Medicine today is seeing very rapid development of new technologies for the prevention, treatment and diagnosis of disease. Decision-makers in the health service and health care professionals have to make choices and define strategies on the basis of criteria of safety, efficacy and benefit.

The National Agency for Accreditation and Evaluation (ANAES) evaluates these various strategies, produces a summary of available information and disseminates its conclusions to all partners involved in health care. Its role is to provide assistance with the individual and collective decision-making process:

- it keeps the public authorities informed of the state of scientific knowledge, its implications for medicine, organisation and financing, and its impact on matters of public health;
- it helps health care establishments provide the best response to patients' needs in order to improve health care;
- it helps health professionals define and implement the best strategies for diagnosis and treatment, in line with prerequisites.

This document fulfils this mission. The technical and economic information it contains has been independently produced using rigorous scientific methods and comes from a review of the international literature and consultation with experts.

Professor Yves MATILLON
Executive Director
This study was carried out at the request of the CNAMTS. The full report is available in French from ANAES.

**CONTEXT**

At the request of the Caisse Nationale d’Assurance Maladie des Travailleurs Salariés1 (CNAMTS), ANAES carried out a study called “Appropriateness of systematic screening for prostatic cancer by prostate specific antigen (PSA)”.

The PSA test is very commonly used in opportunistic screening. The aim of the study was to determine whether the conditions required for systematic screening are satisfied, and, from a public health viewpoint, whether such screening is acceptable and useful to the patient.

**SUMMARY**

Although prostatic cancer is the second most common male cancer in the developed world in terms of incidence, it ranks only seventh in terms of mortality. Its incidence has risen over the years. This rise could be due to increased diagnosis of prostatic cancer at the localised stage, as a result of more frequent blood tests to determine PSA concentration, and more frequent transurethral resections of the prostate. Mortality related to prostatic cancer has not risen in the same way.

A number of guidelines on screening for prostatic cancer have already been published.

Screening is justified if the disorder fulfils the ten WHO criteria (Wilson and Jungner), which have been used as reference criteria in a number of countries where various organisations have looked into the question of whether mass screening for prostatic cancer is appropriate, and have concluded that it is not (criteria not satisfied). These are the National Cancer Institute, the US Preventive Services Task Force, the American College of Physicians, the International Union against Cancer, the American College of Radiology, the American Neurological Society, and the American Cancer Society, the Canadian Cancer Society, the Canadian Task Force on the Periodic Health Examination, the Canadian Cancer Society, the Canadian Urological Society, the American Cancer Society, and the American College of Radiology.

Randomised controlled trials to evaluate the potential benefit of mass screening for prostatic cancer are currently being carried out in the United States, Canada, and certain European countries, coordinated by the Netherlands.

ANAES also used the WHO criteria as the basis for this report.

The condition should be an important public health problem:

- In France, the standardised incidence (per 100 000 inhabitants) of prostatic cancer ranges between 24.9 (Isère) and 37.9 (Tarn). In Europe, the range is between 17.1 (Poland) and 74.7 (Sweden) (1992 data).
- Standardised mortality (per 100 000 inhabitants) is 16.7 in France, while in Europe the range is between 11.9 (Poland) and 22.2 (Norway).

The incidence of prostatic cancer has increased regularly over the years, but at present both the incidence of the disease and mortality related to it are decreasing, which has led to a number of hypotheses, i.e. that fewer PSA tests are being ordered, and that screening is reducing the “pool” of cancers which are at the pre-clinical stage. In fact it is difficult to assess the true prevalence of the disease, as the only available data are derived from autopsy series in which histological prevalence ranges from 12% in the 40-49 age bracket to 43% in patients over 80.

In terms of years of life lost, the impact of this cancer is much lower than that of lung cancer or gastrointestinal cancers.

Although many risk factors have been suspected (familial factors, ethnic factors, history of vasectomy, diet, sex hormones, exercise) none have been proved and, in the current state of knowledge it is not yet possible to provide any guidance on primary prevention.

Prostatic cancer is therefore a less important public health problem than its incidence and prevalence would suggest.

There should be a recognisable latent stage, and the natural history of the condition, including development from latent to declared disease, should be adequately understood:

- The development of prostatic cancer is androgen dependent. Ninety-five percent of prostatic cancers are adenocarcinomas. Prostatic cancer has a very long natural history, and although there does not appear to be any spontaneous regression, progression during the patient’s lifetime is not inevitable. Although 30 to 40% of men over 50 may have prostatic cancer, only 8% are likely to develop a clinically significant cancer and fewer than 5% are likely to die of it. In addition, data in the literature on untreated prostatic cancer show high survival rates at 5, 10 or 15 years.
- Small adenocarcinomas are asymptomatic and are detected incidentally during PSA

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1 Social security fund for salaried staff.
repeated PSA tests would not lead to a significant increase in the level of tumours detected at a localised stage over that obtained using a single test.

Other tests can be used to screen for prostatic cancer, such as digital rectal examination and transrectal ultrasonography of the prostate. They have the same limitations as PSA with regard to true measurement of the prevalence of the disease.

The most powerful strategy might be a combination of PSA and digital rectal examination, with a biopsy being performed when one of the two tests is positive. However, no optimum strategy which takes account of both organisational and economic criteria has yet been defined.

The test should be acceptable to the population, and screening should result in benefits for public health:

There are no randomised or case-control studies which demonstrate that routine screening for prostatic cancer has any benefit in terms of specific mortality or quality of life. Studies using various screening strategies are currently in progress (United States, Canada, Europe). Although these studies have not yet produced any definitive results, they illustrate the importance of factors which cannot be planned for, i.e. the problems of recruitment and transfers from one group to the other in these randomised screening studies. In 1997, the data in the literature seemed to show that if objective information is provided about the benefit and potential side effects of screening and treatment for prostatic cancer, the patient either prefers not to take part, or finds it impossible to reach a decision, while the patient’s family and close friends are more favourable to the idea. The acceptability of the tests also seems to be related to uncertainties about screening rather than to the technical aspects.

In addition to the WHO criteria, an analysis of the benefits of screening needs to include economic factors:

Conclusions from economic studies have mostly opposed mass screening, although there is felt to be a place for some spousaneous screening. Although study results have concluded that the cost of screening cannot be regarded as prohibitive compared with that of other programmes, a better knowledge of the gain in terms of life expectancy is needed before any decisions can be taken regarding allocation of resources for this kind of screening.

In addition, both mass and individual screening imply improved patient information, particularly to refute the idea that early discovery of prostatic cancer improves survival and cure levels. Patients should be made aware of the lack of data on the benefits of screening in asymptomatic men, and the damaging effects that have been reported under curative treatment. The doctor therefore has a responsibility to present the implications of screening in an objective way. Patients should be aware that a suspicious test result will lead to other investigations.

There should be a suitable test for screening:

A blood test to determine PSA concentration can identify a biological abnormality which suggests that the patient has prostatic cancer. However, in routine practice there are problems of variation in results depending on the methods used (threshold value). Most studies have found that the test has a positive predictive value in selected populations. They certainly overestimate the prevalence of the disease in the general population. The few case-control studies available report sensitivity of between 46 and 81%, and specificity of between 91 and 99.5%.

Modified PSA tests have been proposed (PSA velocity test, PSA density test, age-referenced PSA concentration, free PSA); but their use has not proven to be superior to the measurement of blood PSA concentration. In addition, the carrying out of repeated PSA tests would not lead to a significant increase in the level of tumours detected at a localised stage over that obtained using a single test.

The positions and recommendations expressed in this document are those of ANAES, and none of the experts consulted is regarded as individually responsible for them.
and potentially to the need to take a difficult decision about curative treatment which is associated with a very high level of morbidity.

At the end of this study and on the basis of a review of the economic literature, it would seem to be premature to consider introducing a mass screening programme for prostatic cancer in asymptomatic men.

Finally, it seems that in order to be able to weigh up the appropriateness of introducing routine screening for prostatic cancer, an economic evaluation needs to be carried out, based on the results of cost-effectiveness studies, and taking into account the costs involved in organising screening campaigns.

So, in 1998, the benefit of mass screening for prostatic cancer has not been established.

GUIDELINES

The most common cancer in men over 50 is prostatic cancer. After a period of increased incidence, there has been a slight decrease in new cases since 1994; this could be related to depletion of the subgroup of prostatic cancers at the subclinical stage, as a result of better detection. In parallel, mortality seems to have begun to decrease, though this trend is still too recent and too small to be interpreted. Available data on years of life lost show that the impact of this cancer is much lower than that of lung cancer or gastrointestinal cancers.

Many questions remain about the effectiveness of treatment for localised prostatic cancer. The best treatment has not been defined; the morbidity of the various forms of treatment and their impact on quality of life were important factors in reaching this conclusion. It has not yet been proved that curative treatment is better than watchful waiting (although this has been suggested for certain age ranges and certain types of tumour). In 1998 it was not possible to identify which of the prostate tumours detected will be life-threatening to the patient during their lifetime and which will not be the cause of death. However, the degree of differentiation of the tumour is the most significant prognostic factor. Men with a family history of prostate cancer in most of the developed countries and the first results of randomised studies currently being carried out to evaluate the benefit of screening (United States and Europe) have clearly demonstrated that information needs to be provided for patients, and how difficult it is to do this, as well as the need to take individual preferences into account.

Acceptability of screening tests by the population needs to be better defined, and economic criteria also have to be taken into account.

In conclusion, current knowledge does not support any recommendation for mass screening for prostatic cancer. Further thought and discussion are needed with regard to patient information and the appropriateness of individual screening by proper prescription of the PSA test.

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