

- low risk after negative results of cervical cytology and its implication for screening policies. *Br Med J* 1986, **293**, 659-664.
9. Ferraroni M, La Vecchia C, *et al.* Pattern of cervical screening utilisation in Italy. *Tumori* 1989, **75**, 521-5262.
 10. Segnan N, Ronco G, Ponti A. Practice of early diagnosis of breast and uterine cervix cancer in a northern Italian town. *Tumori* 1990, **76**, 227-233.
 11. Report by the Evaluation Committee. Population screening for cervical cancer in the Netherlands. *Int J Epidemiol* 1989, **18**, 775-781.
 12. EEC, Eurosanitè. Prevention of female cancers: early diagnosis and screening. Bruxelles, 1991.
 13. Koopmanschap MA, Van Oortmarssen GJ, *et al.* Cervical cancer screening: attendance and cost-effectiveness. *Int J Cancer* 1990, **45**, 410-415.
 14. Marteau TM. Reducing the psychological costs. *Br Med J* 1990, **301**, 26-28.
 15. Wilkinson C, Jones MJ, McBride J. Anxiety caused by abnormal result of cervical smear test: a controlled trial. *Br Med J* 1990, **300**, 440.
 16. Marteau TM. Psychological costs of screening. *Br Med J* 1989, **299**, 527.
 17. Nathoo V. Investigation of non responders at a cervical cancer screening clinic in Manchester. *Br Med J* 1988, **298**, 1041-1042.
 18. Campion MJ, Singer A, Mithell HS. Complacency in diagnosis of cervical cancer. *Br Med J* 1987, **294**, 1337-1339.
 19. Habbema JDF, Van Oortmarssen GJ, *et al.* Model building on the basis of Dutch cervical cancer screening data. *Maturitas* 1985, **7**, 11-20.
 20. Gustafsson L, Adami HO. Natural history of cervical neoplasia: consistent results obtained by an identification technique. *Br J Cancer* 1989, **60**, 132-141.
 21. Prorok PC. Mathematical models and natural history in cervical cancer screening. In Hakama M, Miller AB, Day NE, eds. *Screening for Cancer of the Uterine Cervix*. IARC Scientific Publications no. 76. Lyon, 1986, 185-195.
 22. Lyng E. Screening for cancer of the cervix uteri. *World J Surg* 1989, **18**, 71-78.
 23. Robertson AJ, Anderson JM, *et al.* Observer variability in histopathological reporting of cervical biopsy specimens. *J Clin Pathol* 1989, **42**, 231-238.
 24. Ismail SM, Colclough AB, *et al.* Observer variation in histopathological diagnosis and grading of cervical intraepithelial neoplasia. *Br Med J* 1989, **298**, 707-710.
 25. De Vet HCW. Interobserver variation in histopathological grading of cervical dysplasia. *J Clin Epidemiol* 1990, **43**, 1395-1398.
 26. Van Ballegooijen M, Koopmanschap MA, *et al.* Diagnostic and treatment procedures induced by cervical cancer screening. *Eur J Cancer* 1990, **26**, 941-945.
 27. Fletcher A, Metaxas N, *et al.* Four and a half year of follow up of women with dyskaryotic cervical smears. *Br Med J* 1990, **301**, 641-644.
 28. Singer A. The abnormal cervical smear. *Br Med J* 1986, **293**, 1551-1556.
 29. Lund E, Bjerkedal T. Cancer cervicis uteri *in situ*. Increased perinatal mortality and prematurity after conization. *Nor Laegeforen* 1986, **106**, 543.2.

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Breast Cancer Screening: Methods, Human Benefits, Human Costs

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INTRODUCTION

IN THEIR renowned *Monograph on Screening for Disease*, Wilson and Jungner [1] began their list of requirements for justification of a population screening programme by emphasising that the disease under scrutiny should be an important public health problem, i.e. the disease should be relatively frequent and have serious consequences. Breast cancer is the commonest form of cancer in women in Europe and it has been estimated that in one single year (1980) there were approximately 135 000 incident cases [2].

There is, however, considerable variation in the incidence of breast cancer within Europe [3]. The highest incidence rates recorded in Europe around the mid-1980s were in Geneva, where the age-adjusted incidence rate was 73.5 per 100 000 and in Eindhoven (72.7 per 100 000). In sharp contrast, the lowest

recorded incidence rates were in Kyrgyzstan (19.6 per 100 000) and Nowy Sacz (22.5 per 100 000) and Warsaw (22.9 per 100 000) in Poland [3]. There are also extremely low incidence rates reported in republics of the former U.S.S.R. [4].

This variation is sufficient that any discussion on the issue of whether to undertake a breast cancer programme should take into account the national incidence or mortality rates. Cost-benefit in relation to screening clearly depends on the prevalence and thus the detection rate of breast cancer. Recent experience of screening in southern Europe suggests that the detection rate at initial screening in women aged 50-64 years is lower than the 6-7 per 1000 found in northern and western Europe. A further factor which must be kept in mind is that the economic situation in many parts of eastern and southern Europe would exclude implementation of breast cancer screening programmes on the simple grounds of costs and priorities.

A broad understanding has been reached about the causes of breast cancer in that western habits of reproduction and, possibly, nutrition are involved in determining the risk of this form of cancer. It appears from our current knowledge that even if we

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understood the causes in greater detail, it would be difficult to change them in the short term. Secondary prevention via early detection and treatment appears to be the most promising approach to breast cancer control for the foreseeable future.

EFFECTIVENESS OF MAMMOGRAPHY

There have been six randomised, controlled trials of breast cancer screening based on periodic mammographic examination in which mortality from breast cancer in a group of women offered screening was studied. All indicated that such screening reduces breast cancer mortality.

The early results of the Health Insurance Plan (HIP) randomised investigation in New York [5] were confirmed by the Swedish two-countries trial [6] and case-control studies in the Netherlands [7, 8] and Italy [9]. Results obtained in the U.K. [10, 11] and Malmö in Sweden [12] are less convincing. Most of the discrepancies between the studies can be explained by differences in the participation rates of women invited for screening and by the degree of pollution by mammographic examination in the control groups [13].

A number of important consensus were reached at the EUSOMA Consensus Conference in Paris in 1993 [14]. Screening for breast cancer by inviting women for periodic mammographic examination, followed by diagnosis and treatment as necessary, leads to a significant reduction in breast cancer mortality. The overall reduction observed in the six randomised trials among women aged 40–74 years was 22%.

Screening women over 50 by mammography has been shown to be effective and worthwhile with the randomised trials demonstrating a significant reduction in mortality of 24 per cent [14]. It was concluded that screening women aged 50 and over should be part of public health programmes organised on an invitation basis with full quality control and monitoring. While it is clear that screening women aged 50 and over is effective, there is uncertainty over the effect on women aged under 50. It is important that any screening in women aged under 50 is only performed as part of a properly controlled research programme, and that younger women who request mammography should only be given this after informing them of the uncertainties and advising them of the possible consequences [14].

Apart from the impact on breast cancer mortality, there are a number of other issues which have been resolved:

1. Mammography is not a "perfect" screening test, but it has been shown to have fairly high sensitivity and specificity, and is definitely better than clinical examination of the breast;
2. with modern film-screen combinations, good image quality can be combined with low radiation dose such that the risk of cancer induction is now further lowered;
3. the optimal interval between screens, in women aged 50 and over, is of the order of 2 years, taking into consideration cost-benefit.

On the basis of this knowledge, screening projects have been undertaken in collaboration with the European Community in the following regions: Belgium (Antwerp-Limburg), Ireland (Dublin, Cavan, Monaghan), France (Strasbourg), Spain (Navarra/Pamplona), Portugal (central region/Coimbra), Greece (west Peloponnes) and Italy (Florence). National programmes are underway in Finland, the Netherlands and the U.K.

REQUIREMENTS FOR SCREENING PROGRAMMES

Any programme for the introduction of a breast cancer screening programme must strive for high quality. There are a

number of important elements which must be taken into account, and their quality assured, if the favourable results achieved in clinical trials can be translated into a meaningful effect in a population.

A high participation rate is an important requirement. This can be achieved only by effective public health education and media advertising. Where possible, use should be made of available population registers in order to direct personal invitations to women. As well as informing the general populations, the medical profession and other health professionals must be well-informed about the programme: both the organisation and the evaluation of the programme will benefit greatly from cooperation from local health professionals.

In organising the logistical aspects of the screening programme, a central organisation has been shown to be more effective: this can utilise both fixed and mobile screening units. Evaluation mechanisms should be built into all stages of the structure of the programme.

Successful screening with mammography requires not only modern equipment but excellent and thoughtful radiologists: the most successful programmes have the best radiology results. In the context of a screening programme, radiologists need to acquire an equilibrium between sensitivity and specificity, i.e. to balance the need to find all possible cancers with that of keeping the number of unnecessary biopsies to a minimum. This is very different from the situation which is usual in clinical practice. Without proper preparation, there will be too many 'false-positives' tests, i.e. with biopsy or cytological results that indicate a normal or benign result, which are synonymous with a low predictive value of a positive test. This has a serious human cost which is often underrated by health professionals.

It is important to have an effective protocol in place for dealing with women who are found to have a suspicious lesion, many of which may turn out not to be cancer. The psychological trauma of screening is increasingly recognised as an important issue in establishing screening programmes. Excellent cooperation must be established between specialists and women in whom a suspicious lesion is found. Not only is there a need for treatment protocols to be in place which account for new modalities, protocols for dealing with women found to have suspicious lesions also need to be developed. These protocols, including details of further investigations to be conducted, should be designed to keep trauma to a minimum.

Treatment protocols should take into account new treatment modalities in which the breast is conserved whenever possible. This is the major human benefit of early detection of breast cancer apart from the impact on mortality.

Another element in the evaluation of screening programmes, as well as trials of screening, is the need to monitor mammographic activities outside the programme. It is also important when preparing for evaluation of the long-term effect of a screening programme, that the results should be linked closely with a prospective registration of the clinical course of the disease.

CONCLUSIONS

The favourable results obtained in randomised clinical trials demonstrating significant reductions in breast cancer mortality by use of mammography have led to the establishment of population-based screening programmes in several countries and regions of Europe. These programmes will benefit from the observations and findings from previous trials.

There are, however, a number of outstanding unanswered

questions regarding screening for breast cancer [14]. The most important is to determine whether breast cancer screening in women aged under 50 reduces breast cancer mortality and, if so, by how much. There is also the need for more information to determine the extent to which older woman (aged 70 and older) are likely to benefit from screening programmes. The issue of the most appropriate screening interval is still live and there is a need to obtain quantitative estimates of the net gain in terms of deaths avoided in relation to the extra costs arising from more frequent mammographic examinations.

On the basis of current evidence, breast self-examination programmes are not an effective method of population screening and cannot be recommended as public health policy [14]. The majority of breast cancers are still found initially by the women themselves and, consequently, women should be advised to continue regular examination of their breasts. Every step taken to reduce the mortality from breast cancer is an important one.

1. Wilson JMG, Jungner G. *Principles of Practice of Screening for Disease*. Public Health Papers no. 34. Geneva, World Health Organization, 1968.
2. Jensen OM, Estève J, Møller H, Renard H. Cancer in the European Community and its member states. *Eur J Cancer* 1990, 26, 1167-1256.
3. Levi F, La Vecchia C, Lucchini F, Boyle P. Cancer incidence and mortality in Europe, 1983-1987. *Soz Präventivmed* 1993, 38, Suppl. 3, S155-S229.
4. Zaridze D, Basieva T. Cancer incidence in the Commonwealth of

- Independent States, the Baltic States and Georgia—the former USSR. *Eur J Cancer* 1993, 29A, 1609-1621.
5. Shapiro S, Venet W, Strax P, Venet L. Current results of the breast cancer screening randomised trial. The Health Insurance Plan (HIP) of Greater New York study. In Day NE, Miller AB, eds. *Screening for Breast Cancer*. Toronto, Huber, 1988, 3-15.
6. Tabar L, Fagerberg CJG, GAD A, et al. Reduction in mortality for breast cancer after mass screening with mammography. *Lancet* 1985, i, 829-832.
7. Collette HJA, Day NE, Rombach JJ, de Waard F. Evaluation of screening for breast cancer in a non-randomised study (the DOM-project) by means of a case-control study. *Lancet* 1984, i, 1224-1226.
8. Verbeek ALM, Hendriks JHCL, Holland R, Mravunac M, Sturmans F, Day NE. Reduction of breast cancer mortality through mass screening with modern mammography. First results of the Nijmegen project, 1975-1981. *Lancet* 1984, i, 1222-1224.
9. Palli D, Rosselli Del Turco M, Buiatti E, Carli S, Ciatto S, Toscani L, Maltoni G. A case-control study of the efficacy of a non-randomised breast cancer screening programme in Florence (Italy). *Int J Cancer* 1986, 38, 501-504.
10. UK Trial of Early Detection of Breast Cancer Group. First results on mortality reduction in the UK. Trial of early detection of breast cancer. *Lancet* 1988, ii, 411-416.
11. Roberts MM, Alexander FE, Anderson TJ, et al. Edinburgh trial of screening for breast cancer. Mortality at seven years. *Lancet* 1990, i, 241-246.
12. Andersson I, Aspegren K, Janzon L, et al. Mammographic screening and mortality from breast cancer: the Malmö mammographic screening trial. *Br Med J* 1988, 297, 943-948.
13. Wald N, Frost C, Cuckle H. Breast cancer screening: the current position. *Br Med J* 1991, 302, 845-846.
14. Wald NE, Chamberlain J, Hacksaw A, et al. Report of the European Society of Mastology Breast Cancer Screening Evaluation Committee (1993). *The Breast*, in press.

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Colorectal Cancer Screening: Methods, Benefits and Costs

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INTRODUCTION

FIVE YEARS after the diagnosis of a colorectal cancer, no more than one-third of patients are alive. The results of treatment are unsatisfactory, and prevention of the disease in the general population is difficult at present. Therefore, screening, which results in detection and removal of early cancers and precursors, will hopefully contribute to a reduction in this disease [1].

Colorectal cancer is one of the most frequent cancers in Europe, with about 130 000 new cases and 90 000 deaths every year in the EC countries. As for most cancers, incidence and mortality increase with age, with a steep rise at 50 years of age.

METHODS FOR SCREENING

Digital rectal exploration

This results in detection of only 10% of colorectal cancers, and is an unpleasant experience; both of these factors make it unsuitable as a screening method.

Rigid sigmoidoscopy

This may result in detection of 25% of these cancers but is also unpleasant and carries a small risk of intestinal perforation, making it a poor method for screening although there is some evidence that sigmoidoscopic surveillance can reduce mortality from rectal cancer. Flexible sigmoidoscopy (60 cm) is more attractive than the rigid type because more than half of these cancers are located within reach of this instrument. Even though it is less unpleasant than rigid sigmoidoscopy, however, preliminary figures have shown low acceptability, and the economic costs are substantial.

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