Executive summary

Health Council of the Netherlands. Population screening act: prostate cancer screening using MRI. The Hague: Health Council of the Netherlands, 2011; publication no. 2011/37

In this advisory report, the Committee on Population Screening of the Health Council evaluates a license application from the Erasmus Medical Centre, Rotterdam and the University Medical Centre St Radboud, Nijmegen. The application relates to a population screening pilot for prostate cancer. Based on the Population Screening Act (WBO), a license is required from the minister of Health, Welfare and Sport. The minister asked the Health Council to advise her on the license application. To this end, the Committee on Population Screening of the Council evaluated the application based on the WBO.

Background

According to a large-scale population screening trial, screening using the prostate-specific antigen (PSA) test leads to a drop in prostate cancer mortality.[1] However, this effect took years to become apparent. The disadvantages such as (over) diagnosis and (over) treatment and consequences thereof, such as impotence and incontinence, are immediate. Internationally, the belief remains that population screening for prostate cancer using PSA testing is irresponsible as long as it has not been demonstrated that the benefits of screening outweigh the disadvantages.

The planned study

The application is for a scientific population screening study into prostate cancer using the PSA test (PSA screening). According to the project proposal, a total of 15,000 men from Rotterdam aged 40 to 70 years old will be invited to take part. Random chance will assign men to follow-up positive PSA tests – with a cutoff value greater than or equal to 2.0 ng/ml – using either Transrectal Ultrasonography (TRUS triage) or Magnetic Resonance Imaging (MRI triage). During TRUS, a standard of at least 6 biopsies (tissue samples) are taken of as many areas of the prostate (sextant biopsy). MRI yields a more detailed image of the prostate. According to the applicant, MRI triage will lead to fewer biopsies being needed and, when necessary, a lower average number of biopsies (2 to 4) because only observed abnormalities are biopsied. A disadvantage is that a man with abnormalities has to undergo an MRI twice (requiring a trip from Rotterdam to Nijmegen): once for diagnostic testing, once for the biopsy.

Scientific integrity

The Committee rules negatively on the scientific integrity of the application. It compares the study proposal with a phase three pragmatic study, for which it has been internationally agreed upon that the control group must be monitored using the currently (most) responsible (effective and safe) test. The PSA test remains the primary test in this design, and as PSA screening with TRUS triage is no considered responsible population screening, it is also inappropriate as a control for this study.

According to the Committee, the study cannot lead to a change in policy if the hypothesis can only raise the likelihood that MRI triage is at least equivalent to TRUS triage: TRUS is far cheaper than MRI, and MRI triage cannot be acceptable if not demonstrably better.

The primary outcome measure used by the application is a measure for tumour aggressiveness, the Gleason score. According to the Committee, this score is insufficient for determining full follow-up policy for an individual patient.[4] For a score of less than 7 (the cutoff in the application), the odds of eventually dying of prostate cancer are not sufficiently lower than for a score greater than or equal to seven (10 versus 29 percent).

Reliable estimates of sensitivity and specificity of (endorectal multi parametric) MRI within population screening for prostate cancer using the PSA test are lacking, but for now, MRI appears to have little added value.[5] It also remains

unclear why the more complicated endorectal multi parametric method was selected.[6]

A cutoff of 2.0 ng/ml for a positive PSA test is very low. This choice is surprising, as the usual cutoff of 4.0 ng/ml is already associated with 25 percent referred men and a significant risk of false positive results and over diagnosis. The Committee feels the risks of a lower cutoff for study subjects to be unacceptable.

As the Committee concludes the study fails to meet the criterion for scientific integrity, it has not – in accordance with past advisory reports – tested the application for conformity to the remaining legal criteria.

Conclusion and recommendation

The application does not meet the legal criteria outlined in the Population Screening Act (WBO). The Committee recommends the Minister of Health, Welfare and Sport to deny the requested license.