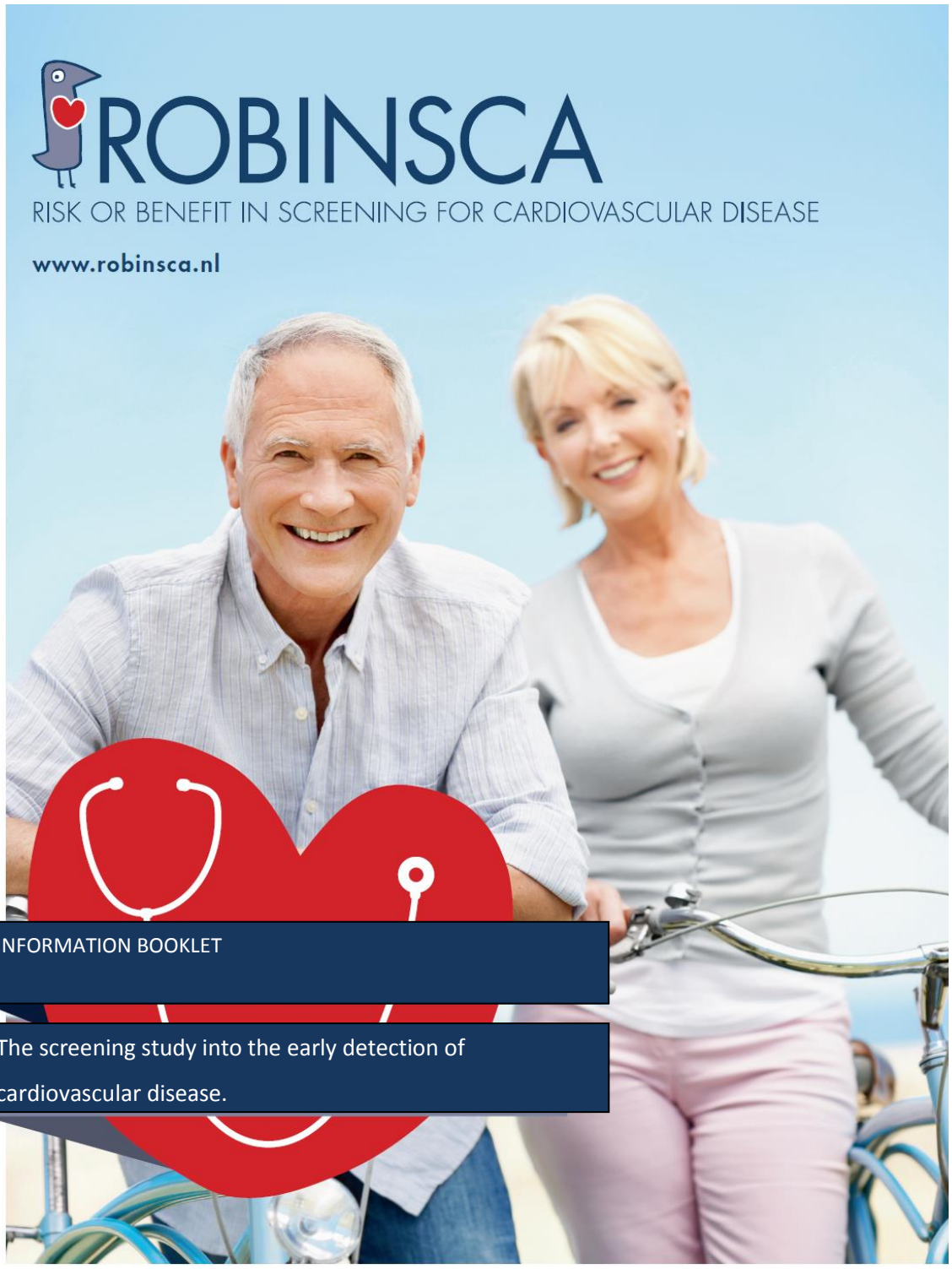

INFORMATION BOOKLET

The screening study into the early detection of cardiovascular disease.

Erasmus MC
Universitair Medisch Centrum Rotterdam

umcg

erc
European Research Council

This information booklet describes the ROBINSCA study. It is intended to help you decide whether you want to be considered for participation in the study. The booklet tells you about the background to the study, what the study will involve and what the implications of participation are.

What is ROBINSCA studying?

ROBINSCA is doing research into cardiovascular disease, which is referred to in this booklet by the initials 'CVD'. CVD is a serious public health problem. In 2012, about 39,000 people in the Netherlands died from CVD. One of the common causes of CVD is the build-up of fat on the inside walls of the arteries. Doctors call that 'arteriosclerosis' or 'hardening of the arteries'. Hardening of the arteries is a process that often goes on for years. It is made worse by things such as high blood pressure, smoking, obesity and too much cholesterol in the blood.

What is the purpose of the study?

The ROBINSCA study has been set up to see whether the number of people who get CVD or die from it can be reduced by checking people for early signs that they may be at risk, and giving medicine and advice to the people identified as being at risk. We will also be trying to find out whether the benefits of early detection outweigh the drawbacks. The benefits we'll be looking for are things such as fewer people getting CVD or dying from it. Possible drawbacks include making people worried about their health and putting people through the stress of medical tests. And, of course, screening people costs money.

Outline of the study

In this package, you'll find a questionnaire. We will check the answers you give to the questions to see whether they suggest that you are at more risk of developing CVD in the future and whether you are therefore the sort of person we need to take part in our study. Once we have found enough people of the kind we need, we will divide them into three groups:

1. Control group: the people in this group won't receive any extra medical tests as part of the study.
2. Intervention group A: the people in this group will be invited to go to a clinic once to have their blood cholesterol level checked and their blood pressure measured. We will use the test results and questionnaire answers from these people to work out how high their CVD risk is.
3. Intervention group B: the people in this group will be invited to go to a hospital once to have a CT scan, so that their 'calcium score' can be determined. A calcium score is a measurement of how much hardening of the arteries is taking place around the heart. We will use these people's test results to work out how high their CVD risk is.

People in intervention groups A and B who are thought to have a higher risk of CVD will be given lifestyle advice and/or medication by their GPs, with the aim of making it less likely that they'll go on to develop CVD. All participants will be monitored for five years. At the end of the five years, we will see how many of the people in the study have developed CVD or died from it. We will then see how the people who have become ill

or died from CVD are spread across the three groups. That will tell us whether the early identification and treatment of people who are at more risk of CVD is useful. The results will also tell us which method is most helpful and how much it costs.

How will the study be organized?

You will be able to take part in the study if your questionnaire answers suggest that you may be at more risk of CVD. Participants will be divided into three groups by random selection, which means that everyone will have an equal chance of being put into each group. We have to choose the groups that way so that the results from the different groups can be compared. You will not be able to switch from one group to another. You will receive a letter telling you which group you have been assigned to, plus a leaflet containing general advice on healthy living.

About the study groups

GROUP 1*: Control group*

If you are chosen for the control group, you will not need to do anything. However, we may contact you from time to time over the next five years to ask you to fill in a questionnaire. It will take you about ten minutes to go through it. The questionnaire that's included with this information booklet contains a variety of questions, some of which relate directly to the risk of cardiovascular disease. If your answers suggest that it might be a good idea for you to have your risk of cardiovascular disease assessed more carefully, we will let you and your GP know. To contact your GP, we need your consent, which you can give using the form provided. It is up to you whether you contact your GP.

Perhaps you feel disappointed about being put in the control group – perhaps you think that you won't benefit from taking part. However, we don't yet know whether any fewer people in the other groups will get CVD or die from it. The study's been set up to find out whether that's the case or not. In a study such as this, the control group is just as important as the other groups, because we have to be able to compare the findings. You will still receive all the normal care that we are used to in the Netherlands.

GROUP 2*: Intervention group A*

If you are assigned to this group, we will invite you to give a blood sample and have your blood pressure measured. That will involve going to a participating blood sampling centre in your region, so you don't have far to travel. Your appointment will last about fifteen minutes.

What we'll do with your test results

Using your blood test results, your blood pressure result and your questionnaire answers, we'll assess whether your risk of CVD is low, average or high. You and your GP will each receive a letter telling you about our findings.

What happens afterwards

If the assessment suggests that your risk of CVD is average or high, you will need to make an appointment with your GP. You will be given advice about healthy living and you may be given medication. That might be medication to reduce your blood pressure and/or your cholesterol level. You will also receive all the normal care that we are used to in the Netherlands.

GROUP 3*: Intervention group B*

If you are assigned to this group, we will invite you to give a blood sample and have a CT scan of the blood vessels around your heart. That will involve going to one of the following hospitals: Groningen University Medical Centre (Groningen), Gelre Hospital (Apeldoorn) or Bronovo Hospital (The Hague).
With this booklet there is an information sheet describing what you can expect from a CT scan. Your appointment will last about 15 minutes in total.
Your blood sample will be stored for five years. At the end of the five years, we will do a number of tests, like the tests we do for intervention group A.

What we'll do with your test results

Using your CT scan results, we will determine a 'calcium score': a measure of how much the arteries around your heart have hardened. Your calcium score may be low, high or very high. You and your GP will each receive a letter telling you about our findings.

What happens afterwards

If your calcium score is high or very high, you will need to make an appointment with your GP. You will then be given medication. That might be medication to reduce your blood pressure and/or your cholesterol level. You will also receive all the normal care that we are used to in the Netherlands.

What we do five years later

As indicated above, people in intervention group B will also give blood samples. The blood won't be used straight away, but stored. After five years, we will measure the levels of fat in the blood and make a CVD risk assessment. We will then compare the risk assessments with the calcium scores. That will help us to tell which test method is best for identifying people who are at risk. By the time we analyse your blood sample, the results won't be relevant to you. Your GP would need to have your blood re-tested to find out whether

anything needed to be done to reduce your risk. If you do nevertheless want to know the results, you can get them from the research team after five years.
Five years after making our risk assessments, we will count up how many people in each of the three groups have gone on to develop CVD, or have died from it. We will also work out what the cost of each kind of test method was. That will be done using information obtained from GPs, health insurers, the Central Bureau for Genealogy and Statistics Netherlands.

What side effects can you expect?
None of the tests have side effects. People who are assessed as having a high risk of CVD may be given medication to reduce their cholesterol or blood pressure. The medications are widely used and rarely have side effects.

What are the benefits and drawbacks of taking part in the study?
If you are in the control group, taking part won't have any direct benefits or drawbacks for you. You will still receive all the normal care that we are used to in the Netherlands. Your participation will help us to gain more knowledge on how we can prevent CVD.

Benefits for intervention groups A and B
If you are in intervention group A or intervention group B, you may benefit from taking part. That is because you will be told what your CVD risk is. So, if you're at risk, you'll be able go to your GP, who can help you bring down your risk and make it less likely you will get CVD or die from it.

Drawbacks for intervention groups A and B
You might find that taking part in the study causes you stress, because of having tests and waiting for the results. You might be put on medication by your GP to reduce your cholesterol and/or blood pressure. If you are given medication, it might later turn out that you didn't really need it. In other words, it might be discovered that you have been on medication – and possibly experienced drawbacks, such as regularly having to take pills – without receiving any benefits. Another possibility is that you are not given medication, and it later turns out that you could have benefitted from it. The study is intended to shed light on those kinds of situations.
If you are in intervention group B, you will have a CT scan. That will involve X-rays passing through your body. The amount of radiation is very small, so the associated health risk is very small as well.

Detection of unrelated abnormalities
The CT scan will show only the area around your heart. The technician who assesses the scan will not be looking for abnormalities in other organs. Nevertheless, there is a small possibility that an abnormality near to your heart, which is unrelated to hardening of the arteries, will be discovered by chance.

The unrelated abnormalities that might be discovered can be divided into two groups:

1. Abnormalities for which *no* further investigation or treatment by a doctor is recommended.
2. Abnormalities for which further investigation or treatment by a doctor *is* recommended; these abnormalities can be subdivided into serious and non-serious.

If an abnormality is detected for which *no* further investigation or treatment by a doctor is recommended, we will take no action. Occasionally, however, something will be noticed that looks as if it might cause a health problem. If so, it's best for a doctor to take a closer look at you. The abnormality might be something that isn't very serious, such as a minor inflammation. On the other hand, it might something very dangerous, such as cancer or an aneurysm (a bulge in an artery). A list of some of the abnormalities that might be found is provided in the table below. Having an abnormality investigated can be good for your health, but it can also be a source of worry and uncertainty, and you might need an unpleasant form of treatment. It could even be that you have something that can't be treated. In that case, you will have learnt that you are unwell but that your doctors can do little for you.

You can decide whether you want to be told about any unrelated abnormality that is observed. You have the right to know, but you also have the right not to know, so please indicate on the consent form whether you want to be told about any unrelated abnormalities that are discovered by chance. If you give your consent, the hospital will tell your GP about anything that is discovered. Your GP will then contact you.

If you indicate on the consent form that you *don't* want to be told about any unrelated abnormalities, you might nevertheless be told. That won't happen, however, unless the doctor sees something that could be dangerous not only for you, but also for the people around you. Naturally, the doctor will never go against your wish not to be told without first considering the situation very carefully. What's more, the doctor won't make a decision alone, but will get advice from an independent committee, made up of people with no ties to the study. The people deciding whether you should be told will not be given your name, only an identification code.

Unrelated abnormalities for which further investigation and/or treatment is recommended

Non-serious

Examples:

- Lung abnormality, such as mild inflammation, COPD (chronic bronchitis or pulmonary emphysema)
- Minor obstruction of part of the lung
- Enlarged lymph gland

Serious

Examples:

- Lung abnormality that might indicate lung cancer
- Abnormal (possibly malignant) mass in the space between the lungs
- Damage to the large blood vessels, such as the aorta or pulmonary artery

What happens if you don't want to take part in the study?

Participation in the study is voluntary. You can also withdraw at any time, without giving a reason. It will not make any difference to your medical care whether you decide to take part or not.

What if new information becomes available?

The study will run for five years. We have planned the study carefully, but we recognize that things can change in five years. For example, new information may become available, which makes us think again about our research. If that happens, we will let you know and you will be able to decide whether you want to continue taking part. Naturally, we will stop the research immediately if we think that taking part has become less safe or less pleasant for you.

What will we do with your data?

All the research data (results, questionnaire answers and requested data) will be used exclusively for the ROBINSCA study. Furthermore, the researchers who handle the data will not know who the data are about. Your personal details (name, address and date of birth) will be linked to a code. The researchers will see only the code and therefore won't use your name in articles or reports that they write. A small number of study personnel will have access to your name and address, so that you can be sent an invitation and results, for example, and so that we can ask you for further information. The people with access to your details will have to abide by the Data Protection Act and the Erasmus MC Privacy Policy. The information about you that we gather will be used only for the ROBINSCA study. We will not share your medical details with anyone else. All data must be retained for fifteen years after the study has ended, because that is required by the Medical Treatment Contracts Act. After fifteen years, all data will be destroyed.

Will your GP be told if you take part?

Your GP has an important role to play in this study. So, if you want to take part, you will need to give your consent to us telling your GP about your test results. If you don't want your GP to know that you are taking part, unfortunately you won't be able to participate in the study.

What are we asking your consent for?

With the questionnaire, there is a consent form, on which you need to answer the following questions:

- Do you want to take part in the study?
- May we receive information about changes to your name, address and place of residence from the Municipal Personal Records Database (previously known as the General Municipal Register), so that we can inform you about the study results, for example?
- May we share your test results with your GP?

- May we tell your GP if the CT scan shows something unexpected?
- May we obtain information about your health from the doctor treating you and other care providers?
- If you die, may we ask the Central Bureau for Genealogy and Statistics Netherlands about the cause of death?
- May we ask your health insurer about any medical expenses you have incurred as a result of CVD?

All the information we obtain will be used exclusively for the ROBINSCA study. We will not share your medical information with any other organization.

Will you be paid?

You can reclaim your travel expenses.

Are you insured for the cost of the tests?

The tests that you have as part of the study will be paid for by us. You will not need to pay for the tests or claim for them on your health insurance. However, if your GP decides to do further tests, those tests will be outside the scope of the study. The cost of further tests that your GP recommends will need to be settled through your health insurance. If your insurance policy includes provision for an 'excess' amount, it is possible that you will be liable for at least part of the cost of the further tests. The situation may be the same where some medications are concerned.

What if something goes wrong?

Doctors and hospitals have liability insurance, which provides protection if anything goes wrong. However, the risk of something going wrong is extremely small.

Approval by the minister and the Health Council

The Minister of Health, Welfare and Sport asked the Health Council to check our study and decide whether it was safe and whether we had taken everything into account. The Health Council approved the scientific quality of our study and advised that the risk to participants was in proportion to the benefit. The Minister of Health, Welfare and Sport accordingly licensed the ROBINSCA study on 27 August 2013.

Do you have any questions?

If you have any questions about the ROBINSCA study, please call or e-mail the research team:
010 703 0084 or robinsca@erasmusmc.nl
Information about the study is also available from our website: www.robinsca.nl

Independent doctor

If you are unsure whether to take part, or if you have a question that you'd rather not put to one of the researchers, please call or e-mail the appointed independent doctor:

Dr Ed van Beeck, doctor and associate professor at Erasmus MC

Tel. 010 703 8472

e.vanbeeck@erasmusmc.nl

The independent doctor is not directly involved with the study, but knows all about it.

Do you have a complaint about the study?

If so, you have three options:

1. You can call or e-mail the research team. If you are not happy with the response to your complaint, you can call the Patient Information Centre (PIC) at the Erasmus MC outpatient clinic. The PIC's phone number is 010 703 5474. Please ask for the complaints officer.
2. You can call the Patient Information Centre without first contacting the research team. The PIC's phone number is 010 703 5474.
   You can make a complaint to the Secretary of the Erasmus MC Complaints Board, by writing to PO Box 2040, 3000 CA Rotterdam or via the website, www.erasmusmc.nl.
3. The Erasmus MC complaints policy and a leaflet about the handling of complaints are available from the PIC.

CT Scan Information Sheet

If you are assigned to intervention group B, you will be invited to go to a local hospital for a CT scan of your heart. This information sheet tells you more about the CT scan.

What is a CT scan?

A CT scan is a type of X-ray examination. You lie on a 'table', while a large X-ray tube revolves around you, taking images. It only takes a few seconds to obtain a number of images.

What are the implications of having a CT scan?

There are not many things you need to consider. You don't have to do anything to prepare: there's no need to go without food, for example. It doesn't matter if you are taking medication – you can simply continue with it. Being scanned isn't painful and doesn't involve medication or a drip. There is no need to undress, but you will need to take off anything metal, such as jewellery or spectacles. If you have something like a prosthetic implant or pins inside your body, that won't prevent you having a CT scan.

What will the scan be like?

For the scan, you will need to lie on a flat surface. The technician will then push this table into the wide opening of the CT scanner. While inside the scanner, you need to keep as still as possible. You will be inside the CT scanner only for a few moments, during which time you will still be able to talk to the technician over the intercom. The technician can also see you and will keep an eye on how you are. The technician will give you detailed instructions, such as 'breathe in', 'breathe out', 'cough', and 'hold your breath'.

What happens afterwards?

After the scan, you can go home and carry on as usual.

Is it dangerous?

When you have a CT scan, you are exposed to X-rays, which can be harmful. However, the amount of radiation is kept to the minimum, so that the chance of your health being damaged is very small.

Results

After the scan, the radiologists will determine the calcium score for your coronary arteries. Your coronary arteries are the blood vessels surrounding your heart. The calcium score is a number that indicates whether you have hardening of the arteries and, if so, how far it has progressed. You and your GP will each receive a letter telling you about the findings.