Abbott

CARDIOVASCULAR RISK STRATIFICATION

A review of risk stratification of the apparently healthy population for future cardiac events with Abbott's High Sensitive Troponin-I.

WHAT IS TROPONIN-I?

Troponin-I is a well-known, reliable cardiac biomarker that is used in emergency departments as an aid to rule in or rule out myocardial infarction (MI). This review looks at the new application and added value of using Abbott's High Sensitive Troponin-I (hsTnI) alongside traditional risk factors, to stratify individuals who have no apparent symptoms but may be at risk of developing cardiovascular disease (CVD). Its inclusion may help to improve prevention strategies, avoid patients undergoing unnecessary tests and treatments and reduce the burden of this condition on healthcare organisations Abbott's hsTnI was the first commercially available troponin assay for this application.[1,2]

523 MILLION
The number of prevalent cases of CVD around the world in 2019[3]

23 MILLION
The number of deaths projected to be caused by CVD, worldwide by 2030[4]

#1 CAUSE
CVDs are the number 1 cause of death globally: more people die annually from CVDs than from any other cause[5]

A NEW APPLICATION: WHAT THE EXPERTS HAVE TO SAY

Leading cardiologists from across Europe discuss the limitations of current risk assessment strategies for stratifying asymptomatic individuals, and explain how Abbott's High Sensitive Troponin-I, as a cardiac-specific marker, can supplement current risk assessment approaches and support the management of CVD.

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THE IMPORTANCE OF ACCURATE CARDIOVASCULAR RISK STRATIFICATION

CVD remains the leading cause of mortality in Europe, causing 45% of all deaths.[6,7] This represents a significant financial and resource burden on healthcare, yet 80% of heart disease and stroke is preventable.[7] Prevention therefore plays an increasingly important role in improving patient care and quality of life, because damage to the heart and blood vessels can largely be avoided if the disease is detected early and treated appropriately over the long term. The key to prevention is to identify those most at risk, using accurate stratification methods; if patients are identified early, then their condition can be managed more appropriately and more quickly and, with guided care, including lifestyle adjustments, their risk of serious disease can be modified. In low risk individuals, management and unnecessary treatments may be avoided which can potentially help improve resource management and alleviate the burden placed on healthcare systems.

"Risk stratification within the general population is extremely important, so that we can recognise high-risk patients and begin preventative measures, such as changes in lifestyle and diet, that minimise that risk."

PROFESSOR DR. WINFRIED MÄRZ

"It is very important to stratify patients correctly so that they can be directed to where they will receive the best care and management, whether that's staying under the supervision of the family doctor, or being referred to specialist hospital services."

PROFESSOR STEFANO CARUGO

CURRENT APPROACHES TO CARDIOVASCULAR ASSESSMENT AND THEIR LIMITATIONS

Primary care physicians, such as family doctors or general practitioners (GPs), and cardiologists mostly rely on risk stratification systems such as the one formulated by the European Society of Cardiology (ESC) that predicts fatal atherosclerotic CVD events over a 10-year period.[6] The Systematic Coronary Risk Evaluation (SCORE) algorithm is derived from data from 12 European cohort studies covering a wide geographic spread of countries, and encompasses three million person-years of observation and 7,934 fatal cardiovascular events.[8] The SCORE risk estimation is very similar to the Framingham Risk Score commonly used in the US; scores are based on the following risk factors: biological sex, age, smoking, systolic blood pressure, lipid profile and diabetes.[9]

The common thread that links all the scoring mechanisms currently used is that they all rely heavily on lifestyle risk factors and age; they do not include cardiac-specific markers, and are not accurate for all patient cohorts, for example, diabetics and those with familial hypercholesterolaemia. The addition of a cardiac-specific marker to these traditional approaches can aid in the accurate identification of patients at risk of developing CVD and in turn, enhance patient care.

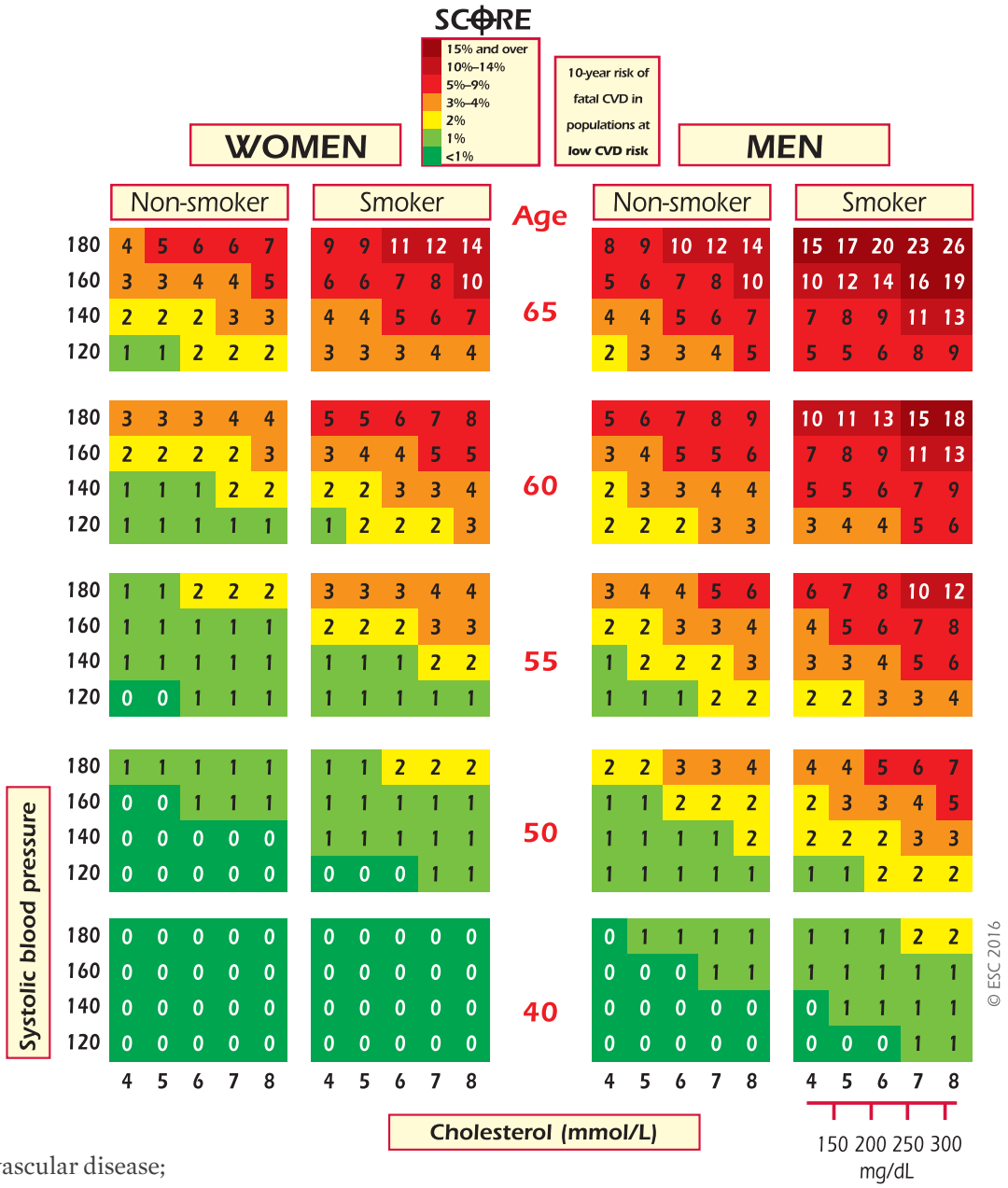
While patients may appear to fall quite clearly into high or low risk, it can be a real challenge to identify the true level of risk in those who fall between the extremes and are classified as being at moderate risk of developing disease. A cardiac specific biomarker, such as High Sensitive Troponin-I, could help to correctly differentiate these patients and assist with clinical decision-making.

"The current scores we use are not cardiac-specific, but incorporate classical lifestyle risk factors. They are frequently not applicable to all patients, for example, the SCORE project is not appropriate for either diabetics or patients with familial hypercholesterolaemia, which accounts for a significant proportion of the population. In addition, some biomarkers – like the generic inflammatory marker C-reactive protein (CRP), for example – are not cardiac-specific, so give an inaccurate estimation of the risk. You get a high CRP if you have toothache, but this doesn't mean that you will get heart disease! We need a biomarker that is more cardiac-specific for screening, because we know from statistics that we have a residual risk besides the usual risk factors that is not covered by the current screening tools but nevertheless needs to be addressed."

PROFESSOR DIMITRIOS FARMAKIS

SCORE CHART

10-year risk of fatal CVD in populations of countries at low cardiovascular risk based on the following risk factors: age, sex, smoking, systolic blood pressure, total cholesterol.



CVD = cardiovascular disease;
SCORE = Systematic Coronary Risk Estimation.

"What is clear is that patients with moderate risk are not very well-discriminated and could, in reality, be at either high or low risk; we would welcome any tool that can help us to correctly differentiate these patients."

DR. LUIS RODRIGUEZ PADIAL

"Patients with very low risk are obvious; there's no need for further stratification on a young woman with no risk factors. At the other end of the spectrum, you get obviously high-risk patients – diabetics, heavy smokers, older men with hypertension, etc. – who also don't need further stratification. The problem is those people who fall between these extremes – and that's a significant part of the population. This is our target patient group and the reason we need to screen further."

PROFESSOR DIMITRIOS FARMAKIS

HOW CAN CARDIOVASCULAR RISK STRATIFICATION THAT INCLUDES HIGH SENSITIVE TROPONIN-I HELP TO OVERCOME THESE LIMITATIONS?

Troponin-I fits the criteria for a cardiac-specific marker; when added to current prediction tools, it provides greater accuracy for identifying a patient's risk of a cardiac event in the future, even in people with no apparent signs or symptoms.

A clearer, more accurate risk assessment – that includes Troponin-I as a cardiac-specific element – could give clinicians the confidence to provide patients with the right care, needed to manage their cardiac risk. It may also help as evidence to convince patients to take charge of their heart health and modify their lifestyle to help reduce their cardiac risk, with appropriate support.

"Any disease marker that can demonstrate a clear relationship to prognosis can help to convince a patient to strictly follow the guidelines or treatments that we recommend; without this a significant proportion of patients do not follow our advice."

DR. LUIS RODRIGUEZ PADIAL

"The measurement of troponin is useful added to the known lifestyle risk scores. For example, when you have a patient with a medium lifestyle risk – an ESC score of between 1 and 5 or a Framingham score of between 10 and 20% – then the patient's troponin level could lead to a better classification."

PROFESSOR DR. WINFRIED MÄRZ

"The main advantage of Troponin-I as a marker for risk stratification is its cardio-specificity – more specifically its specificity to the myocardium."

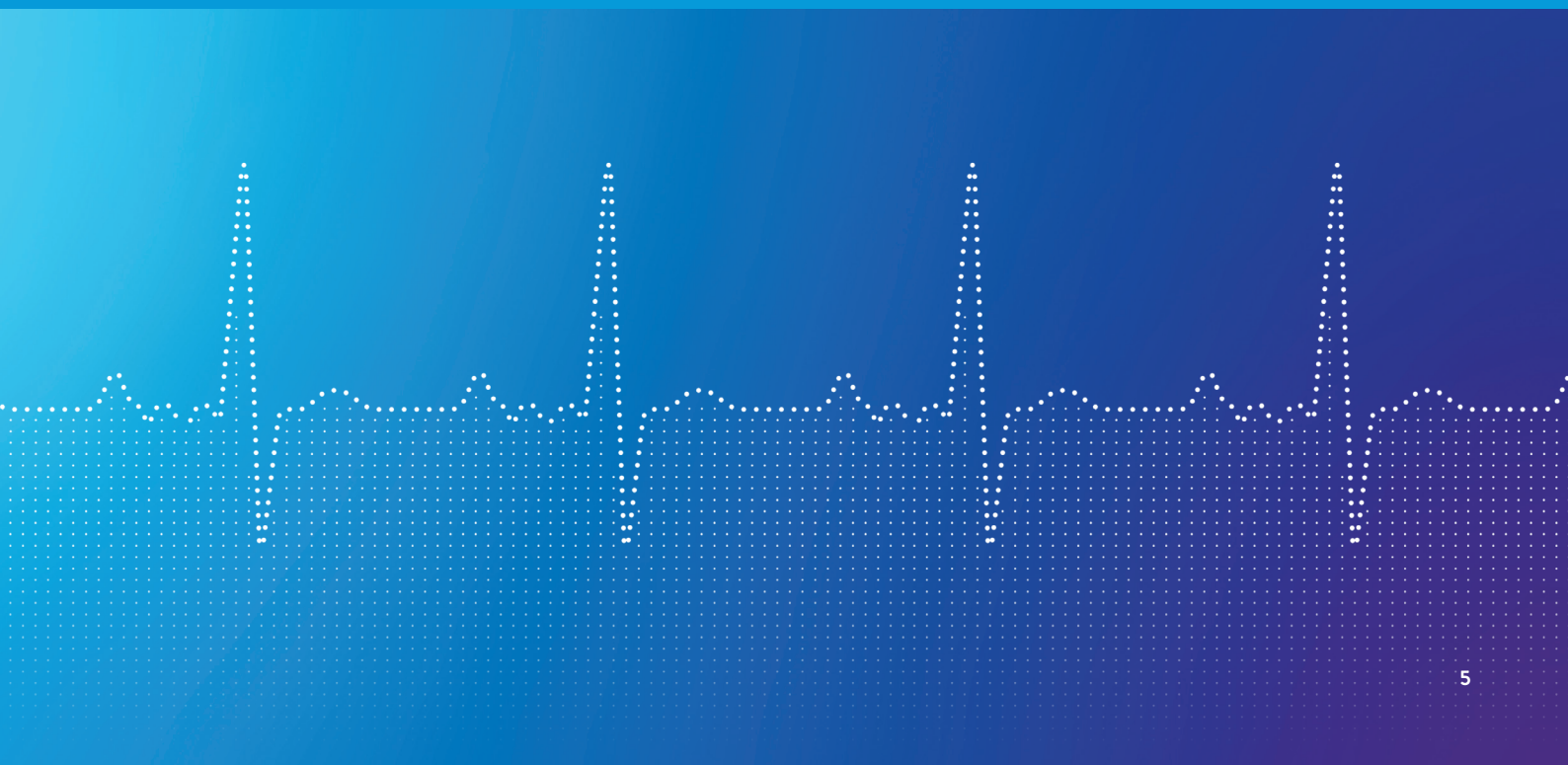
DR. TILL KELLER

"When we are presented with, for example, a relatively young patient with only one risk factor and no obvious heart disease, we need to decide whether to prescribe statins to him or her, potentially for their lifetime; it's not an easy decision to make. To do that, you need strong evidence to convince yourself first, and then to convince the patient that they need lifetime drug therapy."

PROFESSOR DIMITRIOS FARMAKIS

"With cardiologists' workloads continuing to increase, risk stratification of patients is sometimes challenging for the management of resources. A simple tool, such as Troponin-I measurement, could be very useful in this context; it is a far better cardiac-specific marker compared to the non-specific CRP, and could help us to more accurately assess cardiac risk and treat patients more effectively."

DR. CHRISTOPH LIEBETRAU



WHAT PROOF EXISTS TO SUPPORT THIS?

THERE ARE FOUR MAJOR CRITERIA THAT SIGNIFY THE SUITABILITY OF A BIOMARKER:

1. In order to use a biomarker, it must be detectable in a significant proportion of the general population.

"If you want to use a biomarker in the general population, then it has to be well represented in that population. We know that high sensitivity Troponin-I can be detected in 95%[10,11] of the normal population, whereas other troponins are only found in a quarter of the population."

PROFESSOR DIMITRIOS FARMAKIS

2. Can this biomarker actually help identify risk of disease in the target population?

"For high sensitivity Troponin-I the answer is yes. A number of recent trials – the Hunt trial,[12] BiomarCaRE (Biomarker for Cardiovascular Risk Assessment across Europe consortium)[13] with a cohort of approximately 75,000 people, WOSCOPS[14] and the Jupiter trial[15] – provide compelling evidence that high sensitivity Troponin-I can be used in a target population to identify cardiovascular risk, and not just cardiovascular death, but coronary artery disease and heart failure too."

PROFESSOR DIMITRIOS FARMAKIS

3. Does the change in this biomarker parallel a change in the risk of disease?

"The study showed that troponin levels in patients with cardiovascular risk dropped while they were undergoing statin therapy, and that decline was associated with better prognosis.[14] In another study, troponin was measured at the beginning of statin therapy. In patients with a troponin-I score greater than 6 ng/L, statin therapy resulted in a higher absolute risk reduction compared to subjects whose troponin value was lower."[2]

DR. TILL KELLER

"The WOSCOPS[14] trial concluded that when a patient's Troponin-I goes down, their risk also goes down, regardless of whether the patient takes statins or not."

PROFESSOR DIMITRIOS FARMAKIS

4. Is there an incremental benefit to this biomarker at the outset?

"Much of the current trial data shows that if you use high-sensitivity Troponin-I measurement on top of the SCORE assessment, then there is an incremental benefit in risk stratification; the same applies to the Framingham score."

PROFESSOR DIMITRIOS FARMAKIS

A CLEAR ROLE FOR ABBOTT'S HIGH SENSITIVE TROPONIN-I TO HELP CARDIOVASCULAR RISK STRATIFICATION IN ASYMPTOMATIC INDIVIDUALS TO SUPPORT CLINICIANS IN DELIVERING PROACTIVE PATIENT CARE.

Health check programmes differ between countries, but can start from age 35 upwards with, for example, two yearly recalls.[12] Abbott's High Sensitive Troponin-I, which meets all the criteria discussed above for a biomarker, could be used in conjunction with other parameters as part of any routine cardiovascular health check to indicate an asymptomatic individual's risk level. Its addition gives better accuracy for estimating the risk of future cardiac events in apparently healthy people, helping to inform clinical decision-making.

The test instructions state: "values may also be used, in conjunction with clinical and diagnostic findings, to aid in stratifying the risk of CVD, including cardiovascular death, myocardial infarction (MI), coronary revascularization, heart failure, or ischemic stroke in asymptomatic individuals."[2]

Different cut-offs have been set for men and women for cardiovascular risk stratification, and were derived from selected peer-reviewed published data and validated in a prospective study. They are lower than those typically used for assessing MI in the emergency setting, as shown in the table on the following page.

CARDIOVASCULAR RISK STRATIFICATION OF ASYMPTOMATIC PATIENTS USING HIGH SENSITIVE TROPONIN-I[2]

TROPONIN LEVEL		INTERPRETATION
MALE (pg/mL)	FEMALE (pg/mL)	
<6	<4	**Low risk** of a future cardiac event
≥6 to ≤12	≥4 to ≤10	**Moderate risk** of a future cardiac event
>12	>10	**Elevated risk** of a future cardiac event

IN CONJUNCTION WITH CLINICAL AND DIAGNOSTIC FINDINGS, SEX-SPECIFIC THRESHOLDS HELP ENABLE CLINICIANS TO APPROPRIATELY STRATIFY AN INDIVIDUAL'S RISK OF A FUTURE CARDIAC EVENT AND PRIORITIZE PREVENTATIVE MEASURES FOR EACH PERSON TO HELP IMPROVE THEIR CARDIAC HEALTH.

In asymptomatic individuals, elevated Troponin levels are associated with a higher risk of developing cardiovascular related diseases in the future. High Sensitive Troponin-I measurement offers an additional cardiac specific data point in cardiovascular risk assessment to support effective clinical management and help improve patient care.

The ESC guidelines[5] are clear on how to manage patients based on their risk classification. They recommend that patients at **low** risk of CVD should still always be advised on lifestyle changes, such as maintaining a healthy weight, doing more exercise and stopping smoking.

For those found to be at **moderate** risk, the managing clinician, such as the family doctor or GP, will have a stronger conversation about lifestyle changes, may consider introduction of medication if risk factors remain uncontrolled, and is likely to implement more regular check-ups to monitor the patient and their key criteria.

Patients with an **elevated** risk may be advised to make considerable lifestyle changes as well as potentially prescribed statins and/or blood pressure medication, and may be referred to specialist outpatients departments.

Troponin-I has been found to be raised[15] in some patients who would be classified as being at low risk under the current scoring methods, suggesting that a proportion of apparently 'low' risk patients should in fact be classified as being at moderate risk.

If patients can be better stratified, then their care pathways will be clearer and measures can be put in place to help prevent further disease and potentially save lives. Patients who are truly at low risk may avoid unnecessary tests and treatments, and high-risk patients can be directed to where their condition will be best managed.

Abbott's High Sensitive Troponin-I assay – and innovation with the Alinity i two-step immunoassay using chemiluminescent microparticle immunoassay technology that is also free from biotin interference[1] – has the potential to reduce the growing cost burden of CVD to the healthcare system, through more accurate stratification of at-risk patients.

"Given the high number of unreported diabetics, the high rate of hypertensives not treated or insufficiently treated, and patients with unrecognized cardiac arrhythmias of any kind, troponin risk stratification is a simple tool in primary prevention to exclude cardiac risk in asymptomatic patients and to identify and further investigate high-risk patients."

PROFESSOR DR. CHRISTOPH LIEBETRAU

"High sensitivity Troponin-I fulfils all of the criteria required for a biomarker to be useful in population screening – high detectability, ability to predict risk, ability to respond to preventive interventions and risk modification, and incremental value to established markers; Abbott's High Sensitive Troponin-I assay shows all of these analytical characteristics."

PROFESSOR DIMITRIOS FARMAKIS

ACCESSING ABBOTT'S HIGH SENSITIVE TROPONIN-I TESTING

Troponin-I is well established as a cardiac biomarker in the emergency setting, and its added value in cardiovascular risk stratification in apparently healthy populations is gaining recognition. Education of specialists and primary care physicians is paramount to encourage its use and see it realise its potential in this role.

At present, a Troponin-I test can be requested by primary care physicians, cardiologists, dieticians, diabetologists, and any clinicians interested in cardiovascular health. Abbott's High Sensitive Troponin-I was the first commercially available biomarker for cardiovascular risk stratification in the asymptomatic population. This test can be readily available from laboratories using Abbott's ARCHITECT or Alinity i systems.

"We need to learn from these studies; not even all specialist cardiologists are aware of the prognostic information that high-sensitivity troponin can give us, let alone primary care physicians. Troponin helps us to discriminate patients with a higher risk of developing heart disease in the future, and it is very important to make an effort to spread this message to our fellow cardiologists. It is also an important message for hospital authorities because better risk stratification will reduce costs, in some cases by cutting the use of drugs, in other cases by preventing the development of secondary conditions in patients at risk."

DR. LUIS RODRIGUEZ PADIAL

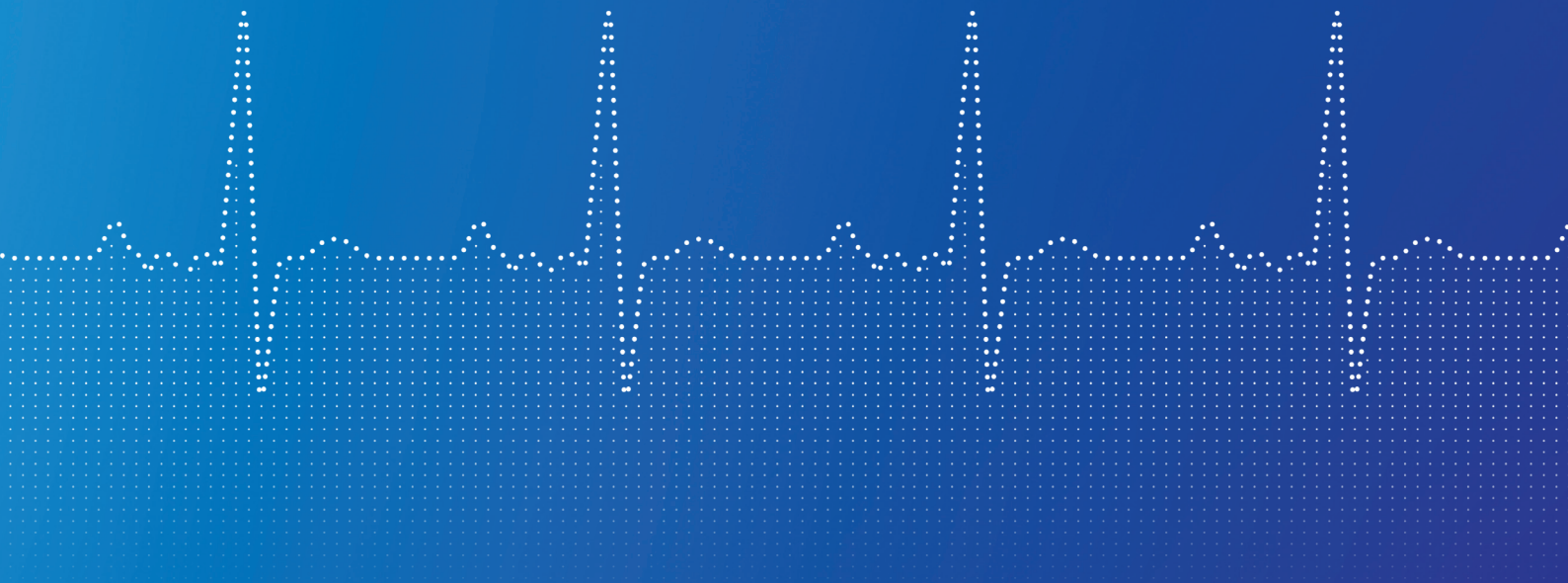
"We can undoubtedly improve the SCORE system by using troponin in the primary care setting as well as in hospitals, and need to improve GPs' knowledge of cardiovascular risk in general, as well as the benefits of this test. We should also take advantage of associations to help educate people everywhere on the improvements to risk stratification that troponin offers."

PROFESSOR STEFANO CARUGO

"The results of the recent studies are clear but now it is important to inform primary care physicians, internists and our fellow cardiologists about the potential of high sensitivity Troponin-I as a screening tool. In addition to this strong scientific data, we are also awaiting economic data that will demonstrate to policy makers that this really is a very cost-effective approach."

PROFESSOR DIMITRIOS FARMAKIS

IT'S MORE THAN A TEST.
IT'S INSIGHT TO ENHANCE CLINICAL DECISION-MAKING.



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