Director: Dr Nigel Gray A.M. MB. BS. Hon. LLD. FRACP, FRACMA

Anti-Cancer Council of Victoria

smac/agenda

5 December, 1989

ACCV MAMMOGRAPHIC SCREENING ADVISORY COMMITTEE (STATE)

The meeting of the ACCV Mammographic Screening Advisory Committee (State) called for **Tuesday, 19 December 1989** will be held at 5.30 pm in the Boardroom, Anti-Cancer Council of Victoria, 1 Rathdowne Street, Carlton South.

AGENDA

1. Apologies: Dr G Giles, Dr R Snyder ? cancelled

2. Report of last meeting (12.4.89) — Attachment 1

3. Business arising from the minutes

   3.1 Letter to Minister of Health (20.4.89) — Attachment 2

   Rh Comments & Report

4. Update on overseas screening studies

   4.1 Swedish Experience — Attachment 3

   4.2 British Experience - Lancet (20.8.88) — Attachment 4

   - BMJ (4.11 & 25.11.89) — Attachment 5

   4.3 - end.

   4.4 "

5. AMEH Project - Progress Report

6. Prime Minister's statement on mobile mammography facilities for country areas

1989

7. Advice to the Minister

   7.1 Attitude to another pilot project in Victoria

   7.2 Present attitude to a national screening program

8. Other matters

Integrated management centres +++
were swamped
Recruitment is hard work ++
Shortage of Radiographers ++
Premature to introduce Screening services. the max
is a second Pilot Project.
Attitudes on the National ...

KEOGH HOUSE, 1 RATHDOWNE STREET, CARLTON SOUTH, AUSTRALIA 3053
☎ (03) 662 3300 Facsimile: (03) 663 3412 Telex: ACCV AA 34158

AUSTRALIA CANCER SOC MEMB

ATTACHMENT 1.

A member of the Australian Cancer Society
Director Dr Nigel Gray A M MB BS Hon LL D FRACP FRACMA

Anti-Cancer Council of Victoria

ACCV MAMMOGRAPHIC SCREENING ADVISORY COMMITTEE (STATE)

Minutes of Meeting
held on Wednesday, April 12, 1989 at 4.30 pm
in the Boardroom, Anti-Cancer Council of Victoria

Present: Dr NJ Gray (Chairman), Professor RRH Lovell (Executive Secretary), Ms J Forwoodd, Dr D Hill, Ms S Hurley, Ms J Maddigan, Dr R Marks, Dr M Moran, Ms D Reading, Dr RD Snyder, Ms S Fitzpatrick

The Chairman opened the meeting welcoming those present. He introduced Ms Dorothy Reading, Director Education Unit, ACCV and advised that Ms Onella Stagoll had been appointed to the position of Coordinator, Women's Health Policy Unit, Health Department Victoria and had succeeded Ms Christine Giles on the Committee.

1. Apologies: Mr JP Collins, Dr GG Giles, Dr N Sacharias

2. Report of last meeting (27/1/88): The minutes, having been circulated were accepted as a true record.

3. Business Arising from the Minutes

   3.1 Letter to Minister of Health: The Chairman referred to the circulated letter and noted that it was in agreement with discussion at the previous meeting.

   3.2 Publicity - Epworth Hospital: Ms Hurley referred to item 8 of the minutes and advised that the misleading advertising material was still being distributed. Dr Snyder advised that the BSC had suggested that the misleading statement be altered and that Epworth had agreed to do this. It was agreed that BSC be asked to raise the matter with Epworth Hospital again.

In the absence of mr Russell, who was expected, the Chairman moved discussion to item 6.

6. Definition of standards for performance & interpretation of mammograms

   6.1 Accreditation guidelines: The RACR 'Accreditation Guidelines for Screening Mammography Facilities' (10//3/89) were noted.

   Several matters were commented on: (1) advertising standards; (2) advising women of the results of their mammogram, especially with regard to the unreferred client and in particular those presenting with symptoms; (3) follow-up of positive screening results; (4) privacy aspects of data collection and minimal requirement to maintain a register.

   It was noted that the RACR would assess presently operating units in Melbourne for accreditation. The Essendon Pilot Project was currently being assessed.

KEOGH HOUSE, 1 RATHDOWNE STREET, CARLTON SOUTH, AUSTRALIA 3053 ☎ (03) 662 3300
Facsimile: (03) 663 3412 Telex: ACCV AA 34158

It was agreed that BSC's comment's on the guidelines should be sought.

It was agreed to request the College, in due course, to furnish the ACCV with a list of accredited mammography screening facilities in Victoria. It was also agreed to suggest to the College that there was a need to inform GPs of accredited facilities.

It was agreed to write to RACR expressing concern about the use of scare tactics as a means of motivating women to attend screening units and to suggest that the RACR take account of the form of advertising employed by units when considering their accreditation.

6.2 Advice to Minister of Health

It was agreed to advise the Minister that the RACR Accrediation Guidelines for Screening Mammography Facilities (10/3/89) have been received and that their operation would be a matter of continuing interest to this Committee.

8. Monitoring mammographic screening in Victoria

It was agreed that it was not possible at present to monitor the use of mammographic screening of symptomless women in Victoria and that it was not currently a matter of high priority. It was noted that the Commonwealth Government was monitoring the pilot projects.

The Chairman moved discussion to item 4.

4. AMEH Project - progress report

Ms Hurley reported that the project commenced operation on October 31, 1988. The project had experienced a number of problems in setting up, especially within a hospital environment. Particular problems, which could have an impact on future centres, included the difficulties in recruiting radiographers and preconceived ideas of rate of work which did not correspond with that foreseen by management. This latter problem resulted in less women being screened than planned. The project aimed to screen 30,000 over two years. As at 10/3/89 (18 weeks) 2086 women had been screened, and at this rate only 30% of target would be screened. Approximately 150 women were attending per week, compared to the original estimate of 250-300. Currently the available appointments have been filled to 80-90% capacity with the exception of the January period.

It was apparent that not as many women as had been thought were willing to attend the project without considerable encouragement. Personal invitation letters were now being sent to a random sample of women offering an appointment time. A detailed evaluation of the project would be conducted in June.

Ms Hurley advised that the recall rate was in the order of 10%, which was as expected.

It was noted that the Minister of Health's nominee on this Committee would report progress to the Minister.

10. Other matters

It was noted that despite emerging evidence that a high proportion of women were not rushing to have mammograms, there was a group of women pressing the need for an item number for screening mammography.

It was noted that the lack of radiographers and radiologists was a worldwide problem. Dr Moran stated that screening mammography was a job of low satisfaction, and he indicated that specific training for mammography radiographers might be what was needed.

5. Pilot projects - consideration of next step

Dr Gray advised that he had written to the Victorian Health Promotion Foundation asking if they would entertain theidea of funding a second pilot project. Their response was "it was decided tht consideration of a second pilot mammography project should be delayed pending experience and evaluation of the first project which is still in progress".

It was agreed to advise the Minister of Health tha the Committee accepted this.

11. Next Meeting

The next meeting would be held perhaps in 3-6 months time, at the discretion of the Executive Secreetary.

12. Other Business

The absence of a surgeon at the meeting was noted. It was suggested that an additional surgeon be invited, and it was agreed to invite Mr Stewart Hart, Executive Secretary, Breast Study Committee.

ATTACHMENT 2

smac/lr-1

April 20 1989

The Hon Caroline Hogg
Minister for Health
Health Department Victoria
PO Box 4057
Melbourne 3001

Dear Minister

re: **ACCV Mammographic Screening Advisory Committee (State)**

By agreement with your predecessor this Committee was established in 1987. Its terms of reference are attached as an apppendix.

The third meeting of the ACCV Mammographic Screening Advisory Committee (State) was held on April 12. In accordance with its terms of reference advice is now offered on the following matters:

1. **Definition of standards for the performance and interpretation of mammograms**

We advised you last year (3/3/88) that the standards for the performance and interpretation of mammograms should be those set out by the Royal Australasian College of Radiologists. The College has now promulgated accreditation guidelines for screening mammography facilities (10/3/89) and these were received by this Advisory Committee. It is understood that the College will gradually implement these guidelines as a result of which a list will be prepared of accredited facilities in Victoria. The operation of the guidelines will be a matter of continuing interest to this Advisory Committee.

2. **Pilot Projects**

Observing that a pilot project conducted by the Amalgamated Melbourne & Essendon Hospital and the ACCV, and funded by the Victorian Health Promotion Foundation, was underway, consideration was given to the possibility of establishing a second pilot project. The attitude of the Victorian Health Promotion Foundation to a second project had been ascertained to be that a second project should be delayed pending experience with the first one. The Advisory Committee was of the same opinion and accordingly has no recommendation to make at present about starting a second pilot project and it will continue to monitor the Essendon project with care.

Yours sincerely

Nigel Gray
Director

ATTACHMENT 3

EARLY DETECTION

This is a DRAFT - NOT for publication - of the Swedish meeting held in August 1989. There is argument between Malmo & Tobar

1. Exchange of X Rays has NOT occurred but probably will
2. Exchange of Pathology & reference panels are occurring
3. A panel is working to compare the way in which Death/Cause is ascertained. Tobar differs from Malmo
4. Tobar + Malmo + Gothenburg + Stockholm will be complete in 2 years & will allow complete analysis.

Given to me by Jan Ponten September 1989

Nigel Carney

REDUCED BREAST CANCER MORTALITY WITH MAMMOGRAPHY SCREENING?- AN ASSESSMENT OF CURRENTLY AVAILABLE DATA

Introduction

Possible measures to decrease breast cancer mortality include prevention and improved treatment. Although there may be some strategies that can now be adopted for prevention, their effect will probably be delayed. Prevention is also difficult since it may entail changes in life-style that will not be accepted by all women despite promises of a reduced future risk of breast cancer. Adjuvant systemic therapy has recently been shown to reduce case-fatality during the first five years by 20-30% (1). Despite these encouraging early results many patients still die of their disease and the long-term benefit of adjuvant therapy is not well known. Evaluation of other strategies to improve the outcome of treatment is clearly warranted e. g. early diagnosis through mass screening.

Most breast cancer deaths are caused by uncontrolled distant metastases. The probability of distant dissemination is related to the clinical stage at presentation. A majority of patients with small tumors without axillary nodal involment achieve long-term survival with local treatment alone. The risk of disease recurrence and early death is considerably higher among patients with large, node-positive tumors. Therefore, it seems reasonable to assume that early detection and treatment should improve the outcome, but this assumption is not self-evident. It is possible that micrometastases become established at a point in time when the tumour is too small to be detectable with currently available techniques e. g. mammography. In such a case, screening would only result in an apparently more favourable stage distribution among the diagnosed cases but would not change the outcome. The applicability of screening as a method to reduce breast cancer mortality should thus be evaluated in the context of controlled trials.

Many factors other than breast cancer mortality contribute to a comprehensive evaluation of screening. These include the benefit of being able to use less radical surgery on small tumours and a decreased need of systemic treatment, the

disadvantages of undue anxiety caused by the screening and risk of diagnosing biologically benign lesions as cancer, the cost, inconvenience, and harm of negative biopsies, and the overall cost of the screening programme. In screening studies several end-points are of interest such as attendance rate, number of detected cases, stage distribution, interval cancers, mortality, etc. However, this paper will focus on the potential benefit of screening in terms of a reduced breast cancer mortality since this invariably has been the main objective of the controlled trials. Moreover, death is the only end-point free of bias and of sufficient importance to justify the resources spent. The paper represents a summary of a workshop held in Stockholm 1989 which was supported by the Nordisk Cancerunion and the Swedish Cancer Society. The aim of the workshop was to review and evaluate the available trial data, to asses the "state of the art", and to define research issues.

Summary of available studies

Table 1 presents a summarized description of the major screening studies. The table is not comprehensive. It only includes controlled studies for which mortality data already have been published or will become available in a near future. Most of the studies have been randomized, either individually or by clusters (e. g. parishes, municipalities). In the British study, on the other hand, the population of certain areas were selected for screening with the population of other selected areas serving as reference (2).

HIP study - After 10 years the breast cancer mortality was about 30% lower in the study group compared to the control group (Table 2). The benefit emerged at about 3 years post-entry and decreased to about 23% at the end of 18 years (3). It should be noted that the study group was offered only four annual screening rounds with no intervention thereafter. The results may have been different if the screening programme had been continuous. Analyses of mortality differences by age showed that during the early follow-up period there was no benefit for women aged 40-49 years at entry whereas there was a major difference for women aged above 50 years. At longer follow-up a differential in favor of the study group appeared at entry ages 40-44 years after about 8 years and at ages 45-49 years after about 5 years. These differences were based on relatively small numbers of deaths and were not significant (Table 3). The early advantage for the older women was maintained although the relative difference between study and control groups became smaller.

WE study - In a 8-year report the results showed an increasingly significant deficit of breast cancer deaths in the study group corresponding to a 31% mortality reduction (4). The differential emerged at about 4 years post-entry (5). Subset analyses showed that the effect was significant and greatest in the age-groups 50-59 years and 60-69 years at entry: the respective mortality reduction was 40% and 35%. At ages 40-49 years and 70-74 years the mortality reductions (8% and 25% respectively) failed to reach statistical significance.

Malmö study - After 10 years there was no significant difference in breast cancer mortality between the study and control groups: breast cancer mortality was only about

4% lower in the study group (6). In women aged above 55 years at entry the estimated reduction of breast cancer mortality was 20% whereas among those aged 45-54 years years there was 29% higher breast cancer mortality in the study group. None of these results was significant. The differential among the older women appeared about 7 years post-entry.

UK study - The reduction in breast cancer mortality during the first 6-7 years in the population offered screening was 20% compared to the reference population. This result failed to reach statistical significance. The differential appeared after about 3 years. Subset analyses according to age have not been published. In the BSE districts no benefit in terms of breast cancer mortality was observed.

Stockholm study - A preliminary analysis showed ..... *(7)*

Mortality data from the Scottish, Canadian, and Göteborg studies have not been published.

Table 1 does not include studies which used a case-control methodology such as the Dutch DOM and Nijmegen studies (8, 9). In such studies screening has generally been offered to all women of certain ages in a defined area. The effect of screening is then estimated by calculating the relative risk of death due to breast cancer among women who have attended screening compared to non-attenders. This methodology is based on the assumption that the risk of developing a fatal breast cancer in the absence of screening would be the same among attenders and non-attenders. The HIP study showed a similar breast cancer mortality among non-attenders in the study group compared to women in the control group, an observation that supports the use of the case-control methodology (3). However, the Swedish and UK studies studies have indicated that women at high risk of dying from breast cancer tend to be non-attenders, some perhaps refusing the invitation to screening because they are fearful that a known breast lump will be diagnosed as cancer. This observation casts some doubt on the validity of case-control studies that compare attenders and non-attenders in screening programmes.

Table 1: *Summary of major controlled trials of breast cancer screening*

Study	Year of initiation	Age at entry (years)	No. of women: Study	Control	Study design	Screening interval (months)	Method of allocation
HIP (3)	1963	40-64	31 000	31 000	1: Phys. exam.+ mammography 2: Control	12	Individual random.
Malmö (6)	1976	45-69	21 000	21 000	1: Mammography 2: Control	18-24	Individual random.
WE (4)	1977	40-74	77 000	56 000	1: Mammography 2: Control	24, 33*	Cluster random.
UK (2)	1979	45-64	1: 46 000 2: 64 000	3: 127 000	1: Phys. exam.+ mammography 2: BSE training (x1) 3: Reference population	12, 24†	By domicile
Scottish (2)	1979	45-64	23 000**	23 000	1: Phys.exam.+ mammograpy 2: Control	12, 24†	Cluster random.
Canadian I (10)	1980	40-49	25 000	25 000	1: Phys. exam.+ mammography 2: Phys. exam at entry (i.e. x1)	12	Individual random.
Canadian II (10)	1980	50-59	20 000	20 000	1: Phys. exam.+ mammography 2: Phys. exam	12	Individual random.
Stockholm (11)	1981	40-64	40 000	20 000	1: Mammography 2: Control	28	Individual random.
Göteborg (12)	1982	40-59	22 000	30 000	1: Mammography 2. Control	18	Individual random.

BSE: Breast self-examination
* Respective average for 40-49 and 50-74 year age group
† Respective interval for physical examination and mammography
** Included also in the mammography group of the UK trial

Conclusions

The effect of screening on breast cancer mortality - Comparison of the results of the screening studies is difficult because of differences in setting and study design. The HIP study, for instance, compared annual clinical examination plus mammography (with technology of the 1960s) with no intervention. The Swedish studies compared mammography alone (with technology of the 1970s and 1980s) with no intervention. The screening interval was 18 months in the Malmö study compared to 24-33 months in the WE study. In the Malmö study 24% of the women in the control group had had a clinical mammography compared to 13% in the WE study. Because of the increased public awareness of breast cancer during recent decades women with breast cancer probably tended to present earlier - even without screening - during the 1970s than the 1960s. Therefore, the effect of introducing screening may have been different in the HIP-study compared to the Swedish studies.

Despite the differences mentioned it seems reasonable to conlude that mass screening for breast cancer can achieve a significant reduction of the mortality from the disease but the effect in quantitative terms is unclear. The estimated percentage reduction of breast cancer mortality in different studies are subject to a considerable random variation (Table 4). Both single-view mammography alone and physical examination plus more complete mammography have shown to be effective as screening modalities. The benefit from adding physical examination to mammography is unknown.

Table 4: *Estimated percentage reduction of breast cancer mortality in selected screening studies. The 95% confidence interval is indicated.*

Study (follow-up)	% reduction (95% C.I.)
HIP† (10 years)	29 (11; 44)
WE (8 years)	31 (14; 45)
Malmö (10 years)	4 (-35; 32)
UK* (6 1/2 years)	20 (-1; 36)
Stockholm (x years)	xx (xx; xx)

† Breast cancer cases detected within 5 years
* Population offered physical examination plus mammography versus reference population

Screening benefit by age - Most of the available trials were not designed to evaluate the effect of screening by age. Subset analysis of the HIP study generated the hypothesis that the effect on short term mortality was restricted to women aged above 50 years. The results of the WE, Malmö, and Stockholm studies are consistent with this hypothesis although the numbers in each separate study are too small to permit meaningful conclusions. Since none of the studies were designed to evaluate age-effects it has been suggested that they should not be used to reach conclusions on the issue. On the other hand it may also be reasonable to consider the HIP result as an hypothesis that can be tested in other data sets. On this basis the observation of no early benefit among those aged 40-49 years at entry has been replicated in other trials. A lack of benefit from screening among young women could possibly be explained in terms of a difference in tumour biology between breast cancer in young and old women, or a lower sensitivity of screening in young women. It remains to be seen if long-term follow-up of the more recent trials will show an emerging mortality difference for women aged 40-49 years as in the HIP study. A long latent period before a benefit eventually emerges is consistent with the long natural history of breast cancer.

In summary, the available data suggest that the short term benefit - in terms of percentage mortality reduction - of initiating screening in women aged 40-49 years is substantially less than for women over the age of 50. On the other hand, mortality reductions at younger ages may result in a greater gain of woman-years than mortality reductions at older ages. If an eventual mortality reduction is found for young women, it would be appropriate to evaluate the degree of benefit - in terms of number of saved woman-years - in the same way that is now possible for women aged above 50. Pending such data screening of young women should be considered experimental. It should only be done in such a way that the results can be evaluated i. e. as a controlled clinical trial or programme with prospective data collection and evaluation.

Frequency of screening? - The interval between screening rounds in different studies has varied from 1 to 3 years. There is no experimental data on the benefit of shorter versus longer intervals. The additional benefit with e. g. a 1 year interval compared to a 2-3 year interval is probably small. Future trials testing this question would thus have to

be large.

Analyses of the distribution of interval cancers in the WE study have indicated that the incidence of such cancers tend to increase during the third year after the initial screening (13). This observation suggests that the screening interval should not exceed two years. In women for which the screening has a low sensitivity e. g. because of dense breast tissue it might be appropriate with an even shorter interval e. g. 18 months. However, until experimental data are available these conclusions should be considered tentative because interval cancers are only a proxy measure of the effectiveness of screening in terms of a reduced breast cancer mortality.

In practice, resources for screening are limited in most countries. Pending further data on the significance of screening intervals, it is an open question if more benefit is derived from screening a smaller population with shorter intervals than screening a larger population with longer intervals.

The significance of compliance - A screening programme must probably achieve a high degree of compliance in order to be effective. The compliance to the first screening round in the HIP study was 65%. In the Swedish studies the figure has generally been higher: 74-89%. In the UK study compliance to screening including physical examination and mammography was higher (66%) than to BSE instruction (35-53%). Collaboration with health promotion experts appears appropriate in order to improve attendance rates, particularly since many studies have indicated that non-attenders constitute a high-risk group for fatal breast cancer (2, 4, 6).

Upper age limit for invitation to screening? - The most well-documented breast cancer mortality reduction with screening is in the 50-69 year age-group. The reduction among those aged 70-74 years at entry in the WE study was lower (23%) compared to those aged 50-69 years (35-40%), possibly because of a lower attendance rate (79% versus 91%). The problem of competing causes of death also increases with age: the benefit of screening in terms of number of woman-years saved decrease with age even if the percentage reduction of breast cancer mortality is the same in all age-groups. Therefore, it seems reasonable to give priority to screening of women

aged 50-69 years. Since screening of women in their 60s probably will affect breast cancer mortality at least up to 10-15 years after cessation of screening, an upper age limit of 69 years can be expected to reduce breast cancer mortality also among women in their 70s and 80s.

Double readings and multiple views? - Double reading of the mammogram and multiple views probably increase both the sensitivity and specificity of the screening. However, there are no experimental data describing to what extent these features contribute to the reduction of breast cancer mortality. Is the benefit from screening e. g. 10,000 women with double reading greater than from screening 20,000 women with single reading? It is possible that the experience of the radiologist should decide whether double reading is necessary. The number of views as well as the screening interval should perhaps be individualized according to the results of the first examination: women with dense breast parenchyma might perhaps benefit from two view-mammography and a shorter screening interval. These questions require further evaluation in future studies.

Radiation-induced breast cancer - With the reduction of absorbed dose to the breasts to around 0.03 Gy from a two-view examination from modern mammography much of the concern about radiation has dissipated. This has been facilitated by evidence from the Japanese atomic bomb studies and the Canadian fluoroscopy study that the risk of radiation-induced breast cancer is substantially reduced if not undetectable in women first irradiated over the age of 35 (14). Gohagen et al (15) calculated the possible effect of the American Cancer Society recommendations assuming a base-line mammogram at age 35 and annual examinations from the age of 40. Even with this age range and frequency, their calculations suggested a lifetime total of only about 150 radiogenic cancers compared to about 93,000 otherwise incident cancers in a population of 1 million women screened by three view low-dose film-screen mammography. These calculations extrapolated to a population screened by mammography every 2 years from the age of 50 suggests that the effect can be regarded as negligible. Even if this policy was extended to include women screened every 18 months from the age of 40 the numbers of breast cancers induced by mammography would be extremely low,

and substantially exceeded by the benefits of screening.

Efficacy of other screening modalities - The effectiveness of other forms of screening e. g. physical examination and BSE education is not well known. The UK study provided some data on BSE but the early results from that study remain inconclusive because of small numbers. The Canada II trial will provide data on whether a similar benefit is obtained from physical examination plus the teching of BSE to that from the combination of two-view mammography plus physical examination and the teaching of BSE in women aged 50-59. A WHO/USSR trial of BSE alone will provide data on that modality. Future trials in South America and other third world countries may provide data on the efficacy of physical examination alone. In summary, screening using physical examination alone or BSE education should be regarded as experimental.

Summary

Screening for breast cancer by mammography alone or mammography plus physical examination can reduce mortality from the disease. The most clearly documented benefit is in the age-group 50-69 years where a 30% reduction in mortality beginning about 5 years after initiation of screening can be anticipated.

The benefit among women aged 40-49 years is less clear. No benefit in terms of mortality has been observed in these younger women in the 5-8 years after initial screening but may emerge with longer follow-up. Screening in the age-group 40-49 years should be considered experimental and be conducted in the context of controlled trials or with continuous monitoring of the programme that will permit future evaluation of the results.

The benefit for women aged above 69 years appears to be less than among those aged 50-69 years, possibly because of lower attendance rates and competing causes of death.

The optimal screening interval is not known. Analyses of interval cancers have suggested that the interval should not exceed 2 years. In women for whom the screening has a low sensitivity it may be advisable to use multiple view mammography and a shorter interval (e. g. 18 months). Double reading may increase both the sensitivity and specificity of screening but its value is dependent on the experience of the radiologist. It remains an open question whether more benefit is derived from screening a smaller population with short intervals using multiple view mammography compared to screening a larger population with long intervals using single-view mammography.

Available data suggest that the risk of radiation-induced breast cancer from mammography screening in women aged 40 or more using modern low-dose techniques is negligible.

Research issues

1: The long-term benefit of screening with mammography - either alone or in combination with other screening modalities.

2: The value of screening in different age groups e. g. among women younger than 50 years.

3: The benefit associated with different screening intervals, multiple versus single views, and double readings.

4: The benefit associated with other screening tests e. g. physical examination and BSE in comparison to that obtainable from mammography.

5: The disadvantages of screening including the psychological distress of screening, "unnecessary" biopsies, the risk of overdiagnosis of borderline lesions, and the potential risk of false reassurance from a "negative" screening result.

6: The ebenfit associated with physical examination or BSE alone.

7: Cost-benefit analyses in different age-groups and health care settings.

POSTERS

alun - Borlänge hälso- och sjukvård
FALU LASARETT
Tjänstestalle, handläggare

Datum

Er beteckning

Ert datum

Er hänvisning

RANDOMIZATION BY CLUSTER IN THE SWEDISH TWO-COUNTY TRIAL: RECENT RESULTS FROM KOPPARBERG AND IMPLICATIONS FOR INTERPRETATION

Duffy,S.[1], Tabár,L.[2], Krusemo, U-B.[3], Day,N.[1]

As is often the case in large-scale public health intervention trials, the Swedish two-county trial of breast cancer screening was randomized by geographic clusters, not individuals. Two problems arise with such a design: the first is that there may be excessive variability of mortality between clusters relative to within, leading to overestimation of the significance of the effect in a traditional Poisson analysis; the second is that imbalances (even small ones) in mortality between clusters prior to the trial might bias the result. The first problem is dealt with by modelling an additional component of variance (allowing us to estimate a higher SE and therefore a decreased significance). In the two-county trial, however, no such additional variation was observed. In the Kopparberg data, using both traditional Poisson-analysis and the alternative, we obtained a relative risk of breast cancer mortality associated with screening of 0.64 ($p<0.01$) and 95 % confidence interval (0.45, 0.90). The second problem can be addressed if data on mortality are available by geographic area prior to the start of the trial. For Kopparberg we have such data. Incorporating the prior data gives RR=0.65 ($p<0.05$) with 95% confidence interval (0.44,0.94). Thus imbalances between clusters have only slightly altered the RR. The conclusion of the trial remains the same.

[1]MRC Biostatistics Unit, Cambridge, England

[2]Department of Mammography, Central Hospital, Falun, Sweden

[3]Uppsala University Computing Center, Uppsala,Sweden

8

Postadress
791 82 FALUN

Telefon
023-820 00

Postgiro
3 50 30-6

NATIONWIDE POPULATION-BASED SCREENING FOR BREAST CANCER IN FINLAND IN 1987 AND 1988

Kirsti Louhivuori, Finnish Cancer Registry, Liisankatu 21 B, SF-00170 Helsinki, FINLAND

In Finland, the nationwide population-based screening programme for breast cancer by mammography was initiated in 1987. The programme covers the age groups 50-59 years, and the screening interval is two years.

In 1987-1988 about 126,000 women were invited for screening. Of the 112,000 (88 %) women who participated, 5,000 (4.5 %) were invited for further examinations During these, 998 fine needle biopsies were taken, and 418 women (0.37 %) were finally found to have breast cancer. The ratio of screening prevalence (0.37 %) to average annual incidence in the age group 50-59 years in the 1980's (0.16 %) was 2.3.

FLOW CYTOMETRIC INDICATORS OF BENIGN BREAST DISEASE, SCREEN-DETECTED BREAST CANCER AND CLINICAL BREAST CANCER

Olli-P. Kallioniemi[1], Alpo Kärkkäinen[2] and Matti Hakama[3]
Tampere University Central Hospital[1], Pirkanmaa Cancer Society[2] and University of Tampere[3], Tampere, Finland

DNA aneuploidy and high S-phase fraction (SPF) as analyzed by flow cytometry are related to poor prognosis in patients with breast cancer. To gain information on the biological properties and malignant potential of screen-detected breast cancer (SDBC), we compared the flow cytometric characteristics of 37 SDBCs from the first round of screening with those of clinically detected cancers (n=60) and benign breast disease (n=30).

DNA aneuploidy was detected less frequently ($p<0.05$) in SDBC (17/37, 46%) than in clinical breast cancer (41/60, 68%). All benign breast tumors were DNA-diploid. Although DNA aneuploidy was already detected in a localized SDBC measuring 6 mm in diameter, the occurrence of DNA aneuploidy was higher in large/node-positive than in small/node-negative SDBCs. Median SPF was lowest in benign breast disease (1.9%), followed by SDBC (3.5%) and clinical breast cancer (9.6%). The differences in median SPF values between SDBC and clinical breast cancer persisted in subgroups defined by stage, histological type or DNA ploidy.

Our results suggest that many SDBCs from the first round of screening have extremely slow growth rate and low malignant potential. Such tumors are not only smaller but also biologically different from clinical breast cancers and should thus not be treated too aggressively.

ATTACHMENT 4

The Lancet · Saturday 20 August 1988

FIRST RESULTS ON MORTALITY REDUCTION IN THE UK TRIAL OF EARLY DETECTION OF BREAST CANCER

UK TRIAL OF EARLY DETECTION OF BREAST CANCER GROUP*

Summary Between 1979 and 1981 the UK Trial of Early Detection of Breast Cancer enrolled women aged 45–64 living in eight locations in the United Kingdom. Annual screening by clinical examination of the breast, with mammography in alternate years, was provided over 7 years for 45 841 women; 63 636 were offered teaching in breast self-examination and were provided with a self-referral clinic; and 127 117, for whom no extra services were provided, form a comparison population. Over the 7 years from the start of the trial a reduction in the risk of dying from breast cancer in women offered screening relative to that in the comparison population was observed. The reduction was 14% (RR 0·86, 95% CI 0·69–1·08) when no allowance was made for underlying differences in breast cancer mortality between the populations, but rose to 20% (RR 0·80, 95% CI 0·64–1·01) when adjusted for differences in pretrial mortality rates. These differences fall short of statistical significance. No reduction in mortality was observed during the first 5 years but thereafter the gap widens. These results, though in themselves inconclusive, are consistent with the hypothesis that screening can achieve a worthwhile mortality reduction. No difference in mortality has so far been observed between women offered teaching in breast self-examination and the comparison population

*Trial Coordinating Centre.—J. Chamberlain, D. Coleman, R. Ellman, S. M. Moss.

Participating Centres.—Edinburgh, A. P. M. Forrest, M. M. Roberts, F. E. Alexander, T. J. Anderson, A. E. Kirkpatrick; *Guildford*, B. A. Thomas, J. L. Price, N. Gibbs, P. S. Boulter, P. Pocock; *Huddersfield*, G. Harris, J. Philip, J. Rustage, C. Flaherty, E. Riley; *Nottingham*, R. W. Blamey, C. W. Elston, E. J. Roebuck, A. Locker, A. Mitchell; *Dundee*, A. Cuschieri, P. E. Preece, A. J. Robertson, R. A. B. Wood, J. Swanson Beck; *Oxford*, E. Bale, R. Holloway, M. Greenall, M. Vessey, C. Wells; *Southmead*, P. Bradfield, S. Dawes, W. J. Poulsom; *Stoke-on-Trent*, M. E. Summerly, J. E. Scoble.

Trial Working Group.—M. R. Alderson (Chairman), C. Faulder, J. L. Hayward, M. Jack, C. A. Joslin, C. Ray, C. C. Spicer, J. Swanson Beck, A. Tucker.

Data Analysis Subgroup.—H. Cuckle, J. M. Elwood, S. J. Pocock, N. Wald.

Introduction

In 1979 a large multicentre trial of early detection of breast cancer was started in the UK, to assess the effect of screening programmes and of programmes promoting breast self-examination on mortality from breast cancer.[1] At that time the only evidence of benefit from screening for breast cancer came from a randomised controlled trial conducted in New York during the previous decade.[2] Subsequently, other evidence of the reduction in mortality which can be achieved by screening has come from a further randomised controlled trial in Sweden[3] and from studies in the Netherlands[4,5] and Italy.[6] A consistent finding of all these studies has been a reduction in mortality, attributable to screening, among women aged over 50 when first screened. Consequently a national breast cancer screening programme is now being implemented in the United Kingdom,[7] its organisation drawing on evidence both from the overseas studies and from preliminary findings from the UK trial. Until now, however, no information has been available on the size of mortality reduction that could be

achieved in Britain. This paper therefore presents the first analysis of mortality in relation to the two types of early detection programmes introduced in the UK trial. It does not attempt a complete evaluation of all aspects of the trial; details such as test sensitivity and specificity will be included in a subsequent report. Follow-up of all women in the trial is continuing and longer-term comparisons of mortality will be published.

Method

A detailed account of the method is given elsewhere.[1] In summary, the trial is a non-randomised comparison between eight districts offering different services for early detection of breast cancer.

There are two screening districts (Edinburgh and Guildford), two breast self-examination (BSE) districts (Huddersfield and Nottingham), and four comparison districts (Dundee, Oxford, Southmead, and Stoke-on-Trent). In Edinburgh the population of women offered screening consists of those registered with a randomly selected half of general practitioners in the city, women registered with the other half forming a comparison group. Thus the Edinburgh population offered screening contributes both to the UK multicentre trial and to a separate randomised controlled trial within Edinburgh;[4] the latter will be reported separately.

At the start of the Edinburgh and Guildford screening programmes every woman aged 45–64 years who was registered with a general practitioner serving the relevant population was invited to be screened. Screening was offered annually for 7 years, mammography and clinical examination being employed in the 1st, 3rd, 5th, and 7th screening rounds, and clinical examination alone in the 2nd, 4th, and 6th. In Huddersfield and Nottingham every woman, similarly defined by age and general practitioner, was invited to a class to learn about breast self-examination; a self-referral clinic, providing clinical examination of the breast and mammography, was available for women who found breast abnormalities. In the four comparison districts a population of women similarly defined was identified but was not contacted.

In the four intervention districts recruitment was staggered over 3 years from 1979 to 1981. Every woman was allocated a date of entry which was the date of her first invitation, irrespective of whether or not she accepted it. In the four comparison districts every woman was allocated the same date of entry, which was midway through the intervention districts' period of recruitment. These women form the initial cohort and it is their subsequent experience of breast cancer incidence and mortality that is reported here. In successive years of the trial women attaining the age of 45, and those between 45 and 64 moving into the district, were also enrolled; these women are not included in the present analysis. All breast biopsies, all breast cancer diagnoses, and deaths from all causes occurring in women after their date of entry have been recorded. For women with breast cancer, details were extracted from hospital case-notes of history, stage at diagnosis, histological classification, and treatment. This information will be described in a subsequent paper.

In the early years of the trial women who were known to have left their GPs' lists were noted and their records at the National Health Service Central Registers (NHSCRs) in Southport and Edinburgh were flagged. As the programme of inviting women progressed, it was confirmed that the Family Practitioner Committee lists of women registered with general practitioners, on which the trial population is based, were inaccurate. This was mainly because of the inclusion of a proportion of women, estimated to be 10–25%, no longer resident at the recorded address although still registered with the same GP. To ensure a complete and uniform system for recording breast cancers and deaths occurring in trial women, the entire population has now been flagged. This means that women who have moved away from a trial district are still included in the follow-up. Whenever the NHSCRs receive a death certificate or a cancer registration of a flagged woman the trial's coordinating centre is informed and the woman's trial record is updated accordingly.

In the present analysis deaths from breast cancer are those in which breast cancer was recorded as the underlying cause of death on the death certificate. In view of the known inaccuracies in death certification of breast cancer patients[9] a system has been set up whereby two independent referees establish whether or not there was evidence of active breast cancer present at the time of death and whether it was the cause of death. This entails obtaining the case-notes of all women diagnosed as having breast cancer after entry to the trial, and extracting the relevant data from the notes covering the period leading up to the woman's death. There are inevitable delays in this process and therefore analyses of verified breast cancer deaths are not yet available.

Analysis

For each centre the observed number of breast cancer deaths among women with breast cancer first detected after trial entry has been compared with the number expected if there were no difference in mortality between the centres. Two methods have been used to derive the expected values. In one, the expected value was obtained by applying the mortality rate in all eight centres combined to the population in the individual centre, stratifying by age at death and by duration in the trial. This method rests on the assumption that there is no underlying difference in breast cancer mortality between the centres; but, since this is a non-randomised trial, such differences may well exist. Therefore data on breast cancer mortality rates in each of the eight health districts for the 10 years from 1969 to 1978 before the trial began were used to calculate a standardised mortality ratio (SMR) for each centre, the pooled pretrial rates of the eight centres being used as a standard. The expected number of breast cancer deaths in each centre, derived as above, was then multiplied by that centre's pretrial SMR to give a second expected value adjusted for pretrial differences in mortality.

The observed and expected deaths in intervention centres and comparison centres have been used to calculate the risk of death from breast cancer in the intervention centres relative to the comparison centres. Confidence intervals for the relative risks have been derived by logistic regression with age and year since entry as variates (GLIM package[10]).

TABLE I—NUMBER OF WOMEN, ACCEPTANCE RATES, AND WOMAN YEARS OF FOLLOW-UP IN THE EIGHT TEDBC CENTRES

Centre	Intervention	No of women in initial population	Acceptance rate (1st screen or 1st invitation to education)	Follow-up to Dec 31, 1986 (censored at death or 7 years within trial)	
				Total woman yr	Mean yr/woman
Edinburgh	Screening	23 194	60%	143 242	6·2
Guildford	Screening	22 647	72%	148 240	6·5
Huddersfield	BSE	22 481	30%	151 361	6·7
Nottingham	BSE	41 155	53%	253 959	6·2
Dundee	None	22 626	Not applicable	153 418	6·8
Oxford	None	31 474	Not applicable	215 344	6·8
Southmead	None	24 693	Not applicable	168 764	6·8
Stoke	None	48 324	Not applicable	327 170	6·8
		236 594		1 561 498	6·6

Results

A total of 238 932 women were identified in the initial population; of these, 236 594 (99·0%) were either successfully "flagged" at NHSCR or were notified as having died by the local centre before the flagging process was begun. The subsequent analysis is restricted to these 236 594 women and includes all newly diagnosed breast cancers and deaths up to Dec 31, 1986, or 7 years from date of entry where this is earlier. By this date, all women still alive in the comparison centres had completed 7 years in the trial, whilst those in the intervention centres had completed between 5 and 7 years of follow-up. Table I shows the

numbers of women, woman-years, and mean follow-up in each district. In Guildford 275 women attended the screening clinic before their date of invitation and hence before their scheduled date of entry to the trial. All these women had symptoms and were either self-referrals or GP referrals. There were 11 breast cancers diagnosed and 2 breast cancer deaths in these women. On the assumption that if these women had not been permitted to attend the screening clinic they would have been referred to surgical outpatients and diagnosed before entry to the trial, all these 275 women have been excluded from the trial population. In Edinburgh, the protocol did not permit attendance at the screening clinic before the date of first invitation so the problem did not arise. In Huddersfield 85 women attending a self-referral clinic before invitation, including 2 in whom breast cancer was diagnosed, have been excluded. In Nottingham women who attended before invitation on account of symptoms were not separately identified and are therefore included.

Acceptance of Screening

The proportion of women attending in response to invitation for the first screen was 60% (13 975) in Edinburgh and 72% (16 498) in Guildford. However, the population registers are known to be inaccurate, and the true compliance rates are therefore somewhat higher. Subsequent attendance was dependent on the protocol for reinvitation in each centre. For the 5th screening round—the latest for which complete data are available—11 269 women (53% of those still present) attended in Edinburgh and 13 167 (65% of those still present) in Guildford.

Attendance for BSE Education

In Huddersfield, 30% (6699) of women attended for an education session within twelve months of receiving the initial invitation and a further 5% attended later. In Nottingham, 52% (21 760) of women attended within twelve months, with less than 1% attending later. Again, these are underestimates of the true acceptance rates.

Breast Cancer Diagnosis

Table II shows the numbers and rates of non-invasive and invasive breast cancers diagnosed in women in each of the eight centres. This includes cancers diagnosed among women who have moved away from the district. The cumulative diagnosis rate over the 5–7-year follow-up period is significantly higher in the two screening centres combined (2·57 per 1000 woman years) than in the comparison centres combined (1·70 per 1000 woman years). The rate for in-situ cancer is 5 times higher and for invasive cancer 1·4 times higher. The cumulative diagnosis rate in the two BSE centres combined (1·95 per 1000 woman years) is also higher than that in the comparison centres.

TABLE II—BREAST CANCERS DIAGNOSED IN EACH OF THE TEDBC CENTRES DURING THE FIRST 5–7 YEARS AFTER ENTRY

	Carcinoma-in-situ		Invasive carcinoma		Total breast cancers	
	No	Rate/1000 woman yr	No	Rate/1000 woman yr	No	Rate/1000 woman yr
Edinburgh	42	0·29	318	2·24	360	2·53
Guildford	46	0·31	342	2·31	388	2·62
Huddersfield	20	0·13	268	1·77	288	1·90
Nottingham	22	0·09	480	1·89	502	1·98
Dundee	7	0·05	241	1·57	248	1·62
Oxford	13	0·06	384	1·78	397	1·84
Southmead	17	0·10	282	1·67	299	1·77
Stoke	11	0·03	517	1·58	528	1·61

Women with more than 1 breast cancer diagnosed during this period are counted only once.

TABLE III—METHOD OF DIAGNOSIS OF BREAST CANCERS DIAGNOSED IN SCREENING CENTRES DURING THE FIRST 5–7 YEARS

	Edinburgh		Guildford		Total	
	Cancers diagnosed	Rate per 1000 women	Cancers diagnosed	Rate per 1000 women	Cancers diagnosed	Rate per 1000 women
Round 1	78	5·5	78	4·8	156	5·2
Rounds 2, 4, 6 (clinical only)	51	1·4	44	1·2	95†	1·3
Rounds 3, 5, 7 (clin + mammo)	95	3·0	141	3·6	236‡	3·3
	224		263		487	
Interval	47		68		115	
Non-attenders	89	1·7*	57	1·7*	146	1·7*
	360		388		748	

*Rate per 1000 woman yr.
†Includes 8 cancers in 684 women (11·7 per 1000) who attended for the first time in response to invitations to later rounds.
‡Includes 15 cancers in 1526 women (9·8 per 1000) who attended for the first time in response to invitations to later rounds.

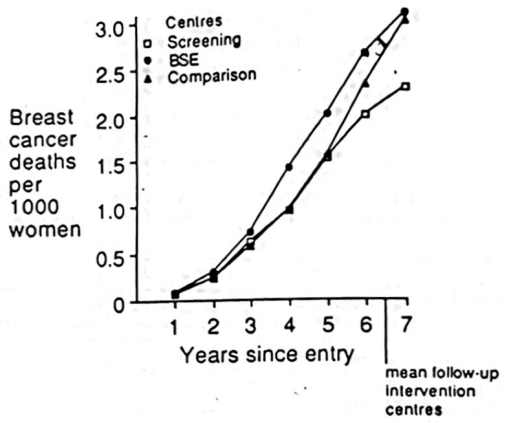
Diagnosis in Attenders and Non-attenders—Screening Districts

Table III shows the numbers of cancers and detection rates at the first screening round and at subsequent "clinical only" and "mammography and clinical" rounds for the two screening centres. The rates in the non-attenders (ie, those who *never* attended for screening) are 1·7 per 1000 women-years in both Edinburgh and Guildford, similar to the rate in the comparison centres.

The interval group includes all those cancers diagnosed in women after a negative screen, irrespective of the interval since screening. These will be the subject of more detailed analysis in a subsequent report.

TABLE IV—OBSERVED AND EXPECTED DEATHS FROM BREAST CANCER IN THE EIGHT TEDBC CENTRES DURING THE FIRST 5–7 YEARS FROM ENTRY, EXCLUDING DEATHS FROM BREAST CANCERS DIAGNOSED BEFORE ENTRY

	Observed breast cancer deaths	Expected breast cancer deaths	Expected, adjusted for pretrial breast cancer SMR
Edinburgh	51	56·9	59·2
Guildford	51	60·9	63·4
Screening centres combined	*102*	*117·9*	*122·6*
Huddersfield	61	63·8	62·5
Nottingham	120	100·7	105·7
BSE centres combined	*181*	*164·5*	*168·2*
Dundee	61	64·0	53·8
Oxford	89	90·0	90·9
Southmead	65	71·1	66·9
Stoke	147	137·5	137·5
Comparison centres combined	*362*	*362·6*	*349·1*



Cumulative breast cancer mortality rate per 1000 women in screening centres, BSE centres, and comparison centres in successive years since entry to trial.

Diagnosis in Attenders and Non-attenders—BSE Districts

In both the BSE districts, the diagnosis rate in the attenders at education sessions is higher (2·1 per 1000 woman years in both centres) than in the non-attenders (1·8 and 1·9 per 1000 woman years in Huddersfield and Nottingham, respectively).

Mortality from Breast Cancer

Table IV shows the observed and expected deaths from breast cancer in the eight districts. The mortality does not differ significantly between either the two screening districts or the two BSE districts, and therefore for each pair the results have been combined.

The risk of death from breast cancer in screening centres and BSE centres relative to that in comparison centres has been calculated. Analysis without adjustment for pretrial breast cancer mortality rates gives a relative risk of 0·86 (95% CI 0·69–1·08; p = 0·23) for the screening centres, and 1·10 (95% CI 0·92–1·32; p = 0·29) for the BSE centres. Adjustment for past rates changes these to 0·80 (95% CI 0·64–1·01; p = 0·06) and 1·04 (95% CI 0·86–1·26; p = 0·69), respectively. Thus none of these relative risks differs significantly from 1·00.

TABLE V—OBSERVED AND EXPECTED DEATHS FROM BREAST CANCER IN COMPARISON CENTRES, SCREENING CENTRES, AND BSE CENTRES IN THREE DIFFERENT TIME PERIODS SINCE ENTRY TO TRIAL

	Yr since entry to trial		
	1–3	4–5	6–7
Comparison centres			
Observed deaths	68	119	176·5
Expected deaths*	73·6	126·2	149·3
Woman yr of follow-up	377 274	246 327	241 095
Screening centres			
Observed deaths	29	45	28
Expected deaths*	28·5	49·2	44·9
Woman yr of follow-up	136 050	89 196	66 236
Relative risk vs comp centres	1·10	0·97	0·54†
95% CI	0·71–1·71	0·68–1·38	0·36–0·81
BSE centres			
Observed deaths	45	80	56
Expected deaths*	39·1	67·3	61·9
Woman yr of follow-up	188 813	123 331	93 176
Relative risk vs comp centres	1·25	1·26	0·78
95% CI	0·85–1·84	0·95–1·70	0·57–1·07

*Expected breast cancer deaths are adjusted by pretrial SMRs (see text).
†p < 0·01.

TABLE VI—METHOD OF DIAGNOSIS OF BREAST CANCER IN WOMEN IN THE SCREENING CENTRES WHO DIED FROM BREAST CANCER DURING THE FIRST 5–7 YEARS

	Ever screened					Never screened	
Screening centre	Screen-detected (yr 1)	Screen-detected (yr 2–7)	Interval	Total	Rate per 1000 woman yr	No	Rate per 1000 woman yr
Edinburgh	6	10	9	25	0·21	26	0·52
Guildford	4	11	10	25	0·27	26	0·79
Total	10	21	19	50	0·24	52	0·65

TABLE VII—ATTENDANCE FOR EDUCATION AMONG WOMEN IN THE BSE CENTRES WHO DIED FROM BREAST CANCER DURING THE FIRST 5–7 YEARS

	Attenders for education		Non-attenders for education	
BSE centre	No	Rate per 1000 woman yr	No	Rate per 1000 woman yr
Huddersfield	13	0·24	48	0·49
Nottingham	57	0·42	63	0·55
Total	70	0·36	111	0·52

The accompanying figure shows the cumulative breast cancer mortality for the three types of centre over the 7-year period, adjusted by each centre's pretrial SMR. Table V shows the observed and expected breast cancer deaths, adjusted by pretrial SMR and grouped by type of centre and year in trial. There is a significant reduction (RR = 0·54, p < 0·01, 95% CI 0·36–0·81) in the screening centres in years 6 and 7.

Table VI gives the numbers of breast cancer deaths in the screening centres according to the method of diagnosis. The age-standardised rates per 1000 woman years in the non-attenders for screening are 0·79 in Guildford and 0·52 in Edinburgh—both higher than any of the rates in the comparison centres (0·39–0·45).

Table VII gives the numbers of breast cancer deaths in the BSE centres in attenders and non-attenders for education. The age-standardised rates per 1000 woman years in the non-attenders are 0·49 in Huddersfield and 0·55 in Nottingham; again these are higher than the rates in any of the comparison centres.

Discussion

The observed reduction in breast cancer mortality in the screening centres during the first 6–7 years of this trial falls just short of statistical significance. The confidence intervals around the relative risks are consistent either with no effect or with a mortality reduction of comparable size to those found in the New York and Swedish Two-Counties trials[2,3] after a similar follow-up period. Moreover, although we have corrected for differences between centres in pretrial breast cancer mortality, this non-randomised comparison requires a more cautious interpretation than would a randomised controlled trial. However, these findings are

compatible with the results of the other trials which show that screening for breast cancers reduces mortality. Further woman years of follow-up will provide a more definitive answer and by narrowing confidence intervals will give a firmer estimate of the size of mortality reduction (if any) achieved.

Table VIII presents comparable data from the New York and Swedish Two-Counties trials at a similar stage of follow-up. The New York and Swedish trials showed mortality reductions of 34% and 31%, respectively, compared with 20% in the UK trial, and this was despite the fact that in Sweden screening was less frequent than in the UK trial and did not include clinical examination. Moreover, breast cancer mortality in the UK comparison centres is higher than in the Swedish control population, suggesting there is greater scope for improvement in the UK.

There are several possible explanations for the smaller benefit observed. Firstly, there may be artifactual reasons. The screening populations in the UK included some women who did not receive their invitations and hence did not have the opportunity for screening, thus diluting its possible effect. Also, despite randomisation in the Edinburgh population, a higher socioeconomic class distribution has been found among those offered screening than in the remainder of the Edinburgh population (Alexander FE, Roberts MM, Lutz W, Hepburn W, unpublished). The pretrial breast cancer SMR for the whole of Edinburgh may therefore be inappropriate; since breast cancer mortality is positively correlated with class, the expected breast cancer mortality of the screening population may be underestimated.

Secondly, even if we allow for the fact that some invited women may no longer have been at the registered address, acceptance of screening was considerably lower than that observed in the Swedish trial. The importance of this factor in reducing the possible effectiveness of the screening programme is shown by the fact that 51% of the deaths occurred in the 28% of women who were never screened. The incidence of breast cancer in the non-participants was similar to that in the comparison centres (tables II and III) but mortality from breast cancer was higher even after adjustment for age. This suggests that women at high risk of dying of breast cancer tend to be non-participants, some perhaps refusing the screening invitation because they are fearful that a known breast lump will be diagnosed as cancer. This possible selection of poor-prognosis cases into the non-participating group casts doubt on the magnitude of reduced relative risk of death in case-control studies that compare participants and non-participants in screening programmes.[4,6]

Thirdly, the sensitivity of screening may be lower than that in the Swedish trial. One indication of this is given by the rate at which symptomatic and advanced cases present at varying intervals after a negative screen, and this will be the subject of a later analysis. Some idea of the ability of screening to detect cases at a curable stage is also given by the death rate among screened women, after exclusion of cases of breast cancer diagnosed at the first screen. Those cancers picked up at the first screen and subsequently causing death were presumably incurable at trial entry; such deaths are unavoidable by better screening. After the first screen, however, an ideally sensitive screening programme would detect all cancers before they reached an incurable stage. Mortality among screened women whose first screen was negative should therefore be very low. There were 44 fatal cases among 30 470 women initially screened and found negative in Edinburgh and Guildford, giving a cumulative mortality rate from cases diagnosed after the first screen of 1·4 per 1000 screened women. The comparable rate in Sweden (among women aged 40–70) was 0·65 per 1000. Given comparable underlying incidence rates, this suggests that, at least initially, the sensitivity of screening in detecting curable cancers was lower in this trial than in Sweden.

The confidence intervals surrounding risk of death from breast cancer in BSE centres relative to comparison centres are wide and the possibility that a real benefit exists cannot yet be ruled out. Further analyses of the effects of BSE in each of the centres are in progress. The apparent excess mortality in BSE centres during the middle years of the trial, shown in tables VI and VII and the figure, is unexplained.

From table V and the figure it can be seen that only in the sixth year did the number of deaths in the screening group begin to show a reduction, and the difference between screening centres and comparison centres appears still to be widening in year 7. Population-based mortality analysis after longer follow-up is essential. With longer follow-up and the inclusion of information on later cohorts entering the trial, analysis by age at entry will also be important for assessing whether women derive any benefit from screening under the age of 50.

Even after exclusion of cancers detected at the first screening the mean annual detection rate is higher than in the comparison centres. This may indicate, as suspected in the Swedish Two-Counties study,[3] that some of those cancers treated might not have become evident in the absence of screening (overdiagnosis), or it may indicate a progressive improvement in screening sensitivity as experience increased (initial underdiagnosis). Low sensitivity in the first round of screening might result in a delayed effect on mortality relative to that in Sweden.

TABLE VIII—COMPARISON OF TEDBC FINDINGS WITH THOSE FROM THE HIP AND SWEDISH-TWO COUNTIES TRIALS

—	UK TEDBC	New York[2,11] (HIP)	Sweden[3,12] (two-counties)
Population invited to screening	46 173	31 000	67 571
Age range	45–64	40–64	40-69*
Attendance at 1st screening	66%	65%	91%
Interval between mammographic screenings (yr)	2	1	2–3
Interval between clinical screenings (yr)	1	1	Not applicable
Mean follow-up† (yr)			
Control group	7·0	7·0	7·0
Study group	6·5	7·0	7·0
Rate of breast cancer detection (per 1000 woman yr) in control group	1·7	1·9	1·8
Detection rate at 1st screening (per 1000 women)	5·2	2·7	5·0
Cumulative breast cancer mortality† per 1000 women during follow-up			
A. Control group women	2·8	4·0	2·1
B. Study group women	2·2	2·6	1·4
B1. Study group, attenders only	1·9		1·1
B1a. If 1st screen negative	1·4		0·6
B2. Study group, non attenders	3·2		4·5
Relative risk for total study group vs control group	0·80	0·66	0·69

*The age range offered screening was wider but figures in the table refer only to the 40–69 yr age group.
†Calculated for the initial populations without censoring at death from other causes.

An early indication of mortality reduction may be given by a reduction in the incidence of cancers that are already advanced at the time of diagnosis. At attempt has been made to record both clinical and pathological stage at diagnosis in this trial. Since this is a multicentre study with patients managed by several different clinical teams, and stage abstracted retrospectively from case-notes, there was a lack of consistency between centres in categorising stage. Further work is required to establish, from the data that have been collected, a method of staging which permits comparison between different centres. This matter will be discussed in a subsequent report.

This paper is presented in accordance with our original undertaking to publish results as soon as there was a reasonable (80%) chance of being able to demonstrate as significant a 30% reduction in mortality, should it exist. Clearer conclusions should be possible after further years of follow-up. The results from all screening trials, including those which have not so far produced statistically significant results, may provide a more realistic indicator of the likely outcome of routine screening services than the results of two clearly successful trials alone. In the current phase of rapid implementation of mammography screening, our findings emphasise the need to achieve high participation rates and high sensitivity of screening if the programme is to achieve its full potential.

This lengthy multicentre trial has only been made possible by the enthusiasm and dedication of many staff working in each of the eight participating centres. In particular we want to thank the surgeons pathologists, radiologists, radiographers, Family Practitioner Committee staff, and, above all, clerical research staff without whom the necessary data could not have been collected. Research staff in the NHS Central Registers cheerfully undertook the enormous task of flagging the entire population and continue to provide the information required for evaluation. Programming and clerical staff at the coordinating centre have, over several years, checked, coded, and prepared the large and complex computerised data-base now being analysed. The computer centre at Queen Mary College, London, has provided assistance throughout the trial and we are most grateful for their interest and support. Finally we would like to thank the women enrolled into the trial for their participation in this research. The work in seven of the participating centres has been supported by the DHSS central funds and in the eighth by the Scottish Home and Health Department. The coordinating centre is supported by DHSS Research Management Division.

Correspondence should be addressed to Prof J. Chamberlain, DHSS Cancer Screening Evaluation Unit, Institute of Cancer Research, 15 Cotswold Road, Belmont, Sutton, Surrey SM2 5NG.

REFERENCES

1. UK Trial of Early Detection of Breast Cancer Group. Trial of early detection of breast cancer: description of method. *Br J Cancer* 1981; 44: 618–27.
2. Shapiro S. Evidence on screening for breast cancer from a randomised trial. *Cancer* 1977; 39: 2772–82.
3. Tabar L, Gad A, Holmberg LH, et al. Reduction in mortality from breast cancer after mass screening with mammography. *Lancet* 1985; i: 829–32.
4. Verbeek ALM, Hendricks JHCL, Holland R, Mravunac M, Sturmans F, Day NE. Reduction in breast cancer mortality through mass screening with modern mammography. (First results of the Nijmegen Project 1975–81). *Lancet* 1984; i: 1222–24.
5. Collette HJA, Day NE, Rombach JJ, Waard F de. Evaluation of screening for breast cancer in a non-randomised study (the DOM Project) by means of a case-control study. *Lancet* 1984; i: 1224–26.
6. Palli D, Rosselli del Turco M, Buiatti E, et al. A case-control study of the efficacy of a non-randomised breast cancer screening program in Florence (Italy). *Int J Cancer* 1986; 38: 501–04.
7. Working Group (chairman A. P. M. Forrest). Breast cancer screening. Report to the Health Ministers of England, Wales, Scotland and Northern Ireland. London: HM Stationery Office, 1987.
8. Roberts MM, Alexander FE, Anderson TJ, et al. The Edinburgh randomised trial of screening for breast cancer: description of method. *Br J Cancer* 1984; 50: 1–6.
9. Brinkley D, Haybittle JL, Alderson MR. Death certification in cancer of the breast. *Br Med J* 1984; 289: 465–67.
10. Baker RJ, Nelder JA. The GLIM system release 3. Numerical algorithms groups. Oxford: Oxford University Press, 1978.
11. Shapiro S, Venet W, Strax P, Venet L, Roeser R. Ten- to fourteen-year effect of screening on breast cancer mortality. *J Natl Cancer Inst* 1982; 69: 349–55.
12. Tabar L, Fagerberg G, Day NE, Holmberg L. What is the optimum interval between mammographic screening examinations? *Br J Cancer* 1987; 55: 547–51.

DOES PROLONGED BREASTFEEDING ADVERSELY AFFECT A CHILD'S NUTRITIONAL STATUS?

L. A. BRAKOHIAPA, A. BILLE, E. QUANSAH, K. KISHI[1], J. YARTEY, E. HARRISON, M. A. ARMAR, S. YAMAMOTO[1]

Noguchi Memorial Institute for Medical Research, University of Ghana, Legon, Accra, Ghana; and Department of Nutrition, School of Medicine, University of Tokushima, Kuramoto, Tokushima, Japan[1]

Summary In 202 children who visited a children's hospital in the city of Accra, Ghana, breastfeeding beyond the age of 19 months was found to be associated with malnutrition. The effect of weaning on food intake was then studied in 15 breastfed malnourished children in a rural community. Before weaning (complete cessation of breast-feeding) protein and energy intakes of all the malnourished children were about half those of 5 normal children. 10 of the malnourished children were weaned, and their intakes rose to the levels of the normal children; the 5 who continued breastfeeding maintained their low intakes. These results indicate that prolonged breastfeeding can reduce total food intake and thus predispose to malnutrition. They also suggest that in Ghana and other developing countries the proper weaning age may be about 18 months.

Introduction

PROLONGED breastfeeding is a common practice in Ghana and other developing countries.[1,2] It has the advantages of providing high quality nutrients and of helping to prevent the diarrhoeal diseases that result from contamination and improper preparation of weaning foods. Such diseases can lead to malnutrition. On the other hand, the incidence of malnutrition among children breastfed for 3–6 months is reported to be less than among those breastfed over long periods.[4] Which effects predominate—the favourable or the adverse? We have investigated the relation between prolonged breastfeeding and malnutrition in an urban clinic and a rural community in Ghana.

Methods

The study was conducted in two phases. In the first we obtained data in 202 children aged between 12 and 24 months who visited Princess Marie Louise Hospital in Accra (the clinic in which kwashiorkor was first named). Mothers were interviewed about the weaning time and eating habits of their children. An infantometer was used for length measurement and a baby scale with 5 g subgraduations for weight. In both phases the main index for distinguishing malnourished from normal children was the weight for length index, according to the NCHS standard;[5] but weight for age and length for age were also assessed. The cut-off point of malnutrition for weight for age was 90% and below,[6] for length for age 95% and below,[7] and for weight for length 80% and below.[8] The results of these three indices were completely concordant in separating malnourished from normal infants.

In the second phase, we studied the effect of weaning on the food intake of randomly selected children aged 12–24 months in a small farming village in the suburbs of Accra. The subjects were chosen on the basis of their anthropometric measurements—5 normal children who were already weaned, and 15 malnourished children who were being breastfed. The malnourished children were randomly divided into an experimental group of 10 and a control group of 5. In both groups three-day food intake was measured during the first, third, and fourth experimental weeks. During the

1988

ATTACHMENT 5

4 Hale AR, Hale M. *A review of the industrial accident literature*. London: HMSO, 1972.
5 Cooper JB, Newbower RS, Kitz RJ. An analysis of major errors and equipment failures in anesthesia management. Considerations for prevention and detection. *Anesthesiology* 1984;60:34-42.
6 Sivak M. Human factors and highway-accident causation: Some theoretical considerations. *Accident Analysis and Prevention* 1981;13:61-4.
7 Turner BA. *Man-made disasters*. London: Wykeham Publications, 1978.
8 Perrow C. *Normal accidents: living with high-risk technologies*. New York: Basic Books, 1984.
9 Reason J. Absent-mindedness and cognitive control. In: Harris JE, Morris PE, eds. *Everyday memory actions and absent-mindedness*. London: Academic Press, 1984:113-31.
10 Anderson RD. The physician's contribution to hospital medication errors. *Am J Hosp Pharm* 1971;28:18–25.
11 Davis NM, Cohen MR. *Medication errors: causes and prevention*. Philadelphia, Pennsylvania: George F Stickley, 1981.
12 Long G. The effect of medication distribution systems on medication errors. *Nurs Res* 1982;31:182-4.
13 Betz RP, Levy HB. An interdisciplinary method of classifying and monitoring medication errors. *Am J Hosp Pharm* 1985;42:1724-32.
14 Hiatt HH, Barnes BA, Brennan TA, *et al*. A study of medical injury and malpractice. *New Engl J Med* 1989;321:480-4.
15 Mills DH. Medical insurance feasibility study. *West J Med* 1978;128:360-5.
16 Department of Health and Social Security. *Hospital inpatient enquiry: summary tables*. London: HMSO, 1985.
17 Office of Population Censuses and Surveys. *Report on confidential enquiries into maternal deaths in England and Wales, 1979-1981*. London: HMSO, 1986.
18 Lunn JN, Mushin WW. *Mortality associated with anaesthesia*. London: Nuffield Provincial Hospitals Trust, 1982.
19 Buck N, Devlin HB, Lunn JN. *Confidential enquiry into perioperative deaths*. London: Nuffield Provincial Hospitals Trust, 1987.
20 Dearden CH, Rutherford WH. The resuscitation of the severely injured in the accident and emergency department—a medical audit. *Injury* 1985;16: 249-52.
21 Eddy DM. Variations in physician practice: the role of uncertainty. In: Dowie J, Elstein A, eds. *Professional judgement: a reader in clinical decision making*. Cambridge: Cambridge University Press, 1988.
22 Cameron HM, McGoogan E. A prospective study of 1152 hospital autopsies: II. Analysis in inaccuracies in clinical diagnoses and their significance. *J Pathol* 1981;133:285-300.
23 Mercer J, Talbot IC. Clinical diagnosis: a post-mortem assessment of accuracy in the 1980s. *Postgrad Med J* 1985;61:713-6.
24 Adams ID, Chan M, Clifford PC, *et al*. Computer aided diagnosis of acute abdominal pain: a multicentre study. *Br Med J* 1986;293:800-4.
25 Driscoll PA, Vincent CA, Servant CJ, Audley RJ. Use of advisers in the diagnosis and management of abdominal pain in accident and emergency departments. *Br J Surg* 1988;75:1173-5.
26 Dumford S. Junior hospital doctors: tired and tested. *Br Med J* 1988;297: 931-2.
27 Deary IJ, Tait R. Effects of sleep disruption on cognitive performance and mood in medical house officers. *Br Med J* 1987;295:1513-6.
28 Orton DI, Gruzelier JH. Adverse changes in mood and cognitive performance of house officers after night duty. *Br Med J* 1989;298:21-3
29 Anonymous. The dangers of not going to bed [Editorial]. *Lancet* 1989;i:138-9.
30 Firth-Cozens J. Emotional distress in junior house officers. *Br Med J* 1987;295:533-6.
31 Pillowski L, O'Sullivan G. Mental illness in doctors. *Br Med J* 1989;298: 269-70.
32 Cooper CL, Rout U, Faragher B. Mental health, job satisfaction, and job stress among general practitioners. *Br Med J* 1989;298:366-70.
33 Swansea Physicians' Audit Group. Audit of the quality of medical records in a district general medicine unit. *J R Coll Physicians Lond* 1983;17:208-12.
34 Mansfield BG. How bad are medical records? A review of the notes received by a practice. *J R Coll Gen Pract* 1986;36:405-6.
35 Leplat J, Rasmussen J. Analysis of human errors in industrial incidents and accidents for improvement of work safety. *Accid Anal Prev* 1984;16:77-88.
36 Anonymous. Critical questions; critical incidents; critical answers [Editorial]. *Lancet* 1988;i:1373-4.
37 Gruver RH, Freis ED. A study of diagnostic errors. *Ann Intern Med* 1957;47:119-20.
38 McKenna FP, Duncan J, Brown ID. Cognitive abilities and safety on the road: a re-examination of individual differences in dichotic listening and search for embedded figures. *Ergonomics* 1986;29:649-63.
39 McKenna FP. Accident proneness: a conceptual analysis. *Accid Anal Prev* 1981;15:65-71.
40 Eysenck MW. *Attention and arousal*. New York: Springer-Verlag, 1982.
41 Marteau TM, Wynne G, Kaye W, Evans TR. Resuscitation: experience without feedback increases confidence but not skill. *Br Med J* 1989 (in press).
42 McKenna, FP. Behavioural aspects of single-vehicle accidents. *Traffic Engineering and Control* 1987;28:280-5.
43 Skegg OCG, Richards SM, Doll R. Minor tranquillisers and road accidents. *Br Med J* 1979;i:917-9.
44 Levy R. Alcoholism in house staff physicians: an occupational hazard. *J Occup Med* 1986;28:79-81.
45 Juntunen J, Aap S, Oikinuora M, Aarimaa M, Strid L, Kauttu K. Doctors' drinking habits and consumption of alcohol. *Br Med J* 1988;297:951-4.
46 Balla JI, Iansek R, Elstein A. Bayesian diagnosis in presence of pre-existing disease. *Lancet* 1985;i:326-9.
47 Colquhoun WP, Rutenfranz J. *Studies of shiftwork*. London: Taylor and Francis, 1980.
48 Martin M, Jones GV. Distribution of attention in cognitive failure. *Human Learning* 1983;2:221-6.
49 McIntyre N, Popper K. The Critical attitude in medicine: the need for a new ethics. *Br Med J* 1983;287:1919-23.
50 Christiansen-Szalanski JJJ, Buskyhead JBN. Physicians' use of probabilistic information in a real clinical setting. In: Dowie J, Elstein A. *Professional judgement: a reader in clinical decision making*. Cambridge: Cambridge University Press, 1988:360-73.
51 Simanowitz A. Standards, attitudes and accountability in the medical profession. *Lancet* 1985;ii:546-7.

(Accepted 12 September 1989)

Breast screening: time for a rethink?

M Maureen Roberts

Dr M Maureen Roberts, clinical director of the Edinburgh Breast Screening Project since 1979, died of breast cancer on 9 June. We publish below her reflections on the care and welfare of women with the disease in Britain today, written shortly before her death. The list of references was added by the editor.

I am in reflective mood as I lie here in the sunshine at the end of my life. Breast cancer has caught up with me, after eight good years. It seems a common disease in Britain, and the evidence is strong that it is on the increase. Small wonder that people working with the disease desperately want to do something. Currently the main effort is in breast screening, with millions of pounds being put into a national programme, as recommended by the working group chaired by Professor Sir Patrick Forrest.

What's the use of breast screening?

I want to put the question, Are we going the right way to provide the best possible benefit?

First of all, screening is always a second best, an admission of failure of prevention or treatment. As we are unlikely to be able to prevent the disease what is required is successful treatment—and I don't mean even more aggressive adjuvant chemotherapy: I mean a treatment which works, which offers some kind of normal life. I don't want half promises of several years or a 50% chance of cure after surgery—it simply isn't good enough for women with the disease. As an example, Lippman believes that breast cancer could be the next human cancer capable of treatment and is working on innovative measures based on growth factors.[1] Others are using genetic approaches.

The next point to consider is, What can screening actually achieve? Two randomised trials, the Health Insurance Plan and the Swedish two county trial, showed a reduction in mortality of 30% in women offered screening.[2,3] Other trials, such as the Malmö,[4] United Kingdom,[5] and Edinburgh (unpublished) trials, found a non-significant reduction in mortality. We cannot ignore them, and it is not enough to say that our techniques weren't good enough a few years ago but are adequate now. We all know that mammography is an unsuitable screening test: it is technologically difficult to perform, the pictures are difficult to interpret, it has a high false positive rate, and we don't know how often to carry it out. We can no longer ignore the possibility that screening may not reduce mortality in women of any age, however disappointing this may be.

Another problem is that screening is offered to only the small proportion of women aged 50-64, there being no evidence that it is of benefit to other women. When we calculate the number of women likely to benefit each year we find that it is a surprisingly small

dinburgh Breast
creening Project
\ Maureen Roberts, *clinical*
irector

orrespondence to: Dr Joan
ustoker, CRC Breast
:reening Primary Care
lucation Initiative,
epartment of Community
edicine and General
actice, 2 Polstead Road,
xford OX2 6TN.

Med J 1989;299:1153-5

percentage of those who develop breast cancer. For example, of 2400 new patients with the disease seen annually in Scotland, 800 are aged 50-64, 270 will be invited for screening, 180 will attend, and 54 will benefit if there is a 30% improvement in mortality. Of course, it won't be like that because a larger number of cancers will be detected at the first visit and many fewer subsequently. Nevertheless, it is clear that the proportion of women with breast cancer who potentially may benefit is small. Some would prefer to exclude the over 65s from this cost-benefit calculation, but why should we take such an approach to the elderly? We must also note that the benefit is a reduction in mortality. This is not offering any certainty of cure or normal life to the women who attend, merely a prolongation of years for a few. Not only that: we cannot predict who will have these extra years.

It seems now that the Forrest committee was premature in its recommendation. At the time screening certainly seemed more likely to be of benefit than it does now, but I cannot help believing that it was a political decision. The government is prepared to put a large amount of scarce resources into a national breast screening programme, yet is unwilling to take on the tobacco industry at a political level; this despite overwhelming evidence that a truly preventive programme would save thousands of lives each year from lung cancer and other diseases. It was clearly a matter of politics, a decision taken in an election year and now out of perspective.


THE SCOTSMAN, EDINBURGH

Maureen Roberts

Might breast screening actually be detrimental?

I have to go on and ask the next question: If screening does little or no good could it possibly be doing any harm? We are all reluctant to face this.

Firstly, I'm thinking about the false positive rate. One in 10 women are being asked to come back for further investigations, which is an unacceptably high proportion. It clearly does not cause all women psychological harm, but it is traumatic for many. In most cases it is also unnecessary.

Some 10% to 17% of all the cancers will be diagnosed as non-invasive. The screeners are delighted, but non-invasive cancer is a difficult condition for women, and no studies have been done about their thoughts and feelings. We do not know how much it represents an overdiagnosis of cancer, nor do we know its natural course or how to treat it.

For most women who have invasive cancer diagnosed they become "patients" like other women. The difference is that they did not discover the problem, it was discovered for them. There is also an undeniable if subtle pressure on them to be grateful for this. Undoubtedly many are grateful, but no studies have been done to find out what women feel and think. Neither do we know how these women cope with recurrence. After all, they were almost promised (if only by implication) a good outcome if they attended for screening.

The current national programme seems prestigious and has consequently attracted many good people who want to set up a high quality service. Though standards will vary across the country, quality control is being taken seriously. It is possibly in danger of becoming a highly technological service. There is also an air of evangelism, few people questioning what is actually being done. Are we brainwashing ourselves into thinking that we are making a dramatic impact on a serious disease before we brainwash the public? Many thousands of women will be invited for screening and those who attend are said to be "compliant." The compliance rate is not very high and I wonder what plans are being made to try to raise it.

I hope very much that pressure is not put on women to attend. The decision must be theirs, and a truthful account of the facts must be made available to the public and the individual patient. It will not be what they want to hear. They should be told that the test is to detect cancer while it is still small; that we don't know how much it can influence mortality but there is up to a 30% chance (though maybe much less) that it may prolong life; that the test does not detect all cancers, some of which may appear in the next three years; and that it can indicate only what the breasts are like today and cannot predict whether breast cancer will develop in future. In addition, we do not know how to treat breast cancer. There is no successful treatment; different surgeons will carry out different procedures. Only a minority of women will be given this result, however, and those who are normal can feel suitably reassured—except that they must remember that they can develop the disease at any time: screening is not prevention.

In view of all this it is difficult to know how to propose a health education programme for women. But the currently expressed or strongly implied statement that if women attend for screening everything will be all right is not acceptable. Modern ideas concentrate on healthy living rather than the search for disease. How to present screening in this context needs further research, which should be a priority. Meanwhile, crucial, scarce resources have been set aside until the end of the century to carry out statistical trials of screening which have been deemed important. It cannot be coincidence that the age and social class of those men who are influential in decision making are similar to those of their wives who appear to be at greater risk of the disease and also have the best chance of benefiting from screening. I'm sure this is entirely subconscious, but it must be why breast screening research has been so readily and expensively funded, possibly to the detriment of other, equally serious problems.

Treatment policies

I'd like to turn now to the treatment of women found to have cancer. In the absence of a successful procedure surgeons will carry on treating the small invasive

tumours found on screening by mastectomy or local excision with conservation of the breast. Policies will vary, but it has already been expressed by many surgeons that "as we should give these women the best possible chance they should have mastectomy." Others will believe in conservation and use it as a bonus point for screening—"you save your breast if the tumour is found when it is small."

As no one knows how to treat non-invasive cancer many surgeons will advocate mastectomy and many women may prefer this. On the other hand, a national trial is being proposed based on conservation and systemic measures. The implication is that treatment will be different in different parts of Britain.

What's to be done?

I've drawn a dismal picture of screening, but it can be improved. I believe that the first thing is to create a nationwide, high quality diagnostic service for breast disease for women of all ages. The new screening clinics could form the basis. They require good clinical staff and surgical back up, cannot be radiological alone (though quality of mammography is of extreme importance), and must offer easy access for women and general practitioners. Clinicians, preferably women, would gain experience of the whole range of breast disease and its management.

The clinics should be run firmly in the context of health care and be sympathetic, open, and truthful, so that women can discuss problems with ease. A programme needs to be set up to encourage women to attend early, to try to reduce the number who currently present with inoperable disease (35%). Women could be made to feel that these clinics (or centres) are their own. As women, especially older women, feel vulnerable to a variety of conditions other services should be offered. The extreme gratitude expressed by women at the Edinburgh Breast Screening Centre, the Woman's Health Shop in Edinburgh, and during the health education campaign conducted as part of the Edinburgh randomised trial of screening for breast cancer showed that they appreciate the services which are offered.

As far as treatment is concerned, surgeons must recognise that they have none and should try to design policies which are consistent so that women aren't treated by different methods depending on where they live. This means that communication is all important. Proper, truthful accounts of diagnosis, screening, treatment, and aftercare must be written and made available everywhere, so that women become well informed and, most important, start to take part in the decision making process for themselves. All the options should be given and the woman should decide if she so wishes.

Finally, it seems that priorities in resource allocation and research should change. I will leave aside the issues of prevention and the search for successful treatment. Meanwhile, the 24 000 women who develop breast cancer each year in Britain require a first class diagnostic and therapeutic service, which should include research to provide necessary psychological back up. New psychological methods designed to improve quality of life (and, indeed, not impossibly quantity of life)—for example, self growth and visualisation, as well as more conventional approaches—should all be considered. More psychological research is required in the screening programme itself, particularly to establish the possible harmful effects on those with cancer. The 15 000 women a year in Britain who need care for recurrent disease must not be forgotten.

Conclusion

I believe that a rethink is required before the programme goes much further. I feel sad to be writing this; sad because naturally after so many years I am sorry that breast screening may not be of benefit. I am also sad to seem to be critical of the many dear and valued colleagues I've worked with over the years, particularly those who have made such a magnificent contribution to the care and welfare of women with breast cancer. But they will recognise that I am telling the truth. I ask them to bring breast cancer screening into its proper perspective and ask again what we really wish to achieve in terms of benefit for women with the disease.

1 Lippman ME. Steroid hormone receptors and mechanisms of growth regulation of human breast cancer. In: Lippman ME, Lichter AS, Danforth DN, eds. *Diagnosis and management of breast cancer.* Philadelphia: W B Saunders, 1988:326-47.

2 Shapiro S, Venet P, Strax P, Roeser R. Ten to fourteen year effect of breast cancer screening on mortality. *JNCI* 1982;69:349-55.

3 Tabar L, Fagerberg G, Duffy SW, Day NE. The Swedish two county trial of mammographic screening for breast cancer: recent results and calculation of benefit. *J Epidemiol Community Health* 1989;43:107-14.

4 Andersson I, Aspegren K, Janzon L, *et al.* Mammographic screening and mortality from breast cancer: the Malmo mammographic screening trial. *Br Med J* 1988;297:943-8.

5 UK Trial of Early Detection of Cancer Group. First results on mortality reduction in the UK trial of early detection of breast cancer. *Lancet* 1988;ii:411-6.

(Accepted 14 July 1989)

ANY QUESTIONS

In a small town in India we use industrial oxygen in place of medical oxygen. What are the risks, if any, of this substitution?

Oxygen for medical and industrial use is prepared by compressing air and cooling it until liquefied to allow fractional distillation to separate oxygen from nitrogen and the inert gases. Medicinal oxygen prepared in the United Kingdom is over 99% pure, with nitrogen and inert gases constituting the major part of the impurity. Contaminated gases that might harm patients, carbon dioxide, carbon monoxide, and oxides of nitrogen, are reduced to minute concentrations by the fractionation process.[1]

Gas for industrial use may be less pure than medicinal oxygen. A colleague who used industrial oxygen for anaesthetic purposes in India for 20 years assures me that, though analyses showed some 4% of impurities, nitrogen and the inert gases accounted for most of them.

Industrial oxygen might cause harm in two ways. Firstly, in any application, given that the oxygen concentration is 96%, 4% less oxygen will be delivered than shown on the flowmeter. For anaesthetic applications oxygen is invariably used at greater concentrations than is strictly necessary, so that the small fall in concentration would not result in hypoxaemia; 30% oxygen concentration would fall to 28·8%, way above concentrations that might induce hypoxaemia. The most critical application of oxygen treatment is to reduce hypoxaemia in respiratory failure. Here 24% oxygen may be used to increase arterial oxygen saturation while reducing the risk of carbon dioxide retention. A 4% fall in oxygen concentration of the gas driving the venturi mask would have a marginal effect only on the oxygen concentration delivered. Secondly, the source of industrial oxygen might be contaminated with substances that could harm patients. I have indicated that the distillation process removes such contaminants, and my colleague never experienced problems attributable to such contamination. This suggests that the risk is insignificant. Nevertheless, any doctor using industrial oxygen should arrange for analysis of a sample, and if contaminants other than nitrogen and the inert gases were present in concentrations of more than a few parts per million another source of oxygen should be sought. In particular, oxygen concentrators are proving to be efficient and economical in developing countries.

Though availability and cost have undoubtedly led to the use of industrial oxygen one other benefit related to its use is that the 4% of nitrogen and inert gases present may help to prevent the closure of alveoli associated with the use of gases that can be totally absorbed—namely, 100% oxygen and nitrous oxide.—J M CUNDY, *consultant anaesthetist, London*

1 Grant WJ. *Medical gases; their properties and uses.* Aylesbury: HM and M Publishers, 1978:73-93.

CORRESPONDENCE

- *All letters must be typed with double spacing and signed by all authors.*
- *No letter should be more than 400 words.*
- *For letters on scientific subjects we normally reserve our correspondence columns for those relating to issues discussed recently (within six weeks) in the BMJ.*
- *We do not routinely acknowledge letters. Please send a stamped addressed envelope if you would like an acknowledgment.*
- *Because we receive many more letters than we can publish we may shorten those we do print, particularly when we receive several on the same subject.*

Breast screening: a response to Dr Maureen Roberts

Dearest Maureen,

How much sympathy I have with many of the points made in your wistful posthumously published article,[1] yet I cannot see how they lead to your assertion that the Forrest committee was premature in its recommendation and your view that breast screening may not be of benefit.

Of course screening is not an optimal means of controlling any disease—far better to prevent it (as, for example, polio) or to treat it successfully (as, for example, testicular cancer). But neither of these options exist for breast cancer, and we are left with screening as a third best measure of control.

As you say, the two principal studies which provide statistically sound evidence of its likely effects suggest that reductions in mortality from breast cancer of around 30% are achievable in women aged over 50 when first invited to be screened.[2,3] Three further trials have been reported more recently[4,5] (Roberts MM, *et al*, in preparation), but none has shown a statistically significant reduction in mortality, although all point to a difference of up to 20% in favour of the women who were offered screening. There are some design flaws in each of these, the first being a non-randomised comparison, the others having insufficient statistical power because of their small sample size. A further study which derived observed and expected mortality rates for women in the United States breast cancer detection demonstration project[6] also concluded that the protection against death afforded by screening was 20-25%. Despite their shortcomings, the findings of these later studies suggesting lesser benefit cannot be ignored. But you seem to be interpreting their inconclusive results as proof that screening is of no benefit while ignoring the earlier more positive trials, thus throwing the baby out with the bath water.

Several retrospective case-control studies of breast cancer screening[7,8] have also indicated that screening is beneficial, showing that the risk of a screened woman dying from breast cancer is one third to one half that of an unscreened woman. These studies overestimate benefit because they cannot overcome the bias that women likely to have a good prognosis take up the offer of screening whereas those likely to have a poor prognosis do not.[9] The extent to which these retrospective studies exaggerate the effect of screening is not known, but, like all that has so far been published, they are consistent with the hypothesis that screening can prolong the life of some women.

Were the Forrest committee deliberating today I would be surprised if it reached a different conclusion. The question raised by the evidence from the more recent studies is not whether screening is capable of having any effect but whether it has sufficient effect to justify its implementation.

It is therefore important to look at those factors which influence the size of benefit—namely, attendance of the invited population, sensitivity of the screening test, frequency of routine screening, adequacy of follow up of abnormal findings, and effectiveness of treatment—and to monitor the costs and disadvantages of the programme.

Of the factors influencing benefit, acceptance of screening is likely to be the hardest to achieve in the United Kingdom. You made no secret of your deeply held personal view that the level of anxiety induced by an invitation to be screened was an absolute deterrent to women like yourself. But most do not find the thought of screening so alarming. In the first year of the United Kingdom programme the overall response has been 67%, and in view of inaccuracies in addresses on family practitioner committees' registers response among those who actually received the invitation must be higher. You may argue that they are attending because we have given them false expectations. If this is so it is to be deplored, and I agree that this rather mundane public health programme has probably been given too much hype.

As for the disadvantages, we must strive to reduce the false positive referrals and biopsies. In the national programme so far 7% of women who turned out not to have breast cancer were referred for further investigation but only 0·6% required a biopsy. Although less than that estimated in the Forrest report, this referral rate is still too high, although it is reassuring to find that the anxiety it provokes is less than that among women with breast symptoms and is not long lasting.[10] Overdiagnosis of non-invasive cancer is indeed a worry and, just as in the cervical neoplasia screening programme, may be the price we have to pay for a test that is sufficiently sensitive to pick up progressive cancer at a stage when it is still curable. However, there is still doubt about whether, and how much, overdiagnosis occurs in breast screening.

The financial cost is another question. The funding for the breast screening programme in England and Wales came from the government's central reserves and thus its implementation has not been at the expense of any pre-existing health care expenditure. Nevertheless, I concur with your opinion that breast screening comes fairly low down the list of priorities for preventive medicine. Far better, as you say, to take on the tobacco industry at a political level, or, on a world scale, to use the money to ensure a clean water supply to Third World communities. But while we strive by political means to achieve these wider aims are we to ignore the small advances in health care, made possible by technology, which slowly chip away at the burden of mortality and morbidity?

You also question the priority for putting further research money into breast screening, although your uncertainties about the programme can surely only be answered by research. Coming from such an ardent feminist as yourself, I was surprised to read your comment about the age and social class of those men influential in decision making on research priorities: age and social class are well taken but one hopes that the voices of women, who are well represented on the relevant research committee, may also help to influence decisions.

You, and others," suggest that the current breast screening programme was introduced to win votes in an election year. This statement confuses two issues. I trust you did not believe that the Forrest committee reached its conclusion for political, as opposed to humanitarian, reasons? The second is the decision by the government to implement that recommendation. The timing of the announcement on implementation might perhaps have been a vote catcher, otherwise why did the report wait, apparently unheeded, for four months from the time it was submitted until its acceptance? But had it not been accepted the outcry from the other political parties and the women's movement would have been enormous.

Your proposed solutions to the dilemma of a disease where treatment is successful only when applied early and where there is still uncertainty about the relative merits of different treatments are very negative. Provision of drop in clinics attracts only a tiny proportion of women at risk of the disease, probably not including the 35% you mention who currently present with inoperable disease. And standardisation of treatment across Britain would exacerbate, not alleviate, doubts about its efficacy, for it is only by clinical trials of alternative treatments that their benefits and side effects can be assessed.

My solution agrees with yours to the extent that complete and honest information must be given to both profession and public, based on the research findings currently available. My interpretation of these findings leads me to believe the following. During the next 20 years, I, in my late 50s, stand a one in 40 chance of dying from breast cancer. If screened from age 50 onward I may be able to reduce this risk to one in 55. To me this reduction is worth the slight inconvenience of going for mammography every few years; of having a one in 14 chance of being referred and a one in 170 chance of having a benign biopsy (both of which have happened to me and were more irritating than alarming); and even of artifically increasing my chance of a breast cancer diagnosis. On what evidence do you base your claim that women "will not want to hear" these facts and, by implication, will not want to avail themselves of the protection which screening offers? To me it seems a mildly inconvenient but sensible precaution in the same league, albeit at a greater cost, as a cholera or typhoid immunisation before a foreign trip. In

...nerefore, I believe that breast screening ... for women, though perhaps not for the ...layer.

How I wish, dear Maureen, that I could pursue this cost-benefit argument in friendly conversation with you, as in the past. We must continue the work you did with such dedication to try to control this disease not "brainwashed in the expectation of a dramatic impact" but with realism that screening is the best we can offer at present. It will be a happy day when we can drop the screening programme because a treatment effective against advanced disease has been discovered.

JOCELYN CHAMBERLAIN

Cancer Screening Evaluation Unit,
Institute of Cancer Research,
Sutton, Surrey SM2 5NG

1 Roberts MM. Breast screening: time for a rethink? *Br Med J* 1989;299:1153-5. (4 November.)
2 Shapiro S, Venet W, Strax P, Venet L. *Periodic screening for breast cancer, the health insurance plan project and its sequelae, 1963-1986.* Baltimore: Johns Hopkins University Press, 1988.
3 Tabar L, Fagerberg G, Duffy SW, Day NE. The Swedish two county trial of mammographic screening: recent results and calculation of benefit. *J Epidemiol Community Health* 1989;43: 107-14.
4 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:411-6.
5 Andersson I, Aspegren K, Janzon L, *et al.* Mammographic screening and mortality from breast cancer: the Malmö mammographic screening trial. *Br Med J* 1988;297:943-8.
6 Morrison AS, Brisson J, Khalid N. Breast cancer incidence and mortality in the breast cancer detection demonstration project. *JNCI* 1988;80:1540-7.
7 Verbeek ALM, Hendriks JHCL, Holland R, Mravunac M, Sturmans F, Day NE. Reduction of breast cancer mortality through mass screening with modern mammography. *Lancet* 1984;i:1222-4.
8 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:1224-6.
9 Palli D, Rosselli del Turco M, Buiatti E, *et al.* A case-control study of the efficacy of a non-randomized breast cancer screening program in Florence (Italy). *Int J Cancer* 1986; 38:501-4.
10 Ellman R, Angeli N, Christians A, Moss S, Chamberlain J. Psychiatric morbidity associated with screening for breast cancer. *Br J Cancer* (in press).
11 Rodgers A. The UK breast cancer screening programme: an expensive mistake. *Community Med* (in press).

SIR,—Dr M Maureen Roberts's reservations about the ultimate value of the breast screening programme,[1] made tragic by her own recent death from cancer of the breast and by her late disillusionment with a project to which she devoted the last 10 years of her career, certainly question the wisdom of the Forrest committee's recommendations. If, as Dr Roberts suspected, political motives encouraged premature launching of the national programme this implies that certain considerations may not have received the attention they deserved. Many of these were enlarged on in her article and have to do mainly with psychological and social repercussions of the programme.

I wish to express a theoretical reservation about the value of breast screening based on consideration of well authenticated features of the biology of cancer. I do not presume their relevance. My purpose is to stimulate discussion and criticism by those with more clinical experience of breast cancer than I have myself.

Any benefits to be expected from screening can accrue only if it results in earlier diagnosis and earlier institution of treatment. Yet no diagnosis attainable by the most advanced techniques presently available is early in a biological sense having regard to the overall timescale of the disease. If we assume exponential growth of a tumour at the average tumour volume doubling time of two months, a tumour of only 2 mm diameter will have been resident in the tissues for about three years eight months and will contain about four million cells; by the time it reaches 3 cm diameter it will have been resident for about five years seven months. Thus a tumour diagnosed by screening at the smallest conceivable size detectable will already have gone through 65% of the time taken to reach a size that is easily palpable. Clearly screening is far from being capable of *early* diagnosis.

For *earlier* diagnosis by screening to influence the outcome of the disease the question is whether the earlier intervention obviates later manifestations of progression. There is no question that it greatly facilitates ablation of the primary tumour with minimum trauma—and that is a great blessing to patients. What, however, about metastasis? For earlier intervention to prevent metastasis in a significant proportion of cases dissemination would have to be confined in most cases to a relatively late time in the history of the tumour. This is distinctly improbable: if a tumour is capable of disseminating viable cells I see no reason why this capacity should be inhibited until a late stage of its history. Indeed, the commonly short intervals between diagnosis of the primary tumour and evidence of metastatic disease suggest that dissemination has occurred early in the history of the disease. If death from breast cancer is most often attributable to disseminated disease then the earlier diagnosis achieved by screening would not be expected to affect long term mortality or the date of death of doomed cases. Survival times might be substantially increased, by about two years in the average case but by anything up to 12 years in the case of slowly growing tumours; also the five year "cure" rate would be increased. It is not generally realised that an increase in average survival time and a hiccup in mortality, when both are attributable to the earlier time of diagnosis, may represent no improvement in the control of the disease at all—impressive as these measures may be to the public. To deny the validity of this theoretical construct one or more of its ingredients have to be questioned.

If the Forrest committee did give short shrift to these theoretical considerations under the influence of political exigency, as Dr Roberts suggested, then implementation of the recommendations may have been a very expensive and cruelly disappointing enterprise.

HAROLD B HEWITT

Rickmansworth, Hertfordshire WD3 4DA

1 Roberts MM. Breast screening: time for a rethink? *Br Med J* 1989;299:1153-5. (4 November.)

SIR,—Dr M Maureen Roberts's personal obituary from both objective and subjective experience[1] is, I am sure, a salutary lesson and a banner for those faint in heart who share her misgivings.

I have always been deeply suspicious of alleged benefits accruing from analyses that require statistical reinforcement to prove their point. How often have we seen a counterargument refute the original using similar statistical equations? Cancer of the breast must hold pride of place in this forum—witness the countless arguments presented over the years to support one or other form of treatment.

Nearly all such arguments fail to take into account two basic facts: (*a*) the behaviour of cancer as a biological entity subject to many variables; and (*b*) the lack of real agreement about what constitutes the earliest manifestations of recognisable cancer, in situ malignancy, and atypical hyperplasia.

Rather than spend millions on a project of dubious value should we not direct these funds to more basic study? A serious criticism of research endeavour is that so little attention is paid to those who do not get the disease or, perhaps of more immediate interest, to those who recover from an apparently hopeless clinical condition. As a pathologist I know I share the experience of others who have performed necropsies on those who die of unrelated causes cured of what should have been incurable cancer. What makes another person die of widespread metastatic disease when the minute primary tumour is hidden right to the end? Why do some who smoke heavily not get cancer of the lung? Why is there so often a reverse relation between atheromatous disease and cancer?

The lessons learnt from screening for carcinoma of the cervix should have warned us of the problems, infinitely more difficult in breast cancer detection. Even at best, is a 30% reduction in incidence acceptable in a disease that affects 1 in 10 women? It is impossible to escape the conclusion that Dr Roberts is correct and that the decision to embark on breast screening has been based on political and not medical considerations.

T G ASHWORTH

Walsgrave Hospital, Coventry CV2 2DX

1 Roberts MM. Breast screening: time for a rethink? *Br Med J* 1989;299:1153-5. (4 November.)

SIR,—I have been enthusiastic for breast screening since the Health Insurance Plan first began to publish its results and have been concerned in a breast screening service run by a charity for some years. However, what Dr Maureen Roberts says seems to describe the inherent defects in our system,[1] and I can only agree with her.

In Belfast clinics for the treatment of symptomatic breast disease and breast cancer are poorly equipped and staffed in comparison with the screening service. Once a cancer is suspected by the screening service, and a biopsy is necessary, the patient is moved to a second class service. I hope, with Dr Roberts, that the screening service may form the basis of a national diagnostic service of the highest quality and that this may be backed up by good treatment and counselling services. Only in this way can we justify the vast amounts of money that are being poured into breast screening. It would also be a fitting memorial for a courageous woman.

WILLIAM ODLING-SMEE

Department of Surgery,
Queen's University of Belfast,
Belfast BT12 6BJ

1 Roberts MM. Breast Screening: time for a rethink? *Br Med J* 1989; 299:1153-5.

SIR,—Though I share Dr Maureen Roberts's opinion that the introduction of breast cancer screening was overhasty, the situation will not be improved by abandoning public screening.[1] The only justification for an about face would be if the current independent review of Swedish trials found it necessary to revise the findings of the Swedish two counties study. Otherwise the evidence must be accepted that good quality screening is an ethical service and should be available. If public screening is withdrawn private screening will fill the void, and it is doubtful whether the quality can be as well controlled. The question that needs rethinking concerns the means of keeping costs and emotions within control.

The sensitivity of screening can be marginally improved by intensification, but this sends the cost per extra year of life saved soaring over £1m and can suck resources into screening from services which give better value. These economic arguments against more frequent screening are lost, however, on the individual, who thinks only of the one life that might have been saved by one extra test. I believe that some choice in determining how much screening one has is reasonable and that a charge for screening above what is economically justifiable from a public point of view would provide the fairest and most comprehensible means of controlling demand.

The principles justifying a free at the point of use screening service for healthy adults are weak compared with those for "free" services for the sick

and disabled: screening need is fairly evenly distributed, decisions do not have to be made in haste and under stress, the unit cost is small, and demand is highest among those best able to afford it. It would be nice if all good things were free, but there is little reason why cancer screening should be so rather than oranges or domestic heating. The Department of Health is working hard to promote quality assurance, but it is allowing geographical disparities to develop and costs to escalate in both breast and cervical cancer screening.

Frankness about screening is, as Dr Roberts said, essential. By stating clearly that the "free" service seeks to provide a reasonable but not the maximum possible degree of protection against later development of advanced cancer and by offering further screening (with explanation of the pros and cons) to those who want to spend extra money on it we may be able to promote more realistic expectations.

RUTH ELLMAN

Cancer Screening Evaluation Unit,
Institute of Cancer Research,
Sutton, Surrey SM2 5NG

1 Roberts MM. Breast screening: time for a rethink? *Br Med J* 1989;299:1153-5. (4 November.)

SIR,—I read Dr M Maureen Robert's article with great sadness.[1] The terrible irony of her death from the very disease to which she devoted her professional life will have been apparent to everyone.

The new national breast cancer screening programme was begun only after many years of large-scale trials and feasibility studies.[2-4] Dr Roberts contributed significantly during this period and was an expert witness to the Forrest committee. It was this eminent medical committee, not the government, which recommended the national screening programme. It is not hard to imagine the political uproar that would have followed if the government had chosen to reject that report.

Dr Roberts makes many points with which we can all agree. More research into the psychological aspects of the screening programme is required; new improved methods of treatment are needed (as in most other spheres of medicine), and the use of existing methods needs to be rationalised: health education aspects must be dealt with more honestly and efficiently (and be appropriately funded). It does, however, seem premature and irresponsible to call for an end to the national programme when it has only just completed its first year, especially when the reported results[3] have met the targets set by the Forrest report and quality assurance guidelines for mammography (Pritchard report).

Many of us do fear that the screening programme will ultimately fail in Britain, not least because of the inadequacies of family practitioner committee registers and the lack of "compliance" of British women; but let us at least give it a good try. Whatever else it does, the screening programme will help to "create a nationwide, high quality diagnostic service for breast disease for women of all ages," which is one of the pleas made by Dr Roberts. She also calls for "a programme . . . to be set up to encourage women to attend early, to try to reduce the number who currently present with inoperable disease (35%)." To many of us this seems a good description of the national breast cancer screening programme.

DAVID L ASBURY

Manchester Breast Screening Service,
Withington Hospital, Manchester M20 0PT

1 Roberts MM. Breast screening: time for a rethink? *Br Med J* 1989;299:1153-5. (4 November.)
2 Shapiro S, Venet W, Strax P, Venet L, Roeser R. Ten to fourteen year effect of breast cancer screening on mortality. *JNCI* 1982;69:349-55.
3 Tabar L, Fagerberg G, Duffy SW, Day NE. The Swedish two county trial of mammographic screening for breast cancer: recent results and calculation of benefit. *J Epidemiol Community Health* 1989;43:107-14.
4 UK Trial of Early Detection of Cancer Group. First results on mortality reduction in the UK trial of early detection of breast cancer. *Lancet* 1988;iii:411-6.
5 Richards T. Breast cancer screening in Britain. *Br Med J* 1989;299:877-8.
6 Bowling A, Jacobson B. Screening: the inadequacy of population registers. *Br Med J* 1989;298:545-6.

Ethnic differences in consultation rates

SIR,—I was pleased to see the work by Dr S J Gillam and colleagues[1] showing significant increases in consultation rates among ethnic groups but not the increase in consultation rates for asthma. Perhaps I can reassure them that research into ethnic groups in hospital practice is not necessarily preoccupied with ethnic specific problems.

I have shown that in the east district of Birmingham (with a 10% Asian population) admissions to hospital for severe asthma are 2·5 times more likely to occur in patients of Asian origin than in non-Asians.[2] This difference was significant and held true even when allowing for possible differing prevalences of asthma and of readmissions. There are several possible reasons for this. The first is that there is a greatly increased prevalence of asthma in Asians, but this is unlikely as the prevalence would have to be surprisingly high to account for this difference. The findings of Dr Gillam and colleagues suggest that there are no more Asian than non-Asian patients with asthma in their population but that the Asian patients present more frequently for a consultation. This is one factor that I held to be responsible for my findings because of the difficulties in communication, which makes educating asthmatic patients more difficult and time consuming. There is also a tendency among the Asian patients whom I see for long term prophylactic treatment not to be used in preference for treatment by the crisis approach of "a needle when bad." The reasons for this tendency in my Asian patients are multiple.

Asthma is a common condition, and much has been made of a possible rise in the number of deaths from asthma over the past decade.[3] Our experience is that death from asthma is relatively rare among Asian patients, although to my knowledge there are no local or national published data that support this. If true, however, this might suggest that Asians do not have more severe asthma and do not take their treatment regularly, so resulting in our inability to control long term symptoms of asthma in this group. More time spent educating these patients in the short term might reduce the consultation rates in general practice in the long term, but the problems of achieving this in our Asian patients are complex.

JON G AYRES

Department of Respiratory Medicine,
East Birmingham Hospital,
Birmingham B9 5ST

1 Gillam SJ, Jarman B, White P, Law R. Ethnic differences in consultation rates in urban general practice. *Br Med J* 1989;299:953-7. (14 October.)
2 Ayres JG. Acute asthma in Asian patients: hospital admissions and duration of stay in a district with a high immigrant population. *Br J Dis Chest* 1986;80:242-8.
3 Burney PGJ. Asthma deaths in England and Wales 1931-85: evidence for a true increase in asthma mortality. *J Epidemiol Community Health* 1988;42:316-20.

SIR,—Recent papers by Dr S J Gillam and colleagues[1] and Professor R Balarajan and colleagues[2] show high rates of consulting general practitioners by Asians living in Britain. The accompanying editorial by Dr Tim Carney argues that such findings have implications for resource allocation,[3] but as Professor Balarajan and his coworkers point out the presence of a substantial ethnic minority may affect the mix of cases as well as the overall caseload. It is noteworthy, for example, that the study by Dr Gillam and colleagues found that all non-British ethnic groups consulted less frequently for mental disorders. They suggest that this may be due either to a genuinely reduced prevalence of mental illness in such subjects or to differences in the nature of their interaction with services.

These issues are also relevant to serious psychiatric conditions that are usually treated in a hospital. For example, I have recently compared a group of first generation immigrants from the Indian subcontinent with a matched group of English born controls (unpublished data). All of the patients had been seen for the first time at the Bethlem Royal Hospital and the Maudsley Hospital between 1969 and 1983 inclusive and had been given a diagnosis of a non-organic adult psychosis. Analysis of case notes showed that the Asian patients spent considerably less time as inpatients at these hospitals between the time of their initial contact and the time the notes were scrutinised (1987-8) than the controls.

These findings could reflect a better outcome in the Asian group in line with the results of the World Health Organisation's multicentre studies in different countries.[4,5] On the other hand, they may be a consequence of the nature of the interaction between immigrants and members of medical and psychiatric services. The studies recently reported in this journal indicate that if the latter explanation is the correct one at least part of the answer may lie in the relationship between immigrants and their general practitioners. Clearly, further research is necessary to examine the influence of ethnic and cultural origin on the process of referral and rereferral from the community to the hospital.

SUNJAI GUPTA

Institute of Psychiatry, London SE5 8AF

1 Gillam SJ, Jarman B, White P, Law R. Ethnic differences in consultation rates in urban general practice. *Br Med J* 1989;299:953-7. (14 October.)
2 Balarajan R, Yuen P, Raleigh VS. Ethnic differences in general practitioner consultations. *Br Med J* 1989;299:958-60. (14 October.)
3 Carney T. Ethnic population and general practitioners' workload. *Br Med J* 1989;299:930-1. (14 October.)
4 World Health Organisation. *Schizophrenia. An international follow-up study*. Chichester: Wiley, 1979.
5 Sartorius N, Jablensky A, Korten A, *et al*. Early manifestations and first-contact incidence of schizophrenia in different cultures. A preliminary report on the initial evaluation phase of the WHO collaborative study on determinants of outcome of severe mental disorders. *Psychol Med* 1986;16:909-28.

Referrals from general practice to hospital outpatient departments

SIR,—Drs Philip Harrison and Robert Blewitt make the point that "skin surgery in general practice should be undertaken only when the diagnosis is certain."[1] Surely the purpose of skin surgery is to ascertain the histological diagnosis and can be carried out equally effectively in general practice given the correct techniques, such as those published in the *BMJ*'s *ABC of Dermatology*.[2]

It seems to be a common strategy for some hospital departments faced with inadequate or negligent actions by individual general practitioners to call into question the competence of the many. Although this may be of general and admonitory educational value, might not a more specific and personal educational approach be more constructive—and did it occur in the two cases mentioned?

N E EARLY

Chesterfield S45 0ER

1 Harrison P, Blewitt R. Referrals from general practice to hospital outpatient departments. *Br Med J* 1989;299:1101. (28 October.)
2 Buxton PK. *ABC of dermatology*. London: British Medical Association, 1988.

19/12 5.30 B/Rm.

Director: Dr Nigel Gray A.M. MB. BS. Hon. LL.D. FRACP. FRACMA

Anti-Cancer Council of Victoria

ltr-1

6 December, 1989

Memo to: Members, State Mammographic Advisory Committee

From: Professor R R H Lovell

Subject: Meeting Papers for **19 December 1989**

The enclosed articles are to be included under Agenda item 4.

4.3 "The debate over mass mammography in Britain
- The case for; The case against" BMJ (15.10.88)
Enclosure 1

4.4 "Mammographic screening and mortality from breast cancer:
the Malmc mammographic screening trial" BMJ (15.10.88)
Enclosure 2

KEOGH HOUSE, 1 RATHDOWNE STREET, CARLTON SOUTH, AUSTRALIA 3053
☎ (03) 662 3300 Facsimile: (03) 663 3412 Telex: ACCV AA 34158

AUSTRALIAN CANCER SOCIETY MEMBER

ENCLOSURE 1.

The debate over mass mammography in Britain

The case for

Ruth Warren

For the sake of British women doctors have a particular duty to take seriously the evidence of world trials on screening for breast cancer as Britain heads the world's league table for mortality from this disease. Epidemiological data in two major controlled trials, the Health Insurance Plan study from New York[1] and the two counties Swedish trial,[2] show that mortality from breast cancer may be reduced by mammographic screening, and the evidence is statistically firm in women aged 50-64. The results of the trials concentrate on mortality figures, but the benefits of screening to individual women are wider—namely, reduced morbidity and more modest surgery because of earlier diagnosis.

Recommendations for screening

After the Swedish trial was published a committee was set up under Professor Sir Patrick Forrest to make recommendations; its report appeared in February 1987[3] and was immediately activated by the government on a slim budget, with the Griffiths management structure to enforce implementation throughout England and Wales by April 1990. Doctors might wonder whether this was wise and whether mortality may be reduced in this way. The public believes it can, but is it being deceived? Is more good being done than harm?

The Forrest report recommends performing mammography only from only one view without clinical examination every three years from the age of 50 to 64.[3] Screening with one view only and without clinical examination has been validated in two major trials: the two counties trial and the Nijmegen project.[4] Testing every three years more closely mimics the Swedish trial. Therefore all that needs to be done is to match that work, which was performed in highly motivated research departments, in every district in Britain, and on a smaller budget.

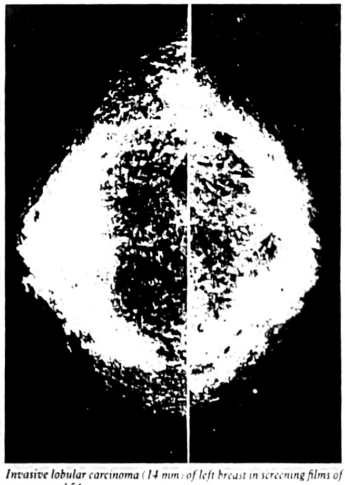
The Swedish National Board of Health on the same evidence has recommended screening every 18 months with two views at the age of 40-55 and screening every two years with two views in dense breasts and one in fatty breasts up to the age of 74.[5] The Netherlands National Council on Public Health recommends two yearly screening with two views from age 50-55 and thereafter two or one views as necessary up to the age of 69.[6] There is a large difference in the amount of money needed for these two requirements and that required for the more limited British recommendations. The British trials, just published, tested every two years and included clinical examination.[7]

The degree of staffing in Britain is not the same as in Sweden. The budget, however, allows for a minimal increase above the recommended levels of staffing before the ceiling of £206 000 for each centre each year is reached. Cytology, essential to the Swedish method, receives little mention and no staffing.

An important feature of the Swedish study is the high degree of compliance achieved. Reliable population lists from the Swedish tax office are used and yield an uptake of 90%. Data from the Swedish figures show that an increase in compliance from 60% to 80% may be as effective in reducing the proportion of advanced cancers (and therefore ultimately mortality)[8] as in reducing the screening interval from three to two years (N E Day, personal communication). Attention to non-attenders is therefore critical to success. The task in Britain should, however, be easier than in Sweden as the mortality for breast cancer is higher (28·4 v 18·6 per 100 000 women[1]) and screening in Sweden reduced the rate by 30%.

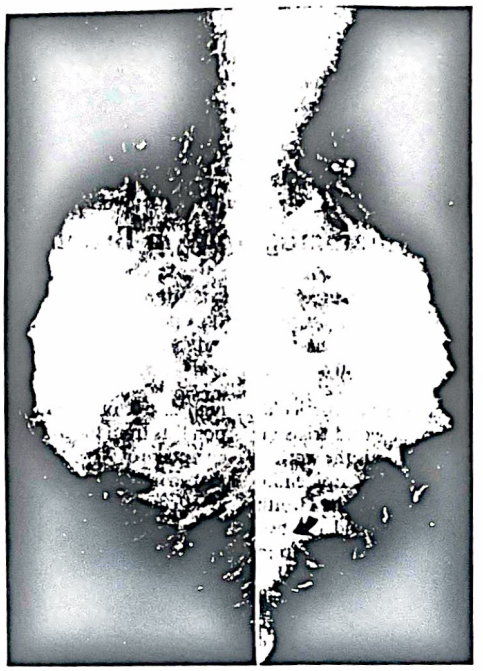
Britain's tight budget means that scrupulous attention needs to be paid to good specificity and high predictive values to avoid unnecessary recalls and high rates of biopsy. Fortunately, this tunes in with the needs of women. The predictive value for the screening of prevalence in Nijmegen is 30% with processing at the time of screening and slightly less in Sweden with batch processing. The predictive value for the screening of incidence increases to 70%.

A woman who receives a recall letter experiences temporarily the diagnosis of cancer. Three recalls for every cancer are acceptable, but 10 or 20 are not. Such specificity is not, however, easily achieved, especially with one view at the initial screening. Attention to the timing of recall letters can minimise anxiety.



Invasive lobular carcinoma (14 mm) of left breast in screening films of woman aged 54

Breast Screening Service, St Margaret's Hospital, Epping CM16 6TN
Ruth Warren, FRCR, *consultant radiologist*



Sclerosing ductal carcinoma (10 mm) of left breast in screening films of woman aged 53

Radiologists diagnosing early lesions is only one part of the process that reduces mortality. The performances of surgeons, pathologists, and radiotherapists are critical, and a special degree of cooperation within assessment teams is essential.

Reaping the benefits

Mass screening is the only current method by which breast cancer, an important cause of mortality, may be tackled, and it may be implemented by the means set out in the Forrest report, but with difficulty within the budget allocated. To fall below the best standards will be to invest and cause anxiety without achieving the expected result. Have the public and politicians understood this? Throwing money at this disease will not automatically gain years of life.

It is worth looking at the managerial process by which this programme has been put into place. Individual performance review is a powerful business tool for achieving results and ideal for producing caterpillar tractors or the sale of hamburgers in a fast food store. It has now been applied to breast cancer through doctors, who are aside from this direct managerial process. The service can be put in place by the target date. The technique is so critically dependant on quality that we may achieve the short term goal (women screened) without the long term result (life years gained).

What factors may make this programme fail? Compulsion and excessive speed are two. High motivation is essential and compulsion may demotivate. The necessary quality may be sacrificed by speedy implementation. The training programme is critical to bring the skills of radiographers, radiologists, pathologists, and surgeons to the necessary standard and must not be rushed.

Mass screening can and, I believe, should be implemented but with some relaxation on the time course of implementation. Sufficient resources should be allocated for effective results. From Europe and the United States there are those who wait to see this programme fail after the well publicised shortcomings of cervical cytology screening in Britain. The critics can be proved wrong if everyone respects the di... of the task. If we do not intend to succeed we sh... not start.

1 Shapiro S, Venet P, Strax P, Roeser R. Ten to fourteen year effect of breast cancer screening on mortality. *JNCI* 1982;69:349-55.
2 Tabar L, Fagerberg CJG, Gad A, *et al.* Reduction in mortality from breast cancer after mass screening with mammography. Randomised trial from the Breast Cancer Screening Group of the Swedish National Board of Health and Welfare. *Lancet* 1985;i:829-32.
3 Department of Health and Social Security. *Breast cancer screening. Report to the Health Ministers of England, Wales, Scotland and Northern Ireland.* London: HMSO, 1986. (Chairman Professor Sir Patrick Forrest.)
4 Verbeek ALM, Hendricks 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:1222-4.
5 Allmänna Råd från Socialstyrelsen. *Mammografi screening. Hälsokontroll för tidig upptäckt av bröstcancer.* Stockholm: Socialstyrelsen, 1986:3.
6 Nationale Raad voor de Volksgenzondheid. *Advies Organisatie bevolkingsonderzoek borstkanker.* Zoetermeer: Nationale Raad voor de Volksgenzondheid, 1986.
7 UK Trial of Early Detection of Cancer Group. First results on mortality reduction in the UK trial of early detection of breast cancer. *Lancet* 1988;ii:411-6.
8 Department of Health and Social Security. *Breast cancer screening: draft health circular.* London: DHSS, 1987. (DA (87)14.)
9 Atkinson EN, Brown BW, Montague ED. Tumour volume nodal status. Metastasis on breast cancer in women. *JNCI* 1986;76:171-8.

ANY QUESTIONS

What advice should be given to help a man weighing 165 kg lose weight? Is intestinal resection a treatment worth considering?

A man of whatever age weighing 165 kg is at considerable risk of premature death and above average morbidity from cardiovascular disease, diabetes, osteoarthritis, spondylosis, and other well recognised hazards. Firstly, serious efforts should be made by conventional dieting as well as strenuous daily exercise. Organisations such as Weight Watchers achieve good short term results with their dietary programmes and the patient should be advised to join one of these.

When all else fails surgical treatment might be considered if reasonable motivation and intelligence are shown by past dietary effort and weight reduction, albeit of shortlived success. Alcoholism, endogenous depression, low intelligence, and a history of cardiovascular disease would be considered contraindications. Endocrine abnormalities, though rarely the cause, have to be excluded. Intestinal bypass was a popular procedure for morbid obesity in the 1960s and 1970s but because of an associated risk of side effects as well as a mortality of 3-4% this has been abandoned. The advent of stapling instruments has made possible much safer, less complicated gastric reduction procedures, of which vertical gastroplasty is the most popular. The stomach is stapled from the fundus adjacent to the cardia to the lower lesser curvature creating a 50 ml proximal compartment draining into the remainder of the stomach through a stoma of less than 1·5 cm diameter, the stoma being supported by a band of Marlex or Silastic to prevent stretching. The mortality is less than 1%—nil in my experience of 125 gastroplasty patients in the past six years. The aim of the operation is simply to reduce gastric capacity and induce early satiety, which with a strict dietary discipline has yielded weight reduction of some 65-70% of excess weight after three years. Gastroplasty is certainly worth considering in a man weighing 165 kg.—MICHAEL BADDELEY, *consultant surgeon, Birmingham*

Correction

BACUP—the first two years: evaluation of a national cancer information service

An editorial error occurred in this article by Dr M L Slevin and others (10 September, p 669). In the last sentence of the second paragraph of the methods 60 151 was substituted for 6015. The sentence should have read, "During the first two years 6015 user surveys were sent out."

The case against

Petr Skrabanek

On the day that the Forrest report was published Norman Fowler announced that the government was going to implement its recommendations. Those who were invited to give evidence to the working party were bound to secrecy about the matters discussed, and as a result dissent was, at least in the short term, effectively silenced.

The Forrest report is a consensus document that does not mention the arguments of the dissenting minority. Its recommendations are based on selective evidence, which ignores data that might undermine its unrealistic estimates. Published evidence is distorted. Ethical issues are avoided.

The other side of the story

The Swedish trial that served as the centrepiece of evidence in favour of population screening is incompletely documented. Only by accident did I discover the data on overall mortality—in the correspondence columns of the Swedish medical journal *Läkartidningen*.[1] The Forrest report makes no mention of the fact that in the Swedish trial the overall mortality in the screened group was slightly higher than in the control group. In other words, not a single life was "saved" in a trial that included over 130 000 women. The Forrest report quotes misleadingly a "30% reduction" in deaths from breast cancer in screened women. As only 34% of the deaths from breast cancer were determined at necropsy in the screened group[1] and as the cause of death was not ascertained by an independent panel the possibility of bias from misdiagnosis, which could reduce or annul the observed reduction in deaths from breast cancer, cannot be excluded. The paper in the *Lancet* used by the Forrest group gave no data on overall mortality, on interval cancers (cancers that appear between screenings), on the number of women with breast cancer excluded before randomisation (about two thirds of the deaths from breast cancer that would be expected to occur in the sample are unaccounted for), or on the case fatality of breast cancer (as opposed to mortality from breast cancer).[2] Another disturbing feature was the constant shifting of the age limits in the Swedish trial. I have recorded the following age ranges in various publications between 1981 and 1986: 40-⩾75, 40-46; >40; 40-69, 40-74, 40-69, and 40-74.

No amount of squirming on the statistical hook will change the fact that there was no net benefit for the women offered screening. The quoted 30% reduction is a relative percentage obfuscating the fact that the yearly benefit was one death fewer in each 15 000 women screened, provided that deaths from breast cancer were correctly ascertained. This "gain" was, however, more than offset by deaths from other cancers and other causes. Somebody should explain to women that this is what the 30% reduction means in absolute terms—not that one woman in three will not die.

The Forrest report distorts the evidence on interval cancers by claiming that no more than 5-10% of interval cancers would be expected if its recommendations were implemented. In large trials such as the Health Insurance Plan trial[3] and the Nijmegen case-control study[4] between one third and one half of all detected cancers were interval cancers.

No mention is made in the report of the positive predictive value of mammography, the single most important piece of information for any screening test. In the Canadian national breast screening study (still in progress) the positive predictive value was 5-10%.[5] This means that out of 100 mammograms showing positive results, 90-95 are false positives. The implementation of the Forrest report, with an estimated positive predictive value of 5% would result in 65 000 mammograms a year showing false positive results.

Disadvantages of screening

The report claims, contrary to existing evidence, that population screening is unlikely to produce a significant overdiagnosis. Yet the authors of the Swedish study reported 30-40% overdiagnosis in the screened group, which persisted for the duration of the trial.[2] In another paper by the same group the screening programme increased the rate of breast operations twofold.[6] One of the coauthors of the Swedish study expressed concern about "a very serious situation" of "unacceptable divergence of opinion" among the pathologists who interpreted the breast biopsy specimens and about the "overall muddling of statistics which invalidates any serious attempts to analyse the screening programme in its entirety."[7]

The harm of screening is not confined to overdiagnosis. Overdiagnosis implies overtreatment, unnecessary biopsies, unnecessary mastectomies, and widespread anxiety and fear. The advocates of screening should assess the harm by stating how many mammograms need to be taken and biopsies performed for one life saved. Wright calculated that if a woman subjected to operation for benign disease is considered to be harmed by screening the ratio of harm to benefit is 62 to 1.[8] I have argued elsewhere that screening healthy people without informing them about the magnitude of inherent risks of screening is ethically unjustifiable.[9]

Widely different estimates on the cost-benefit of mammography have been published. If, as I believe is the case, they are based on false premises they are meaningless. How do you calculate the cost of the benefit when there is no benefit?

Towards effective screening

The wisdom of population screening needs reappraisal. Firstly, it must be established that screening does alter the natural course of breast cancer in an appreciable proportion of screened women. Thirteen out of 14 long term follow up studies of patients with breast cancer failed to show evidence of cure, regardless of the stage at diagnosis. Secondly, if evidence shows that screening prolongs life the next question is whether the best achievable results from university centres translate into the real world of routine screening centres and private clinics. Judging from the ineffectiveness of the British cervical screening programme, there are no grounds for optimism. The horror of the private clinics has already been exposed.[10] Finally, only when these two hurdles have been cleared does the time come to discuss cost. What would be the cost of a permanent national programme? And, more importantly, in terms of opportunity cost is it worth while?

Who will be blamed, and who will assume responsibility for screening in Britain, if, say, in 10 years time mortality from breast cancer shows no improvement? As Richard Feynman, the Nobel laureate, observed after pinpointing the cause of the *Challenger* shuttle

Department of Community Health, Trinity College, Dublin 2
Petr Skrabanek, PHD, *lecturer*

disaster: "Reality must take precedence over public relations, for nature cannot be fooled."

1 Projektgruppen för WE-studien. Replik om mammografi. *Läkartidningen* 1985;82:2674.
2 Tabár L, Fagerberg CJG, Gad A, *et al.* Reduction in mortality from breast cancer after mass screening with mammography. Randomised trial from the Breast Cancer Working Group of the Swedish National Board of Health and Welfare. *Lancet* 1985;i:829-32.
3 Shapiro S, Venet P, Strax P, Roeser R. Ten to fourteen year effect of breast cancer screening on mortality. *JNCI* 1982;69:349-55.
4 Verbeck ALM, Hendricks JHCL, Holland R, Mravunac M, Sturmans F, Day NE. Reduction of breast cancer mortality through mass screening with modern mammography. First results of the Nijmegan Project, 1975-1981. *Lancet* 1984;i:1222-4.
5 Baines CJ, Miller AB, Wall C, *et al.* Sensitivity and specificity of first screen mammography in the Canadian National Breast Screening preliminary report from five centres. *Radiology* 1986;160:295-8.
6 Holmberg L, Adami L-O, Presson I, Lundström T, Tabar L. Demanda surgical inpatient services after mass mammographic screening. *Br Med J* 1986;293:779-82.
7 Gad A. Ten years' experience from a randomised controlled breast cancer screening programme. II. Diagnostic aspects. In: *Proceedings of a conference on cancer screening.* Florence: Centro Per lo Studio e la Prevenzione Oncologica, 1987:37-8.
8 Wright CJ. Breast cancer screening: a different look at the evidence. *Surgery* 1986;100:594-8.
9 Skrabanek P. The physician's responsibility to the patient. *Lancet* 1988;i:1155-7.
10 Fentiman IS. Pensive women, painful vigils: consequences of delay in assessment of mammographic abnormalities. *Lancet* 1988;i:1041-2.

(Accepted 10 August 1988)

How To Do It

Communicate with cancer patients: 2 Handling uncertainty, collusion, and denial

Peter Maguire, Ann Faulkner

Breaking bad news often prompts patients to ask questions about their future like: How long have I got? You then have to help them cope with uncertainty without them becoming demoralised.

Handling uncertainty

When asked: How long have I got? it is tempting to give a finite (Oh, three months) or range (Anything from a month to six months) of time. But such predictions are usually inaccurate, tend to err on the optimistic side, and cause problems for patients and their families. Patients then pace themselves according to the time they believe is left. If they deteriorate earlier than expected and are prevented from achieving planned goals they will feel cheated and bitter. Relatives can find an unexpectedly prolonged survival ("borrowed time") hard to cope with because they have used up their physical and emotional resources. So it is better to acknowledge your uncertainty and the difficulties that this will cause.

Doctor: You asked me how long he has. The trouble is, I don't know. I realise this uncertainty must be difficult for you.
Mrs W: It is. It is terrible knowing that he is going to die but not knowing when. I mean it could be in one month's time or next Christmas.
Doctor: That's the trouble, I just don't know how long it will be.

You should next check if she would like to know the signs and symptoms that would herald further deterioration.

Doctor: What I can do, but only if you would like me to, is tell you what changes would suggest he is beginning to deteriorate further.
Mrs W: Yes, I think that would help me.
Doctor: He will probably complain of feeling breathless, weak, and start going off his food.

You can then encourage her to try to use the intervening time.

Doctor: But as long as there are no signs like that I think you can take it that he is relatively OK. So, you should try to make the most of this time if you can. Is there anything you would particularly like to do?

Later, add that you are prepared to check him regularly, and show a willingness to negotiate the frequency of such check ups.

Doctor: I think it would help if I saw him from time to time to monitor how he is doing. How often would you like me to do that?
Mrs W: Would every month be OK?
Doctor: Yes, fine.

You should explain that if anything unforeseen occurs between these assessments you should be contacted immediately. This gives patients and relatives confidence that they have a "life line."

Doctor: If you are worried at any stage between his appointments you must get in touch with me. I can then assess him and decide what needs to be done.

Few patients or relatives abuse this offer.
When some patients or relatives face uncertainty they show that they do not want any markers.

Doctor: Would you like me to tell you how you might recognise if Peter's health is deteriorating?
Mrs B: No, I'll leave it to you. You're the expert.

Sometimes the uncertainty concerns issues other than "how long." Again you should acknowledge the uncertainty and establish any resulting worries.

Doctor: I sense that this uncertainty is a major problem for you.
Mr J: It is. I feel helpless not knowing what's going to happen or how it's going to happen.
Doctor: What are you worried about in particular?
Mr J: I'm worried about how I'm going to die. I don't want to be a burden on my family, and I'm not sure what to expect after death.
Doctor: Any other concerns?
Mr J: Isn't that enough?
Doctor: Yes, it is, but I just want to make sure I establish all your concerns before we discuss them in detail.

By separating out and exploring each concern the patient begins to see that there is some prospect that they can be tackled.

Cancer Research Campaign Psychological Medicine Group, Christie Hospital, Manchester M20 9BX
Peter Maguire, FRCPSYCH, *director*

Department of Nursing Studies, University of Edinburgh, Edinburgh EH8 9PL
Ann Faulkner, SRN, *senior lecturer*

Correspondence to: Dr Maguire.

ENCLOSURE 2.

Mammographic screening and mortality from breast cancer: the Malmö mammographic screening trial

Ingvar Andersson, Knut Aspegren, Lars Janzon, Torsten Landberg, Karin Lindholm, Folke Linell, Otto Ljungberg, Jonas Ranstam, Baldur Sigfússon

Abstract

Study objective—To determine whether mortality from breast cancer could be reduced by repeated mammographic screening.

Design—Birth year cohorts of city population separately randomised into study and control groups.

Setting—Screening clinic outside main hospital.

Patients—Women aged over 45; 21 088 invited for screening and 21 195 in control group.

Interventions—Women in the study group were invited to attend for mammographic screening at intervals of 18-24 months. Five rounds of screening were completed. Breast cancer was treated according to stage at diagnosis.

End point—Mortality from breast cancer.

Measurements and main results—All women were followed up and classed at end point as alive without breast cancer, alive with breast cancer, dead from breast cancer, or dead from other causes. Cause of death was taken from national mortality registry and for patients with breast cancer was validated independently. Mean follow up was 8·8 years. Altogether 588 cases of breast cancer were diagnosed in the study group and 447 in the control group; 99 *v* 94 women died of all causes and 63 *v* 66 women died of breast cancer (no significant difference; relative risk 0·96 (95% confidence interval 0·68 to 1·35)). In the study group 29% more women aged <55 died of breast cancer (28 *v* 22; relative risk 1·29 (0·74 to 2·25)). More women in the study group died from breast cancer in the first seven years; after that the trend reversed, especially in women aged ≥55 at entry. Overall, women in the study group aged ≥55 had a 20% reduction in mortality from breast cancer (35 *v* 44; relative risk 0·79 (0·51 to 1·24)).

Other findings—In the study group 100 (17%) cancers appeared in intervals between screenings and 107 (18%) in non-attenders; 51 of these women died from breast cancer. Cancers classed as stages II-IV comprised 33% (190/579) of cancers in the study group and 52% (231/443) in the control group.

Conclusions—Invitation to mammographic screening may lead to reduced mortality from breast cancer, at least in women aged 55 or over.

Departments of Radiology, Surgery, Community Health Sciences, Oncology, Pathology, and Internal Medicine, Malmö General Hospital, S-214 01 Malmö, Sweden
Ingvar Andersson, MD, *associate professor of radiology*
Knut Aspegren, MD, *associate professor of surgery*
Lars Janzon, MD, *professor of community health sciences*
Torsten Landberg, MD, *associate professor of oncology*
Karin Lindholm, MD, *head of department of cytology*
Folke Linell, MD, *emeritus professor of pathology*
Otto Ljungberg, MD, *associate professor of pathology*
Jonas Ranstam, MA, *senior lecturer in community health sciences*
Baldur Sigfússon, MD, *associate professor of radiology*

Correspondence to: Dr Andersson.

Introduction

Many clinical studies have shown that the prognosis of breast cancer is related to the stage of the disease at diagnosis and treatment.[1] Mammography is a sensitive method of detecting breast cancer at an early stage, sometimes even at an in situ stage, and hence mortality from breast cancer should be reduced by mammographic screening. Owing to the potential lead time (the amount of time by which diagnosis is advanced through screening) and to length time bias associated with screening (the tendency of screening to pick up slow growing tumours) a randomised trial is necessary to determine whether such a reduction does occur.

The first evidence in favour of mammographic screening came from the study on patients registered with the Health Insurance Plan of Greater New York.[2] This study included physical examination as well as mammography and showed a reduction in mortality from breast cancer of about 30% in women invited for screening. Owing to the design of the study the effect of mammography alone could not be assessed. Furthermore, because of differences in mortality from breast cancer between the United States and Sweden and in the use of diagnostic procedures such as mammography the study's results could not be extrapolated to a Swedish population, Substantial technical advances in mammography were made after the American study, and in 1976 a trial was set up in the city of Malmö in southern Sweden to find whether the mortality from breast cancer could be reduced by repeatedly inviting women to attend for mammographic screening. We report the results.

Subjects and methods

All women born in 1908-32 were identified from the population registry of Malmö. Half the women in each birth year cohort were randomly selected as the study groups and invited to mammographic screening. The remaining women were allocated to a control group and were not screened. Each birth year cohort was randomised separately. Invitation was by personal letter, and all 25 birth year cohorts were successively entered into the study, the date of entry being defined as the date of invitation. The screening programme started in October 1976; all 25 birth year cohorts had been through their first round of screening by the end of September 1978. The planned interval between screenings was 18 to 24 months. Women who had moved out of the city were not contacted for subsequent examinations. Women who did not attend a screening examination but were still living in the city were invited to subsequent rounds. The examinations were free of charge. The study was approved by the ethical committee at the University of Lund, Sweden.

Screening was with up to date film screen mammography, improved equipment being used as it became available. In the first two rounds two views (craniocaudal and oblique) were used. In subsequent rounds either both views or only the oblique was taken, depending on the parenchymal pattern: a single oblique view was taken for women whose breasts were mainly fatty on mammography, and both views were taken for women with dense breasts.

Malmö is served by one hospital for somatic diseases, where virtually all patients with breast cancer are diagnosed and treated by a team specialising in breast

diseases. Patients are treated according to the stage of the cancer. The principles of treatment changed somewhat during the study period; in particular, breast preserving surgery was introduced for patients with limited disease. At the beginning of the study period simple mastectomy was the standard treatment for non-invasive breast cancer (stage 0); this was later replaced by subcutaneous mastectomy. The treatment offered for stage I breast cancer from 1979 was breast conservation or mastectomy. For stage II cancer two different randomised clinical trials were started in 1978 to test adjuvant radiotherapy or chemohormonal therapy, or both, and ran consecutively. Treatment for stages III and IV was individualised throughout the study period. As invitation to screening was never used as a stratification variable in the trials of the treatments all patients were treated according to the same principles.

Statistical methods—The predetermined end of the trial was 31 December 1986; no interim analyses were performed. The study was designed to document a 25% reduction in mortality from breast cancer with a power of 0·90 at the 5% level of significance. The effect of screening on mortality from breast cancer was estimated by the relative risk for the study group versus the control group with a test based 95% confidence interval. Women who had been treated for breast cancer previously were included in the analysis only if a new cancer was diagnosed in the other breast during the study. For comparison, analyses were done including and excluding these women.

Assessment at the end of trial—At the end of the trial women in both groups were classified as alive without breast cancer, alive with breast cancer, dead from breast cancer, or dead from other causes. Over 98% of the patients with breast cancer in both groups were registered with and subsequently treated at Malmö General Hospital. The remaining 2% of patients were identified through the national cancer registry. The number of deaths, together with the cause of death, was retrieved from the national mortality registry. Women who had moved out of the country were followed up through the national registry of immigrants and emigrants.

Validation of end points—To achieve an independent evaluation of the cause of death of patients with breast cancer identified in the study an end point committee was formed to reassess the clinical records and findings of postmortem examinations. The committee consisted of one pathologist and one oncologist; they were blinded to the patients to reduce the risk of bias in establishing the underlying cause of death. They separately reviewed the clinical data and findings of postmortem examinations and then independently determined the cause of death. Biopsy material as well as microscopic material from postmortem examination was analysed if necessary. Additional clinical records could be requested if insufficient material for an accurate decision had originally been submitted. When the two committee members did not agree, the case was re-evaluated and determined by a qualified internist. The underlying cause of death was coded according to the eighth revision of the International Classification of Diseases.[4]

TABLE I—*Composition of Malmö mammographic screening trial by birth cohorts and woman years of observation. Women were aged 45-69 at entry*

	Study group			Control group	
Birth cohort	No of women	No of woman years	No (%) attending first screening	No of women	No of woman years
1908-12	4 183	33 550	2 677 (64)	4 169	33 611
1913-7	4 324	38 041	3 113 (72)	4 321	37 779
1918-22	4 600	42 931	3 496 (76)	4 623	42 991
1923-7	4 323	40 723	3 458 (80)	4 313	40 578
1928-32	3 658	31 052	2 890 (79)	3 769	32 057
Total	21 088	186 297	15 604 (74)	21 195	187 016

TABLE II—*Numbers of breast cancers detected in women in study and control groups by age at diagnosis*

	Cancers detected in study group				
Age at diagnosis	At screening	In intervals between screening*	In non-attenders†	Total	Cancers detected in control groups
45-49	16	6		22	14
50-54	60	24	17	101	77
55-59	55	23	16	94	89
60-64	80	16	19	115	93
65-69	97	16	33	146	89
70-74	47	12	16	75	67
75-79	19	3	6	28	18
Total	374	100	107	581‡	447§

*Breast cancer diagnosed in interval between negative screening examination and invitation for next screening.
†Women who did not attend screening examination and in whom breast cancer was diagnosed before invitation for next screening.
‡In addition, seven women in study group had breast cancer diagnosed after moving out of Malmö. Two patients with malignant cystosarcoma phyllodes and one patient with fibrosarcoma were included.
§Includes three patients with malignant cystosarcoma phyllodes and one with fibrosarcoma.

Results

By 31 December 1986 five rounds of screening and most of the sixth round had been completed. The mean duration of follow up in each group was 8·8 years. Table I shows the age distribution of the women in the study. The attendance rate was higher in the first round (74%) than subsequent rounds (70%) and higher among younger than older women.

BREAST CANCERS

A total of 1035 women developed breast cancer, 588 in the study group and 447 controls (table II). The number of breast cancer years was 2835 in the study group and 1869 in the control group. Seventeen per cent of the cancers in the study group appeared in the intervals between screenings and 18% in women who had been invited for screening but did not attend. Thirty six patients in the study group had bilateral carcinoma: in 16 the cancer was diagnosed on both sides within the study period and in 20 it had been diagnosed in one breast before entry into the study. In the control group 32 patients had bilateral carcinoma, the disease being detected on both sides within the study period in nine patients.

The mean age at which breast cancer was diagnosed was 62·4 years for patients whose carcinomas were detected at screening, 59·9 for patients whose carcinomas were detected in the intervals between screening, and 63·5 for non-attenders; it was 61·8 years for patients in the control group.

The median size of invasive carcinomas detected at screening was 1·0 cm, of carcinomas detected in the intervals between screenings 1·9 cm, of carcinomas in non-attenders 2·5 cm, and of carcinomas in the control group 1·9 cm. The size of the actual carcinoma was measured whenever possible; otherwise the size was measured on the mammograms. The largest diameter was used to compute the median tumour size.

Table III shows the distribution of tumours by stage. Bilateral carcinomas were staged according to the most advanced side if synchronous, and according to the first carcinoma if metachronous. Patients who had carcinoma in one breast before the study and in the other breast within the study were staged according to the carcinoma detected in the study period. Most non-invasive carcinomas (stage 0) were ductal (81 (87%) in the study group and 38 (78%) in the control group); the rest were lobular. A large proportion (26%) of non-invasive cancers were discovered in the intervals between screenings. The proportion of advanced cancers was significantly greater in those who did not

attend for screening than it was in the control group (72% *v* 50%; p=0·0001, χ^2 test). On the whole the distribution by stage was more favourable in the study group, which had a smaller proportion of stage II-IV cancers than the control group (tables III and IV).

Table V shows only minor differences in treatment between the study group and the control group with respect to stage 0 disease. As no women with stage 0 cancer died this somewhat skewed distribution of treatment was unimportant.

MORTALITY

Table VI shows the mortality in the population under study. The cause of death was as given in the national mortality registry, which was complete up to the end of 1985 at the time of analysis. Death certificates had been based on findings of postmortem examinations in 58% of cases in the study group and 57% in the control group. There were only minor differences between the groups in the age specific rate of postmortem examinations and no significant difference in overall mortality between the groups. Mortality specific to cause was similar in the two groups.

END POINTS

During the study 193 patients who had been diagnosed as having breast cancer died, 94 in the control group and 99 in the study group (table VII); in both groups 76% underwent postmortem examination. Breast cancer was considered by the independent evaluators to be the underlying cause of death in 66 patients in the control group and 63 in the study group. Most (51) of the deaths from breast cancer in the study group occurred in women who did not attend for screening and in women whose carcinoma was detected in the interval between screenings. In both groups women with breast cancer showed the same pattern of deaths from other causes.

Of the 193 women with breast cancer who died, 41 had at least one other malignancy (19 in the control group and 22 in the study group); it was the cause of death in 14 patients in the control group and in 17 in the study group, according to the independent evaluators. Twenty six of the 41 patients had undergone postmortem examination, and in three the additional cancer was an unexpected finding and was determined to be the cause of death. In another two cases the additional cancer was found to be the cause of death, although clinically the cause of death was attributed to metastases from the breast cancer.

During the analysis we questioned whether all patients with metastases of breast cancer, irrespective of the cause of death, should be included in the assessment of the effect of screening; whether the comparison should be based only on official death certificates; and whether women in whom breast cancer had been diagnosed before the study should be included. Table VIII shows the results of analyses based on these different definitions of end point.

During the first seven calendar years of the screening programme the cumulative number of deaths from breast cancer was higher in the study group than the control group, but at the end of the trial the opposite was the case (figure). The initial trend of a higher number of deaths from breast cancer each year in the study group was reversed six years after the start of the screening programme (table IX). In the seventh and subsequent years the number of deaths from breast cancer was lower in the study group. By the end of 1987 this trend was more pronounced: in 1987, 18 of the patients who died from breast cancer were in the control group compared with six in the study group.

Mortality from breast cancer in the study group was unexpectedly high at first. To investigate this phenomenon further we compared the effect of screening on women younger than age 55 and aged 55 or older at entry into the study (table X, figure). The excess deaths from breast cancer in the study group occurred

TABLE III—*Number (percentage) of cases of breast cancer by stage in study and control groups*

Stage*	Cancers detected in study group: At screening (n=374)	In intervals between screening (n=79)	In non-attenders (n=106)	Total† (n=79)	Cancers detected in control group† (n=443)
0	61 (16)	24 (24)	8 (8)	93 (16)	50 (11)
I	241 (64)	33 (33)	22 (21)	296 (51)	162 (37)
II	68 (18)	33 (33)	41 (39)	142 (25)	172 (39)
III	4 (1)	7 (7)	15 (14)	26 (4)	27 (6)
IV	0	2 (2)	20 (19)	22 (4)	32 (7)
II-IV as proportion of:					
All carcinomas				190/579 (33)	231/443 (52)
Invasive carcinomas				190/486 (39)	231/393 (59)

*Staging by Union International Contra le Cancrum's TNM classification.[3]
†Two cases of malignant cystosarcoma phyllodes in study group and three in control group and one case of fibrosarcoma in each group were not staged. Stage was unknown in six cases in study group.

TABLE IV—*Cumulative rate of stage II-IV breast cancers* per 100 000 woman years after entry into study*

Year after entry	Control group	Study group
1	152	196
2	286	287
3	401	398
4	513	500
5	661	584
6	795	654
7	890	749
8	971	831
9	1111	930
10	1210	980

*Staged by Union International Contra le Cancrum's TNM classification.[3]

TABLE V—*Numbers (percentages) of women with breast cancer given surgical treatment, adjuvant hormone therapy, chemotherapy, and radiotherapy according to stage of disease. Some women were given more than one treatment*

	Stage 0		Stage I		Stage II		Stage III		Stage IV	
	Control group (n=50)*	Study group (n=92)	Control group (n=161)	Study group (n=294)	Control group (n=170)	Study group (n=142)	Control group (n=27)	Study group (n=26)	Control group (n=28)	Study group (n=21)
Breast preserving surgery	9 (18)	31 (33)	54 (34)	95 (32)	15 (9)	7 (5)		2 (8)	2 (7)	2 (10)
Mastectomy	24 (48)	43 (47)	102 (63)	197 (67)	154 (91)	135 (95)	23 (86)	21 (81)	13 (47)	8 (38)
Subcutaneous mastectomy	17 (34)	18 (19)	5 (3)	2 (1)	1 (1)					
Hormone therapy	1 (2)		2 (1)	6 (2)	66 (39)	60 (42)	11 (39)	6 (23)	19 (67)	8 (38)
Chemotherapy	1 (2)				17 (10)	11 (8)	7 (27)	4 (15)	16 (56)	11 (53)
Radiotherapy	1 (2)	6 (7)	64 (40)	123 (42)	119 (70)	106 (74)	22 (81)	22 (85)	3 (11)	3 (16)

*Data on treatment not available for some patients.

TABLE VI—*Cause of death (according to national registry) in study and control groups from date of entry into screening trial until 31 December 1985*

Cause of death (ICD code*)	Study group (n=21 088): No of deaths	% Of all deaths	% Of group	Control group (n=21 195): No of deaths	% Of all deaths	% Of group
Malignant tumours (140-239)	707	39·8	3·35	739	40·8	3·49
Cardiovascular diseases (390-458)	721	40·6	3·42	673	37·2	3·18
Respiratory diseases (460-519)	97	5·5	0·46	111	6·1	0·52
Diseases of gastrointestinal tract (520-577)	47	2·6	0·22	44	2·4	0·21
Diseases of urogenital tract (580-629)	16	0·9	0·08	20	1·1	0·09
Injuries, suicide, and unknown causes of death (800-999)	100	5·6	0·47	120	6·6	0·57
Other	89	5·0	0·42	102	5·6	0·48
Total	1777	100	8·42	1809	100	8·54

*ICD=International Classification of Diseases (eighth revision).[4]

mainly in the younger cohort and during the first six years of the study. In the older cohort the study group had fewer deaths from breast cancer than the control group during the last three years of the study and in 1987. In the younger cohort 29% more women in the study group than the control group died of breast cancer (28 *v* 22; relative risk 1·29, 95% confidence interval 0·74 to 2·25), whereas in the older cohort 21% fewer women in the study group died of breast cancer (35 *v* 44; relative risk 0·79, 95% confidence interval 0·51 to 1·24).

Discussion

Malmö is a city in southern Sweden with roughly 230 000 residents. It has a fairly stable population, the yearly migration rate to and from the city being about 2% in the age groups participating in this study. The number of woman years lost/1000 women/year owing to breast cancer before age 65 equalled the average for Sweden in the five years preceding the screening programme.[6]

The purpose of the study was to assess whether repeated invitation to mammography reduces mortality from breast cancer. By the predetermined end of this study no significant reduction had occurred in the study group, which is at variance with results of a study conducted in the Swedish counties of Kopparberg and Östergötland.[7]

TABLE VII—*Number (percentage) of patients with breast cancer alive, dead from breast cancer, and dead from other causes at end of follow up period 31 December 1986. Cause of death was assessed by an independent committee*

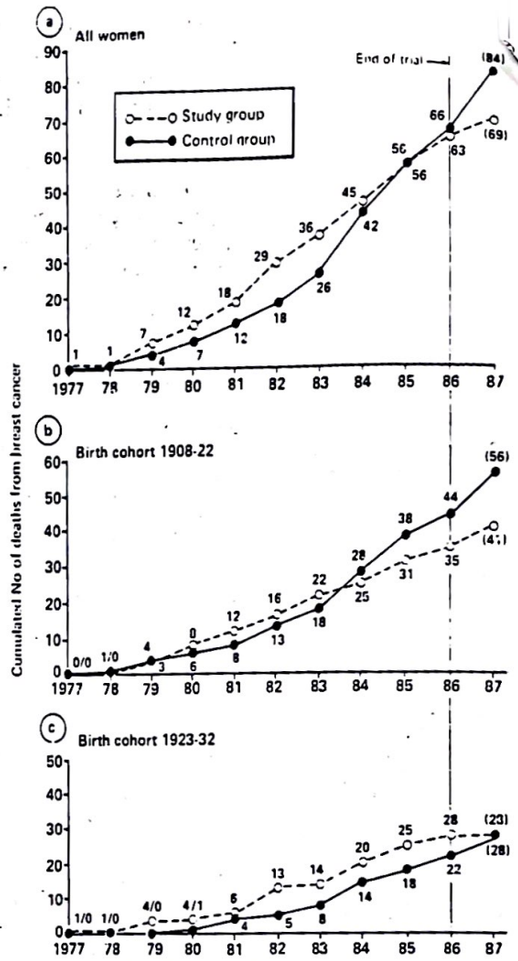
	Cancer detected in study group				Cancer detected in control group*
	At screening	In intervals between screening	In non-attenders	Total*	
		Stage 0			
Alive	60 (16)	24 (24)	7 (7)	91 (16)	48 (11)
Dead from breast cancer	1 (<1)			1 (<1)	1 (<1)
Dead from other causes			1 (1)	1 (<1)	1 (<1)
		Stage I			
Alive	221 (59)	27 (27)	16 (15)	264 (45)	151 (34)
Dead from breast cancer	4 (1)	4 (4)	1 (1)	9 (2)	5 (1)
Dead from other causes	16 (4)	2 (2)	5 (5)	23 (4)	6 (1)
		Stage II			
Alive	58 (16)	22 (22)	32 (30)	112 (19)	130 (29)
Dead from breast cancer	6 (2)	9 (9)	6 (6)	21 (4)	28 (6)
Dead from other causes	4 (1)	2 (2)	3 (3)	9 (2)	14 (3)
		Stage III			
Alive	2 (1)	2 (2)	6 (6)	10 (2)	14 (3)
Dead from breast cancer	1 (<1)	5 (5)	7 (7)	13 (2)	9 (2)
Dead from other causes	1 (<1)		2 (2)	3 (1)	4 (1)
		Stage IV			
Alive			3 (3)	3 (1)	7 (2)
Dead from breast cancer		2 (2)	17 (16)	19 (3)	22 (5)
Dead from other causes					3 (1)
		All stages			
Alive	341 (91)	76 (76)	65 (61)	482* (83)	353† (79)
Dead from breast cancer	12 (3)	20 (20)	31 (29)	63 (11)	66 (15)
Dead from other causes	21 (6)	4 (4)	11 (10)	36 (6)	28 (6)
Total	374 (100)	100 (100)	107 (100)	581 (100)	447 (100)

*In addition seven patients in study group whose breast cancer was diagnosed after they moved out of Malmö were still alive.
†Two cases of malignant cystosarcoma phyllodes in study group and three in control group and one case of fibrosarcoma in each group were not staged. Stage was unknown in six cases in study group.

TABLE VIII—*Deaths from breast cancer until end of December 1985. Potential influence on outcome of using different sources of information and different criteria for establishing end point*

	Study group	Control group
End point assumed by end point committee*	56	56
Excluding patients with breast cancer diagnosed before entry	53	52
Including all patients with breast cancer metastases irrespective of underlying cause of death	58	62
End point based on official statistics*	54	57
Excluding existing breast cancer	50	52

*Death from breast cancer diagnosed during study.



Cumulative number of deaths from breast cancer in study and control groups by calendar year (and preliminary data for 1987). (a) All women. (b) Women ≥55 years at entry into study. (c) Women <55 years at entry

TABLE IX—*Number of deaths from breast cancer and cumulative mortality by year after entry into study*

Years after entry	Control group: No of deaths	Control group: Cumulative mortality (per 100 000 woman years)	Study group: No of deaths	Study group: Cumulative mortality (per 100 000 woman years)
1			1	4·8
2	6	28·7	4	24·0
3	1	33·5	3	38·5
4	3	48·1	7	72·6
5	7	82·5	11	126·9
6	8	122·1	9	171·6
7	13	187·1	9	216·8
8	13	253·0	10	267·6
9	13	329·0	7	308·7
10	2	361·8	2	341·6
Total	66*		63*	

*Relative risk (study group *v* controls)=0·96 (95% confidence interval 0·68 to 1·35, p=0·8085).

The higher case fatality rate of breast cancer in the control group illustrates the lead time and length time bias associated with screening (table VII) and cannot be taken as evidence for the effect of screening on mortality. The slightly higher mean age of patients with carcinoma in the study group compared with the control group is explained by the greater proportion of cancers detected in older women.

There are three main steps in this type of intervention: firstly, to have women attend for screening; secondly, to detect breast cancer; and thirdly, to treat the cancer. Our study differs somewhat in each of these aspects from other studies of the effects of mammographic screening.

The potential benefit associated with screening can

s—*Deaths from breast cancer and cumulative mortality in women aged ≥55 and <55 at entry into study. Mortality is per 100 000 woman years*

Years after entry	Women born 1908-22				Women born 1923-32			
	Control group		Study group		Control group		Study group	
	No of deaths	Cumulative mortality	No of deaths	Cumulative mortality	No of deaths	Cumulative mortality	No of deaths	Cumulative mortality
1							1	12·6
2	5	38·9	4	31·0	1	12·4		12·6
3	1	46·7		31·0		12·4	3	50·5
4	2	62·6	6	78·6	1	25·0	1	63·2
5	5	102·8	6	126·8	2	50·2	5	126·9
6	5	143·5	4	159·3	3	88·1	5	190·8
7	7	201·2	7	216·9	6	164·3	2	216·5
8	10	285·2	4	250·4	3	202·6	6	294·1
9	8	358·9	2	268·8	5	282·7	5	375·7
10	1	389·2	2	329·2	1	318·5	0	375·7
Total	44*		35*		22†		28†	

*Relative risk (study group *v* controls)=0·79 (95% confidence interval 0·51 to 1·24, p=0·3085).
†Relative risk (study group *v* controls)=1·29 (95% confidence interval 0·74 to 2·25, p=0·3732).

be reduced by a high rate of non-attendance. The attendance rate, especially in the older age group, was lower in our study, than in the Swedish "two county" study[7] but higher than in the Health Insurance Plan trial[2,3] and in a non-controlled breast cancer screening programme in Florence,[4] which showed a reduction in mortality from breast cancer in women invited for screening. The attendance rate in our study was similar to that in the DOM project[9] and Nijmegen projects,[10] both of which were not controlled and showed a reduced mortality from breast cancer. In our study cases of advanced breast cancer and, accordingly, deaths from breast cancer were substantially over-represented among women who did not attend for screening. It is our impression that many of these women already had cancer at an advanced stage at the time of invitation, and attending screening would not have improved the course of their disease. As the control group also contained women with advanced tumours the extent to which the attendance rate affected the results of the study is unclear.

In spite of the lower attendance rate the distribution of breast cancers by stage was similar in our study and the two county study. This may be explained by the shorter interval between examinations in our study and the more extensive use of two views rather than one at screening, which is a more sensitive technique.[11,12] The high sensitivity of our technique is confirmed by the large proportion of non-invasive carcinomas and the small median size of invasive carcinomas among cases detected by screening. Furthermore, the percentage of carcinomas detected in the intervals between screenings was not higher than in most other studies.

The results of our trial may also have been influenced by the fact that some women in the control group had mammography. Mammography was available outside the screening programme throughout the study. A random sample of 500 women in the control group showed that 24% had undergone mammography during the study period, most only once. The rate varied from 13% in women aged 65-69 at entry into the study to 35% in women aged 45-49 at entry. Twenty per cent of the breast cancers in the control group were first detected by mammography. In the two county study 13% of women in the control group had undergone mammography.[4]

In our study free access to mammography implied examinations not only of women in the control group but also of women in the study group between screenings, which accounts for the high proportion of non-invasive carcinomas detected in the intervals between screenings. Furthermore, the availability of mammography was undoubtedly one of the reasons for non-attendance in the screening programme. It is thus difficult to assess the net effect of the mammography done outside the programme.

Though the principles of treatment of breast cancer were not presented in the two county study, there is no reason to believe that they were greatly different from those practised in our trial. Also, there were no important differences in treatment of women with breast cancer in the study and control groups in our study.

The assessment of the vital state of the patients at the end of the trial was important and was performed for all of the population being studied. The validation of the end point (that is, the determination of the underlying cause of death in patients with breast cancer) was crucial. For this purpose a high rate of postmortem examination was important; the rate in this study was exceptionally high. In addition, the records of all patients with breast cancer who died in both groups were reviewed by an independent committee blinded to the identity of the patients to validate the underlying cause of death. The importance of such unbiased assessment is underlined by the fact that in at least 15 of the 193 deaths the underlying cause of death was equivocal, and there was thus the possibility of biased classification. Comparing the number of deaths due to breast cancer given in official statistics with those classified by the independent committee resulted in 10% that were discordant. Furthermore, more than one type of cancer was frequently found in the same patient, which made it hard to assess clinically which had metastasised.

The validity of causes of death other than breast cancer was not confirmed. Because the cause of death of patients with known breast cancer was validated, however, and because it is highly unlikely for undiagnosed breast cancer to cause death there is no reason to believe that unrecognised deaths from breast cancer were concealed among those listed as deaths from other causes.

The most likely effect of screening for breast cancer would be early detection of the disease, thus permitting treatment of non-invasive carcinoma and possibly of early stages of invasive carcinoma, which might prevent metastases of breast cancer. Once a cancer has metastasised local treatment is less likely to influence the course of the disease. The life cycle of breast cancer is long, lasting on average about 15 years.[13,14] Accordingly, intervention at the non-invasive or early invasive stage would not influence the death rate until several years later. The deaths during the first years of the screening programme would have been mainly of patients whose disease was at an advanced stage when it was diagnosed, and thus its course would not have been influenced by detection of the disease. Altogether 89% of the women who died from breast cancer in the study group and all of those who died from breast cancer in the control group during the first six years of the study had been diagnosed as having stage II-IV disease.

It is thus reasonable to assume that the effect of screening for breast cancer is delayed, a point that was recently considered in a review.[15] After a six year delay (counting only the deaths from 1983 to the end of 1986) our study showed a 30% reduction in mortality from breast cancer; when preliminary data from 1987 are included the reduction is 42%.

The effect of mammographic screening seems to be different in young and old women,[16] an impression that is supported by our findings. Although there was no overall effect on the mortality from breast cancer, deaths from breast cancer were reduced by 20% in women aged 55 and older at entry into the study, despite a lower participation rate in this group. This seemingly conflicting result could be explained by different tumour biology in old and young women.

Women younger than 55 in the study group had a 29% higher mortality from breast cancer. This higher mortality among younger women was also observed in the two county study.[7] Although this could be a random phenomenon, negative results of a screening examination may have falsely reassured some patients and caused a deleterious delay in diagnosis. Delayed diagnosis may be more dangerous with rapidly growing tumours than with the more slowly growing tumours.

A proportional hazards analysis of patient survival with breast cancer, stratified for stage and adjusted for age at diagnosis, gave a relative risk of 2·3 (p=0·001) for patients whose cancer was detected in the intervals between screenings compared with patients in the control group. This confirms that carcinomas detected in the intervals between screening were more malignant, stage for stage, than those occurring in the control group. It also confirms preliminary results of this study[16] but is at variance with results from the two county study reported by Holmberg *et al.*[17]

Differences in treatment were also considered as a possible explanation for the differential mortality from breast cancer in the beginning of the programme. A study of the chemotherapy and hormonal and *x* ray treatment of all patients who died during the first six years of the programme showed only minor differences between the study and control groups. There is no reason to believe that induction of cancer through irradiation would be the explanation.[18]

From a public health perspective mammographic screening remains controversial.[19,20] The different outcomes in results of breast cancer screening programmes show that it is difficult to use the results from one study to calculate the expected benefit in another population. The results of our study cannot be used to advocate introduction of mammographic screening in all ages in an urban population. Although firm conclusions cannot be drawn from analyses of subgroups in this study, our data support previous studies showing that invitation to mammographic screening for breast cancer may lead to reduced mortality from breast cancer, at least in women aged 55 and over.

We thank the members of the end point committee: Dr Stig Berglund, Dr Stig Borgström, and Dr Nils-Herman Sternby; Vivi-Maj Mirén for outstanding secretarial help and Sivert Carlsson for data systems management. This study was supported by the Swedish Cancer Society, project No 2357-B87-01XA.

1 Nemoto T, Vana J, Bedwani R, Baker HW, McGregor FH, Murphy GP. Management and survival of female breast cancer: results of a national survey by the American College of Surgeons. *Cancer* 1980;45:2917-24.
2 Shapiro S, Strax P, Venet L. Periodic breast cancer screening in reducing mortality from breast cancer. *JAMA* 1971;215:1777-85.
3 Shapiro S, Venet W, Strax P, Venet L, Roeser R. Ten- to fourteen-year effect of screening on breast cancer mortality. *JNCI* 1982;69:349-55.
4 World Health Organisation. *Manual of the international statistical classification of diseases, injuries, and causes of death; based on the recommendations of the eighth revision conference, 1965, and adopted by the nineteenth world health assembly.* Geneva: WHO, 1969.
5 Union International Contra le Cancrum. *TNM classification of malignant tumours.* 3rd ed. Geneva: UICC, 1978.
6 Sjukvårdens och socialvårdens planerings- och rationaliseringsinstitut. *Dödsorsaksstatistik som underlag för planering.* Stockholm: SPRI, 1983:258. (Rapport 122.)
7 Tabár L, Fagerberg CJG, Gad A, *et al.* Reduction in mortality from breast cancer after mass screening with mammography: randomized trial from the breast cancer screening working group of the Swedish National Board of Health and Welfare. *Lancet* 1985;i:829-32.
8 Palli D, Rosselli Del Turco M, Buiatti E, *et al.* A case-control study of the efficacy of a non-randomized breast cancer screening program in Florence (Italy). *Int J Cancer* 1986;38:501-4.
9 Collette HJA, Day NE, Rombach JJ, De Waard F. Evaluation of screening for breast cancer in a non-randomized study (the DOM project) by means of a case control study. *Lancet* 1984;i:1224-6.
10 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:1222-4.
11 Andersson I, Hildell J, Mühlow A, Pettersson H. Number of projections in mammography: influence on detection of breast disease. *AJR* 1978;130:349-51.
12 Andersson I. Radiographic screening for breast carcinoma: III. Appearance of carcinoma and number of projections to be used at screening. *Acta Radiol Diagn* 1981;22:407-20.
13 Tubiana M. L H Gray medal lecture: cell kinetics and radiation oncology. *Int J Radiation Oncology Biol Phys* 1982;8:1471-89.
14 Fournier D, Weber E, Hoeffken W, Bauer M, Kubli F, Barth V. Growth rate of 147 mammary carcinomas. *Cancer* 1980;45:2198-207.
15 Miller AB. Screening for breast cancer: a review. *Eur J Cancer Clin Oncol* 1988;24:49-53.
16 Andersson I. What can we learn from interval carcinomas? *Recent Results in Cancer Research* 1984;90:161-3.
17 Holmberg L, Tabár L, Adami HO, Bergström R. Survival in breast cancer diagnosed between mammographic screening examinations. *Lancet* 1986;ii:27-30.
18 Feig S. Radiation risk from mammography: is it clinically significant? *AJR* 1984;143:469-75.
19 Skrabanek P. False premises and false promises of breast cancer screening. *Lancet* 1985;ii:316-9.
20 Wright CJ. Breast cancer screening: a different look at the evidence. *Surgery* 1986;100:594-8.

(Accepted 11 July 1988)

The course of untreated epilepsy

R D C Elwes, A L Johnson, E H Reynolds

Abstract

As little is known about the course of untreated epilepsy the time intervals between untreated tonic-clonic seizures were examined retrospectively in a series of 183 patients presenting to a neurological department having had two to five seizures. After the first seizure a second attack had occurred within one month in 56 patients, within three months in 93, and within one year in 159. The median interval between the first two seizures was 12 weeks (95% confidence interval 10 to 18 weeks), between the second and third eight weeks (four to 12 weeks), between the third and fourth four weeks (two to 20 weeks), and between the fourth and fifth three weeks (one to four weeks). When patients who had had three, four, or five untreated seizures were considered separately a similar pattern of decreasing intervals was seen. Successive intervals between seizures could be compared in 82 patients. In 48 the interval decreased, in 16 it did not change, and in 18 it increased. These results suggest that in many patients there is an accelerating disease process in the early stages of epilepsy.

Introduction

The prognosis for controlling seizures in epileptic patients has until recently been thought to be generally unsatisfactory. In a comprehensive review Rodin reported that no more than one third of epileptic patients achieve a remission of two years, and he regarded the disorder as chronic in about 80% of patients.[1] This view was based mostly on studies of patients attending hospital clinics and institutions, where patients with chronic epilepsy tend to accumulate. Recent community and hospital based studies of patients with newly diagnosed epilepsy have shown a much more favourable prognosis. In two retrospective community studies about 70% of all patients were found to achieve a four or five year remission.[2,3] In a

rsity Department of
ology, King's College
tal, London SE5 9RS
Elwes, MRCP, *research*
ir
eynolds, FRCPSYCH,
ant neurologist

al Research Council
tistics Unit,
sbury Road,
ridge
hnson, PHD, *medical*
ian

pondence to: Dr
lds.

TABLE I
and sec
in 183 p

Interval
≤1 Mon
-2 Mon
-3 Mon
-12 Mon
-2 Year
-3 Year
>3 Year

TABLE II

From 1st
95% C
From 2n
95% C
From 3r
95% C
From 4th
95% C