Executive summary

Health Council of the Netherlands. Population Screening Act: calcium score and the risk of cardiovascular disease. The Hague: Health Council of the Netherlands, 2013; publication no. 2013/09

Within the context of the Population Screening Act (WBO), the Erasmus MC in Rotterdam filed an application for authorisation for a comparative scientific study, named ROBINSCA. This study compares two risk assessment measures: (1) traditional risk assessment and (2) risk assessment using calcium score. On 20 July 2012, the Minister of Health, Welfare and Sport asked the Health Council to advise on this issue. Based on additional questions from the Committee regarding the application, the applicant updated the application and final modifications were received on 2 April 2013. The Committee bases its recommendations on the updated application.

The scientific study

As part of ROBINSCA, 338,800 men between the ages of 45 and 74 years and women between the ages of 55 and 74 years across four regions in the Netherlands receive a questionnaire on cardiovascular disease and a measuring tape. Thirty-nine thousand respondents who provide consent and whose answers indicate a (previously unknown) elevated risk of cardiovascular disease, are randomly assigned to three groups of 13,000 participants each: no further screening (control group), traditional risk assessment, and risk assessment using calcium score. Participants in the control group are given general lifestyle recommendations in writing, such as eating healthy and exercising more. If they smoke, are at least 50 years old, or have a family history of cardiovascular

disease, they are informed of the possibility for full (traditional) risk assessment via the GP. For the second group with the traditional risk assessment, the questionnaires are supplemented with blood pressure data and blood values determined by a GP laboratory (lipids and glucose levels in particular). In the third group, a calcium score is determined using a CT scan of the heart's contours. Participants with an elevated cardiovascular disease risk in the second and third groups are referred to the GP for (specific) lifestyle recommendations and, if necessary, treatment with cholesterol and blood pressure-lowering medication. Subsequently, mortality and disease due to cardiovascular disease in all three groups is registered for a five year period. The outcomes in the three groups are then compared with each other.

ROBINSCA is population screening requiring authorisation

ROBINSCA is a scientific study and a population screening study according to the WBO. People without complaints or symptoms are invited to complete a questionnaire and measure their abdominal circumference. If this reveals indications for elevated cardiovascular disease risk, they are invited for further risk assessment. If this assessment reveals an elevated risk, they are referred to the GP for lifestyle recommendations and medical treatment, where necessary.

Only certain categories of population screening require authorisation, including studies which involve the use of ionising radiation. The calcium score is determined using a CT scanner, which requires ionising radiation. Therefore, ROBINSCA is population screening that requires authorisation within the meaning of the law. To this end, the Council's Committee on Population Screening examined the study based on legal criteria: the importance to public health, scientific integrity, accordance with legal rules for medical actions and the risk-benefit balance.

Importance to public health

An application for authorisation for population screening that is also a scientific study may be denied if public health interests do not require such a study. In the opinion of the Committee, it is unlikely that a national population screening programme for cardiovascular diseases using a CT scan will ever be deployed in the Netherlands. However, ROBINSCA is first and foremost a scientific study, which can answer questions to scientific questions that may be important to public health. A calcium score is being offered with increasing frequency outside of regular care, for example (abroad) as part of opportunistic screening with a

full-body scan or an extensive athletic assessment. Scientific research, such as ROBINSCA, can provide clarity about identifying risk factors for cardiovascular disease (with or without calcium score) and help structure the demand for calcium scores. Taking the above into consideration, the Committee concludes that authorisation for ROBINSCA need not be denied based on this clause.

Scientific integrity

The Committee rules positively on the scientific integrity of the application. The randomised study design is good, the size of the study population is sufficiently substantiated, and the expected outcomes are scientifically relevant, quantifiable and testable.

Participants in the control group who smoke or have a family history of cardiovascular disease, are advised to contact their GP by the investigators. The Committee does not expect this to bias the study. Few control subjects are expected to visit the GP of their own accord, and if they do visit, the GP can record this.

The risk-benefit balance

The study may benefit participants. A participant with an elevated risk and an indication for lifestyle recommendations and medication runs a lower risk of death due to cardiovascular disease if he follows the lifestyle recommendations and takes his medication.

There are also potential disadvantages. Ionising radiation can have negative health effects, such as radiation-induced cancer. However, the radiation burden due to the CT scan for the calcium score is usually limited; the median radiation dose lies between 0.7 and 2.3 mSv, although outliers are possible. This depends, among other things, on the scanner used. Therefore, it should be verified whether the scanners in participating screening regions meet the requirements for medical scientific research, as outlined in the advisory report. Outliers may not exceed 5 mSv per individual.

The risk of incidental findings is likely low. However, the Committee does require agreements be made with the radiologists performing the CT scan for the calcium score. In order to minimise the chance of incidental findings, they may only focus on the contours of the heart. Furthermore, the Committee also requires incidental findings be recorded. Diagnosis and treatment resulting from incidental findings must also be recorded.

Another disadvantage is the risk of over-diagnosis and overtreatment with cholesterol and/or blood pressure-lowering medication. An elevated risk does not mean the participant will necessarily ever suffer from cardiovascular disease. Participants are properly informed of this risk in advance, and are referred to their GP if they have an elevated risk. Cholesterol and blood pressure lowering medication is relatively safe, and the GP will oversee the safe use of the substances together with the pharmacy.

Considering the limited risks and the intensive involvement of GPs in treatment, the Committee judges positively on the risk-benefit balance for participants.

Agreement with legal rules for medical actions

The information provided to the target group meets legal criteria. There is sufficient information about study design, the scientific importance and advantages and disadvantages of participating.

Participants are given various choices for whether or not to be informed of clinically relevant incidental findings other than the calcium score: not at all, all clinically relevant findings, or only those for which reasonable action or treatment options are available. In accordance with the Dutch Medical Treatment Act (WGBO), an exception may be made to the 'right to not know' following careful consideration, should the importance of knowing about a finding for the participant or others outweigh not sharing it. The applicant provides participants with sufficient information on this subject.

The Committee considers the extensive involvement of the GP in this study to be important. All participants with an elevated risk based on the risk assessment are referred to the GP, who discusses further actions and treatment options with the participant.

Conclusions and recommendations

In the opinion of the Committee, the application meets the legal criteria outlined in the Population Screening Act (WBO). It recommends that the Minister of Health, Welfare and Sport authorise ROBINSCA, with a number of requirements and prescriptions, for a duration of six years.