

# RECOMMENDATIONS ON CANCER SCREENING IN THE EUROPEAN UNION

PREPARED BY THE  
ADVISORY COMMITTEE ON CANCER PREVENTION  
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SCREENING AND EARLY DETECTION OF CANCER  
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## 1. INTRODUCTION

Screening allows detection of cancers at an early stage of invasiveness or even before they become invasive. Some lesions can then be treated more effectively and the patients can expect to live longer. The key indicator for the effectiveness of screening is decrease in disease specific mortality or incidence.

Screening is, however, testing of healthy people for diseases which have so far not given rise to symptoms. Aside from its beneficial effect on the disease specific mortality or incidence, screening might therefore also have some negative side-effects for the screened population.

Health care providers should know all the potential benefits and risks of screening for a given cancer site before embarking on new cancer screening programmes. For the informed public of today, it is furthermore necessary to present these benefits and risks in a way which allows the individual citizen to decide on participation in the screening programmes for her or himself.

The purpose of this document is to give recommendations on cancer screening in the European Union. These recommendations address the people, the politicians and the health administrations of the Member States, the European Commission and the European Parliament.

Principles for screening as a tool for prevention of chronic non-communicable diseases were published by the World Health Organisation in 1968 (1) and by the Council of Europe in 1994 (2). These two documents form, together with the present state of art in each of the cancer screening fields, the basis for the present recommendations.

All data on incidence and mortality are quoted from the recently published EUCAN data covering 1995. An estimated number of 1,488,000 new cancer cases, excluding non-melanoma skin cancer, occurred in the European Union in 1995. Of these, 2% were cervical cancers, 13% were breast cancers, 13% were colorectal cancers, and 8% were prostate cancers. Cervical and breast cancer constituted 4% and 29%, respectively, of new cancers in women, and prostate cancer constituted 14% of new cancers in men. All rates presented here are age standardised with the European Standard Population (3).

## **2. GENERAL PRINCIPLES**

Screening is only one method of controlling cancer. Whenever possible primary cancer prevention should be given first priority. When cancer screening is undertaken it should be offered only in organised programmes with quality assurance at all levels, and good information about benefits and risks. The benefits of a screening programme is achieved only if the coverage is high. When organised screening is offered high compliance should therefore be sought. Opportunistic screening activities are normally not acceptable as they may not achieve the potential benefits and may cause unnecessary negative side-effects.

New cancer screening tests should be evaluated in randomised trials before being implemented in routine health care.

The reduction in the disease specific mortality achieved in trials depends on the sensitivity of the screening test, the compliance among the invited, the screening frequency, the number of screens each person has, the completeness of the follow up, and the benefit of early treatment. The negative-side effects in the screened population depend on the sensitivity and the specificity of the test, and on the possible side effects of early treatment. The findings from trials can be extrapolated to the general population only if the conditions in the trials can be reproduced in the routine health care system. This requires an organisation with a call-recall system and with quality assurance at all levels, and it requires an effective and appropriate treatment service.

Centralised data systems are needed for the running of organised screening programmes. This includes a computerised list of all persons to be targeted by the screening programme. It includes also computerised data on all screening tests, assessment and final diagnoses. Organised screening also implies scientific analysis of the outcome of the screening and quick reporting of these results to the population and screen providers. This analysis is facilitated if the screening data base is linked to cancer register data.

High quality screening is possible only if the personnel at all levels are adequately trained for their tasks. Performance indicators should be monitored regularly.

Ethical, legal, social, medical, organisational and economic aspects have to be considered before decisions can be made on implementation of cancer screening. Resources, human as well as economic, must be available in order to assure the appropriate organisation and quality control. Actions have to be taken to ensure different socio-economic groups equal access to screening. The implementation of a cancer screening programme is therefore a decision to be made locally, depending on the disease burden and the health care resources.

Cancer is a leading disease and cause of death in all of Europe. European collaboration should facilitate high quality cancer screening programmes and protect the population from poor quality screening.

### **3. CERVICAL CANCER SCREENING**

#### **3.1 Epidemiology**

In an unscreened population, the incidence of cervical cancer reaches its maximum around the age of 50. In screened populations the incidence tends to be highest for women above the age of 60. The incidence of cervical cancer reflects both background risk and screening activity during the previous decades. The highest incidence of cervical cancer is now observed in Portugal with 19 per 100,000 and the lowest in Luxembourg with 4 per 100,000. Mortality rates are highest in Denmark, Austria and Portugal with 6-7 per 100,000 and lowest in Luxembourg and Finland with about 1 per 100,000.

#### **3.2 Present situation**

While no randomised trials on cervical screening with Pap smears were ever carried out, the effectiveness of cervical screening programmes has been demonstrated in several countries (4-6). It is estimated that cervical smears every three years can prevent 90% of cervical cancers in a population if all women attend and all detected lesions are adequately followed up (7). High acceptance is thus vital and high degree of organisation is needed to achieve this.

Nationally organised cervical screening programmes exist in Sweden, Finland, Denmark, the Netherlands, and the United Kingdom. A European set of guidelines for cervical screening was developed in 1993. It provides targets for quality assurance of organised screening programmes (8). Ten centres with cervical screening have, in the past, been financially supported by the Europe Against Cancer programme. These ten programmes have recently formed a network focussing on quality assurance, epidemiology and new technologies.

Limited screening resources should be concentrated in the age range 30 to 60 years. A large proportion of cervical abnormalities will regress to normal if left untreated. Screening should therefore definitely not start before the age of 20 and in many countries probably not before the age of 30. The protective effect of screening of women older than 60 years is limited, especially if these women previously had negative tests.

Screening should be undertaken with a three to five year interval. Prolonged intervals may be considered in women with a history of negative tests. The benefit of more frequent screening is very limited, and, in addition, it increases the risk of overtreatment of otherwise regressing lesions.

### **3.3 Recommendations**

#### ***3.3.1 To the Member States***

Pap smears should be the method used in cervical cancer screening.

When screening is offered it should start at the latest by the age of 30 and definitely not before age 20. The upper age should depend on the available resources but should preferably not be lower than 60 years. Limited screening resources should be concentrated in the age range 30-60.

Screening intervals should be between three and five years. Screening more often than every third year should be discouraged. Smear taking in healthy women should be undertaken only in organised screening programmes with quality assurance at all levels.

Cervical cancer screening programmes should be organised in accordance with the European guidelines.

#### ***3.3.2 To the European Commission and the European Parliament***

A common terminology for histology and cytology should be implemented. For the laboratories, a detailed quality control programme should be defined based

on the existing guidelines and implemented at the national level.

Recommendations for training and quality control could be proposed and tested in the network centres. As different treatment options are currently adopted, auditing of cases should be performed by a core group of clinicians. A concerted effort should be made to find the most effective methods for follow up and treatment of cervical abnormalities.

Validation studies of liquid based and automated screening methods with special attention to cost-effectiveness should be undertaken. Well designed studies should be undertaken on the use of HPV testing as a screening method and/or as a supplementary method in the follow up of cervical abnormalities.

Studies should be undertaken of recent trends in incidence of cervical cancer in Europe in order to optimise the lower and upper age limits for screening.

## **4. BREAST CANCER SCREENING**

### **4.1 Epidemiology**

In countries with national population-based cancer statistics, such as the Nordic countries, the incidence of breast cancer has increased during the last four decades. The start of a mammography screening programme is associated with a temporary increase in the incidence of breast cancer, and the European differences in breast cancer incidence therefore at present reflect both background risks and screening activities. At present the incidence is highest with 120 per 100,000 in the Netherlands, where a screening programme started recently, and lowest in Spain and Greece with 61-63 per 100,000. Breast cancer is rare under the age of 30 and the incidence increases with age. The breast cancer mortality is highest in Denmark 38 per 100,000 and lowest in Greece 23 per 100,000. Mortality rates have increased during the last decades in the majority of European countries, whereas it has been stable or decreased slightly in the Nordic countries and in the UK.

### **4.2 Present situation**

Screening for breast cancer with mammography has been studied in a number of randomised trials. Data from five Swedish counties showed a 30% decrease in breast cancer mortality among women invited to screening at age 50-69 (9). Updated data from Sweden also indicate a reduction in breast cancer mortality among women invited to screening at age 40-49 (10). The cost-effectiveness is, however, not clear in this lower age group.

A European breast cancer screening network was established in 1989 with the aims to provide experience for countries with no breast screening service, to explore methods of implementation into the national health systems, to establish contact for exchange of information between Member States, and most importantly to develop guidelines for best practice related to breast screening. The desirable endpoint for each member of the network is to establish a co-ordination of the screening activities

in their country and to operate as service and/or reference centre for these activities.

During its ten years of existence the network has noted that population-based screening requires the full support of national or regional health authorities, and that the decision to start a programme needs to be taken by appropriate health authorities. Screening for breast cancer is multidisciplinary and the quality of the whole process (invitation, diagnosis, assessment of suspicious lesions, treatment and follow-up) needs to be ensured before initiating a programme. Initial and continuous training of all personnel involved is mandatory. Mechanisms are needed to monitor the quality of the screening programme.

The different health care systems in Europe have made it necessary to find different solutions to common problems. The network has demonstrated the importance of high quality radiological examination and the need for centralised expert reading of mammograms taken in a decentralised setting. It has also demonstrated the need for standards on the minimal number of women to be examined in a centre in order to keep up the level of expertise.

The European guidelines for quality assurance in mammography screening is a document with minimal and optimal requirements for quality assurance of organised screening programmes (11). An updated version will be published in year 2000.

### **4.3 Recommendations**

#### **4.3.1 To the Members States**

Mammography should be the method used in breast cancer screening. There is at present no convincing evidence for the effect of screening based on breast self examination or clinical breast examination.

Women without symptoms of breast cancer should be offered mammography examination only in organised screening programmes with quality assurance at all levels. When mammography screening is offered, only women aged 50-69 should be invited.

Screening intervals should be two to three years.

Breast cancer screening programmes should be organised in accordance with the European guidelines (11).

Adverse effects of mammography screening in women aged 40-49 may not be negligible, due to the lower predictive value of mammography in this age group, the possible detection of non-progressive cancers and the higher radiation hazard.

Thus, if screening is offered to women aged 40-49 in some centres or European regions, according to local resources and quality standards reached in screening offered to older women, the following requirements are needed: 1) women should be

clearly informed about the possible benefits and adverse effects of screening, 2) organised programmes should be set up in order to discourage spontaneous screening in units without adequate quality control systems, 3) two view mammography with double reading and 12-18 months of interval should be used, 4) data monitoring and proper evaluation should be mandatory.

#### ***4.3.2 To the European Commission and European Parliament***

Efforts should be continued to improve breast cancer screening in Europe by promoting exchange of experience. This may best be achieved by continuation of the activities of the European breast cancer screening network.

Updated guidelines should be published at regular intervals. Quality management should be ensured, including training and education in business strategy, recruitment, training and retention of qualified staff, quality assurance providing consumer protection, and management of political, governmental, economic, social and technical aspects of a programme.

Research should be encouraged on the impact of screening on breast cancer mortality, progression of mammography detected lesions, ethical questions, population acceptance, method of invitation, cost-effectiveness, and psycho-social effects. These research activities should address mammography screening both below age 50, in the age range 50-69 years, and from age 70 onwards. Support should be given to development of appropriate data registration systems.

A system should be set up for accreditation on a European level of screening programmes applying to become reference centres in the breast cancer screening network.

## **5. COLORECTAL CANCER SCREENING**

### **5.1 Epidemiology**

For men the highest incidence of colorectal cancer incidence is found in Ireland, Austria and Denmark with 58-61 per 100,000 and the lowest in Greece with 25 per 100,000. For women the highest incidence is found in Denmark, the Netherlands and Ireland with 40-43 per 100,000 and the lowest in Greece with 19 per 100,000. Mortality rates for men are highest in Denmark and Ireland with 35-36 per 100,000 and lowest in Greece with 13 per 100,000. For women the mortality is highest in Denmark with 27 per 100,000 and lowest in Greece with 9 per 100,000. Despite advances in diagnostic techniques and treatment the five-year survival rates remain poor.

### **5.2 Present situation**

Faecal occult blood test, sigmoidoscopy and colonoscopy have all been considered as screening tests for colorectal cancer.

The faecal occult blood test is the only test which has been extensively evaluated as a screening tool on the population level. Four European trials have been undertaken (12-16). There are three randomised trials from Funen, Nottingham and Gothenburg, and one non-randomised trial from Burgundy. In the last trial people from small areas "cartons" were allocated to either the screening or the control group. Only two screening rounds were undertaken in Gothenburg. In Funen, Nottingham and Burgundy screening was offered five times. A recent meta-analysis of all randomised faecal occult blood test trials showed a 16% reduction in colorectal cancer mortality (17).

Pilot screening programmes with the faecal occult blood test will start in two areas in England and Scotland in year 2000, and pilot projects are under consideration in one area in Austria and one in Spain. Annual faecal occult blood tests are offered as part of the German cancer screening activities.

More complex faecal occult blood tests, especially immunological tests, have been developed (18-19). They are more sensitive, but their specificity at the population level is not well established. The effectiveness of flexible sigmoidoscopy as a screening tool is currently being tested in randomised trials in England and Italy (20-21).

## **5.3 Recommendations**

### ***5.3.1 To Member States***

As colorectal cancer is a major health problem in many European countries faecal occult blood screening should be seriously considered as a preventive measure. The decision on whether or not to embark on these screening programmes must depend on the availability of the professional expertise and the priority setting for health care resources.

If screening programmes are implemented they should use the faecal occult blood screening test and colonoscopy should be used for the follow up of test positive cases. Screening should be offered men and women aged 50 to about 74 years. The screening interval should be one to two years.

Other screening methods such as immunological tests, flexible sigmoidoscopy and colonoscopy can at present not be recommended for population screening.

### ***5.3.2 To European Commission and Parliament***

Guidelines should be developed both at the European and national levels on quality assurance of faecal occult blood screening programmes.

Efforts should be continued to improve faecal occult blood tests. They must be carefully evaluated at a population level before being proposed in organised screening programmes with a special attention to cost-effectiveness. The effectiveness of flexible sigmoidoscopy as a screening tool should be evaluated in randomised controlled studies.

## **6. PROSTATE CANCER SCREENING**

### **6.1 Epidemiology**

The highest incidence of prostate cancer is observed in Finland 101 per 100,000 being four times higher than in Greece 24 per 100,00. This pronounced difference between European countries may reflect differences in medical procedures in addition to variation in exposure to risk factors. This is supported by a smaller variation in mortality, being highest in Sweden 36 per 100,000 and lowest in Greece 17 per 100,000.

Prostate cancer is predominantly a disease of older age, and due to increasing longevity the number of cases is expected to increase over the coming years (22). Part of the presently observed increase in incidence in some European countries is most likely due to opportunistic screening with the Prostate Specific Antigen, PSA.

## **6.2 Present situation**

The effect of screening on prostate cancer mortality has not been documented. Rectal examination has been part of the annual health check up offered in Germany since the 1970's, but apart from this prostate cancer screening has not been an accepted policy in Europe. Opportunistic screening is, however, increasing. In the US, the incidence of prostate cancer has almost doubled from 1986 to 1992 to decline again from 1992. This is most likely due to PSA screening (23). A slight decline in prostate cancer mortality started in American men in 1992, but the decline is so far without a conclusive explanation (24-25).

The European Randomised Study of Screening for Prostate Cancer (ERSPC) was initiated in 1994 in two and later in seven EU countries. It is the purpose of the study to test a 20% reduction in prostate cancer mortality after two screens in men followed up for ten years. The study aims at randomising 192,000 men to the screening or control groups. In November 1999, 170,000 men have been randomised. Final results are expected in 2008.

ERSPC has joined forces with the Prostate, Lung, Colon, Ovary (PLOC) screening study of the US National Cancer Institute (26). The US study will include 63,625 men. A common analysis has been planned. In the meantime, the collected data offer excellent opportunities for evaluation of the screening test (27-28), potential overdiagnosis (29), quality of life and interval cancers. An up-date of the international co-operation will be published soon (30). A comprehensive review on prostate cancer screening has been published recently (31).

## **6.3 Recommended Activities**

### ***6.3.1 To Member States***

As long as randomised studies have not shown an advantage on prostate cancer mortality or related quality of life, screening for prostate cancer is not recommended as a health care policy.

### ***6.3.2 To European Commission and European Parliament***

The European randomised trial should be completed.

## 7. CONCLUSION

Decisions on implementation of cancer screening programmes should be made within the frame of the general priority setting on use of health care resources.

Cancer screening should only be offered to healthy people if the screening is proven to decrease the disease specific mortality or incidence, if the benefits and risks are well known, and if the cost-effectiveness of the screening is acceptable. At present, these screening methods are:

- Pap smear screening for cervical abnormalities starting at the latest by age 30 and definitely not before age 20,
- Mammography screening for breast cancer in women aged 50-69,
- Faecal occult blood screening for colorectal cancer in men and women age 50-74.

No other screening test should be offered healthy people before these tests have been shown to decrease the disease specific mortality or incidence. Once the effectiveness of a new screening test has been demonstrated, evaluation of modified tests (e.g. alternative tests for faecal occult blood or interpretation of cervical specimens) may be possible using surrogate endpoints.

Potentially promising screening tests should be evaluated in randomised controlled trials, as is currently the case for:

- PSA testing for prostate cancer,
- Mammography screening for women aged 40-49,
- Flexible sigmoidoscopy for colorectal cancer.

Pap smear screening for cervical abnormalities, mammography screening for women aged 50-69, and faecal occult blood screening for colorectal cancer should be offered only in organised screening programmes with quality assurance at all levels, and good information about benefits and risks.

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