.<sup>13</sup> A positive family history is also not incorporated into traditional risk scores.

It is estimated that up to 4.5% of cases of myocardial infarction may be associated with or due to air pollution.<sup>14</sup> This risk factor has also not been incorporated into the risk scores.

Are chronic kidney disease and depression risk factors? They are not included in any risk scores, and yet they are associated with increased cardiovascular events. Both are also strong contenders as emerging cardiovascular risk factors.

### The use of nonsteroidal anti-inflammatory drugs

It was shown in a recent, extensive meta-analysis that all studied nonsteroidal anti-inflammatory drugs (NSAIDs) cause gastrointestinal complications (cyclo-oxygenase-2 to a lesser degree), increase the risk of heart failure (naproxen, the most) and cardiovascular events (except naproxen).<sup>15</sup> There can be up to three major vascular events in 1 000 patients at moderate risk of heart disease, including one death due to a year of high-dose NSAID therapy. NSAIDs also interfere with low-dose aspirin which is given for cardiac protection. Therefore, NSAIDs and aspirin should be given at least eight hours apart. Patients must undergo cardiovascular risk assessment before an NSAID is prescribed. Protective cardiovascular therapy should be offered to high-risk patients. NSAIDs are also not given to patients for at least six months after an acute event, e.g. myocardial infarction, a stroke or percutaneous coronary intervention. In this meta-analysis, it was clear that the higher the cardiovascular risk, the higher the chance of the NSAID causing harm. In addition, the NSAID must be given at the lowest possible effective dose to provide pain relief. It should not be prescribed for long periods in order to reduce cardiovascular risk. Ultimately, a balance between benefit and risk is needed. The FRS is useful in helping this decision to be made.

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