MAMMOGRAPHIC SCREENING

Economic evaluation of a mammography-based breast cancer screening programme in Spain

ROBERTO GARUZ, TARSICIO FORCÉN, JUAN CABASÉS, FERNANDO ANTOÑANZAS, CRISTINA TRINXET, JOAN ROVIRA, FRANCISCO ANTÓN *

The aim of the study was to perform a cost-effectiveness analysis of a breast cancer (BC) mammography screening programme, compared to a do-nothing alternative, in Spain. Screening consisted of a biennial mammography performed on all women 50-65 years old. A marginal analysis including women 45-49 years old was also performed. With the aid of a decision tree model, the numbers of BC cases diagnosed through screening, BC cases missed by screening and false-positive BC cases were calculated. Costs were calculated by feeding local data into Markovian models and the cost-effectiveness ratio calculation was performed in a computer spread sheet. A sensitivity analysis was also conducted. Results were presented in ECUs of 1993. The cost-effectiveness ratio per avoided death is 115,500 ECUs and per saved life year 7,300 ECUs. Including women 45-49 years old in the programme raises this ratio to 229,000 and 9,400 ECUs respectively. The sensitivity analysis showed the efficacy of mammography, compliance of the programme and screening costs to be the more sensitive variables.

Key words: breast cancer, screening, economic analysis, cost-effectiveness analysis

Breast cancer (BC) is the leading cause of death due to cancer among Spanish women and specific rates of mortality have shown an upward evolution from 1953 to 1986.[1,2] Several risk factors associated with this disease are known;[3] however, most of them are not easy to modify. Since survival is related to diagnosis and treatment of the disease in early stages,[4] early detection is crucial to achieve a reduction in mortality. Three major procedures are currently used to reach an early diagnosis: breast self-examination, examination by a health professional and mammography. As will be discussed, only the latter has been shown to be effective in reducing mortality, although some debate exists about the ages at which it should be started and discontinued and about the optimal time interval between examinations.

The aim of this study was to participate, with an economic evaluation, in the wide debate concerning breast cancer that is currently taking place in Spain. We decided to evaluate screening procedures of proven efficacy in terms of mortality reduction, shown through randomized clinical trials. We evaluated, in terms of a cost-effectiveness analysis, a breast cancer screening programme based on mammography, versus the alternative option of treating only those cases already symptomatic or incidentally found (i.e. the current practice). We designed a model inspired in a programme that is currently being conducted in the Spanish Autonomous Community of Navarre. Navarre is a northern region, which has an extension of 10,000 km^2, a population of 500,000 inhabitants and a $ 13,000 per capita income. We gathered data from this programme and also from other relevant sources. The model was then applied with a nation-wide scope. Effectiveness was measured either as saved years of life or avoided deaths and only costs to the health system were considered.

* R. Garuz[1], T. Forcén[2], J. Cabasés[3], F. Antoñanzas[4], C. Trinxet[5], J. Rovira[6], F. Antón[7]
1 National Institute of Health (INSALUD), Area 3, Zaragoza, Spain
2 Navarre Institute of Health, Tafalla (Navarre), Spain
3 Navarre Public University, Pamplona (Navarre), Spain
4 University of La Rioja, Logroño, Spain
5 Department of Public Health, Catalonia, Spain
6 Central University of Barcelona, Catalonia, Spain
7 Hospital San Millán-San Pedro, Logroño, Spain
Correspondence: Fernando Antoñanzas, University of La Rioja, Departamento de Economía y Empresa, San José de Calasanz, s/n, 26004 Logroño (La Rioja), Spain, tel. +34 41 299382, fax +34 41 299393

MATERIAL AND METHODS

Decision-analysis model

To perform the cost-effectiveness analysis a decision tree was designed (*figure 1*) where 2 alternative options were compared:

- no screening programme, which is the current practice in most parts of the country and
- a mammography screening programme through personal appointments, with most women between 50 and 64 years old.

The programme simulation was done on a computer spread sheet, beginning with the cohort of women in the above-mentioned age range and incorporating or exiting every year considered a new cohort of women 50 or 65

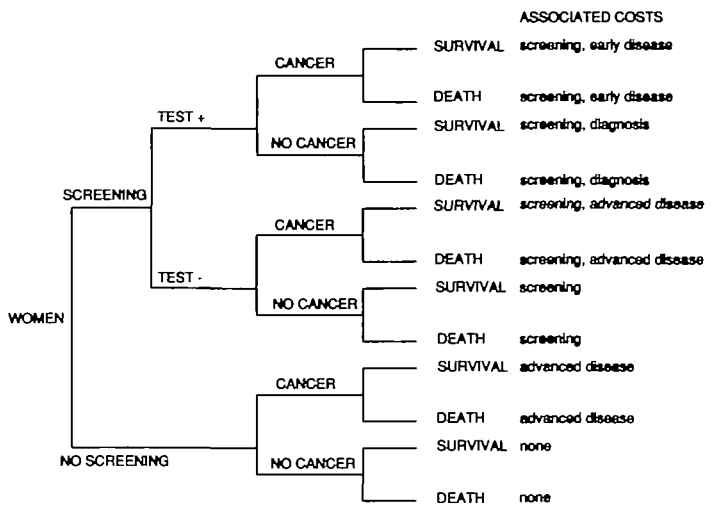

Figure 1 Decision tree for comparison of screening and non-screening alternatives

years old, from the first year and during the 25 years that the simulation lasts (since it is necessary to set a time limit to perform the economic analysis). Moreover, a marginal analysis was conducted to assess inclusion in the programme of women 45–49 years old.

The former were chosen because of the proven efficacy of mammography for that age group, the latter being the group of women included in the programme conducted in Navarre. The time between serial mammographic screenings was set at 2 years and a single-projection mammography was offered. Data were obtained from the 1991 Spanish Population Registry. Since data until the year 2015 are needed, projections were done based on age-adjusted mortality rates[1,2] *(tables 1 and 2)*. Populations were stratified by age cohorts.

In this model, 4 possible categories were defined:

- women in the population registry that can be appointed for mammography,
- women on whom mammography is performed (with or without breast cancer, true positives, false negatives, true negatives and false positives),
- women who do not attend screening (with or without breast cancer) and
- women who have died due to breast cancer or other causes.

Each category comprises a number of women for each age cohort and for each year of duration of the programme. Categories such as 'cancer' or 'death' were considered end-points to the effects of repeated screening in the following years, while 'healthy' and 'false positive' stayed within the model, according to programme compliance and while they were 64 or less years old. The time period for moving between non-end-point categories was 1 year.

The number of breast cancer patients detected by screening depended on the population of susceptible women, programme compliance, test sensitivity and age-adjusted cancer incidence. The number of cancer patients not detected by the programme depended on the values of coverage and incidence. The number of false-positive cases depended on the expected incidence, compliance of the programme and test specificity.

Table 1 Spanish population pyramid for women 45–64 years old in 1991 (per 100,000)

Age (years)	Number	General mortality rate	Breast cancer mortality rate average (lowest-highest)	Breast cancer incidence rate average (lowest-highest)
45–49	1,101,184	167	26 (25–29)	144 (106–184)
50–54	1,005,080	278	37 (33–40)	127 (110–140)
55–59	1,114,822	410	52 (48–57)	128 (118–140)
60–64	1,103,318	635	64 (55–70)	161 (137–180)

Data and assumptions

The sensitivity of mammography was estimated to be 0.90, the specificity was set at 0.98[5–7] and effectiveness at 0.24, as measured by the percentage of breast cancer mortality reduction[8] *(table 3)*. Programme compliance was set at 70%. The general mortality rates and specific breast cancer mortality rates are shown in *table 1*. The

Table 2 Projected number of women 45 or 50 years old from 1992–2015

Year	Number 45 years old	Number 50 years old
1992	222,319	181,242
1993	247,721	206,831
1994	252,184	232,688
1995	241,286	228,529
1996	234,792	245,646
1997	238,961	220,455
1998	248,956	245,644
1999	246,341	250,069
2000	248,474	239,262
2001	257,139	232,823
2002	262,045	236,957
2003	279,238	246,868
2004	283,074	244,275
2005	287,352	246,390
2006	290,941	254,983
2007	286,343	259,848
2008	290,516	277,591
2009	302,844	280,700
2010	313,971	284,942
2011	311,703	288,501
2012	306,654	283,942
2013	315,535	288,080
2014	306,892	300,304
2015	307,713	311,338

Source: Elaboration from *table 1*

mortality was calculated from cohort size and mortality rate.

Sensitivity analyses were conducted using the highest and lowest values. Each cohort was subjected to its yearly mortality risk, which includes that caused by breast cancer. In this regard, all deceased women were subjected to the risk of belonging to the remaining 3 categories even though they died throughout the year. This causes a slight overestimation of the population by the end of each year, but the additional sophistication of the model that would be needed to avoid this was not considered to be worthwhile.

The efficacy of mammography was extrapolated from relevant studies (*table 3*), considering those in which it was performed on women of similar ages and with similar time intervals.[8,10] It was measured as avoided deaths and saved years of life. This reduction in mortality is evident within the first 6 years of the programme for women 50 years or older and from the ninth year for women younger than 50 years and lasts for at least 12 years after the programme has ended. It varies according to age and programme coverage. Saved years of life were calculated from the mortality decrease due to screening and actual life expectancy. Figures of avoided deaths were presented undiscounted and also discounted at 6%.

The benefits derived from a mammography screening programme stem from an earlier diagnosis of BC, at a more limited stage and with greater chances of complete remission. This saved time was initially intended to be measured in terms of months, 1 year or 2 years. However, uncertainty about the average saved time and results from the sensitivity analysis (which demonstrated almost no changes in the final results) made us choose a simplification of the model in such a way that the annual number of cases of BC was similar to the expected incidence since the beginning of the programme.

To gather all necessary data, we combined several information sources, including the aforementioned Navarre Screening Program, Guipuzcoa (a nearby province) Cancer Registry, National Epidemiology Center, National Statistics Institute, Fundación Jiménez Díaz Hospital and results from several studies conducted in Sweden.[8,9]

Costs calculation

▪ Programme costs

Only direct costs to the health system were considered. Costs generated by screened women (transportation, loss of working hours, mammography-associated intangible costs) were not taken into account. The costs were divided into fixed (independent of the number of screened women) and variable (depending on that number). Fixed costs include human resources, advertising, information and amortizations. Variable costs include repairing and maintenance of mammographic equipment, X-ray film, travelling expenses, stationery, training activities, other activities and other expenses (*table 4*). The average cost per screened women depended on programme compliance and was set at 27 ECUs. All these data were taken from the Navarre Screening Programme. These costs include those derived from diagnosis and treatment of mammographic screening-induced tumours. The risk for women having a yearly mammography is 150 per 1,000,000,[12–14] which in our model accounts for a total of 225 tumours with an updated cost of 46,406 ECUs per year.

▪ Diagnosis-associated costs

Diagnostic processes and diagnostic costs depend on how BC presents and tend to be lower in women diagnosed through mammography. Also, false-positive women undergo less diagnostic tests once BC has been ruled out. Thus, 3 diagnostic cost categories exist: BC diagnosed through mammography, 'interval' BC and false-positive BC. Since the number of tests performed depends on the

Table 3 Data an assumptions used for cost-effectiveness analysis

Variable	Mean value	Range	Reference
Sensitivity	0.90	0.71–0.90	5, 7
Specificity	0.98	0.94–0.99	5, 6, 7
Compliance	0.70	0.60–0.85	9
Efficacy according to age (years)			8, 10
45–49	0.13	0.37–0.00	
50–54	0.29	0.43–0.11	
55–59	0.29	0.44–0.09	
60–64	0.06	0.40–0.00	
Costs			
Treatment costs[a]	3,378	3,378–5,493	9, 11
Diagnostic costs[a]	631	455–631	9, 11
Treatment costs[b]	2,699	2,699–4,109	9, 11
Diagnostic costs[b]	454	275–454	9, 11
Diagnostic costs[c]	176		
Cost per screened woman	27	23–31	

a: Cost per non-screened woman
b: Cost per screened woman
c: Cost of diagnostic evaluation of false-positive cases
All costs are in ECUs referred to 1993

Table 4 Annual costs of screening programme (in million ECUs)

Fixed costs		Variable costs	
Human resources	19,345	Repairs and maintenance	2,629
Advertising and information	3,265	X-ray film	1,857
Initial investments amortization	1,733	Stationery	855
Start-up cost amortization	362	Travelling expenses	1,030
Computer hardware amortization	185	Other expenses	144
		Training activities	43
		Other activities	265
Total fixed cost	24,892	Total variable cost	6,826
Total annual cost[a]	31,765		

a. Includes mammography-induced tumour costs, estimated at 46,405 ECUs/year
Source: Navarre Breast Cancer Screening Programme

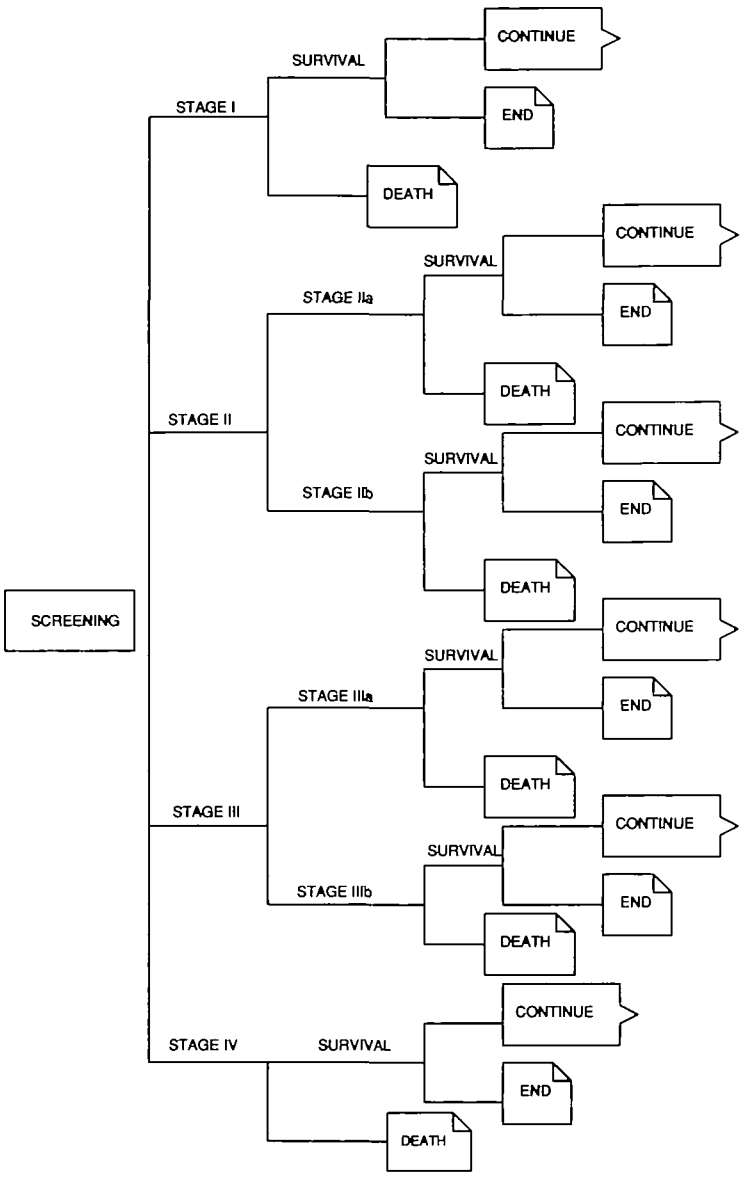

Figure 2 Decision tree for calculation of BC treatment and follow-up costs

tumour stage, the highest and lowest costs were considered, which included all possible tests or only chest X-ray and bone gammagraphy as extension diagnosis tools. Diagnostic processes and their associated costs are shown in *table 5*. To perform a cost-effectiveness analysis the highest costs were used, since current tendencies are toward performing a high number of tests.

- Health care costs

To calculate BC treatment and follow-up costs, a decision tree based on Markovian models was used (decision trees computer program SMLTREE, copyright Jim Hollenberg, 1989). This programme allows the design of a dynamic model in which the different stages of the disease occur according to predefined probabilities. This process simulated a cohort of women diagnosed as having BC. According to lymph node involvement, 4 stages of the disease were considered. This is depicted in a tree-like structure with its branches representing the possible stages *(figure 2)*. Each stage had its own survival and costs associated. This simulation, named

Table 5 Diagnostic costs (in ECUs)

Diagnostic category	Probability	Procedures	Unitary cost	Average cost	Lowest cost
Natural evolution				631	455
Unilateral discharge	0.037	Medical care, mammography, galactography	136		
Bilateral discharge	0.003	Medical care, mammography, cytology, prolactin levels, sella turcica X-ray, CT scanning	226		
Non-palpable mass	0.18	Medical care, mammography, localizing X-ray, needle biopsy	228		
Palpable mass	0.78	Medical care, mammography, ultrasonography, needle biopsy	211		
Diagnosis/staging		Biopsy, hormone receptor assay, carcinoembryonic antigen, chest X-ray, bone scanning, liver ultrasonography, CT scanning, biochemistry	420		
Screening		Needle biopsy, biopsy, hormone receptor assay, carcinoembryonic antigen, liver gammagraphy and ultrasonography, CT scanning, biochemistry	454	454	275
False positive		Needle biopsy, biopsy	176	176	176

Source: Jiménez Díaz Foundation analytical accounting

Monte Carlo,[15,16] entered cohort patients into the tree 1 by 1, in different branches according to pre-set probabilities. The tree is a dynamic and recurrent model in which time is represented by cycles (1 cycle is 1 year). The structure of the first cycle is repeated in each new cycle until the simulation ends, changing the value of the variables. Simulation ended when the whole cohort had reached any of the considered end-points. One of them is 'death' and the other the considered follow-up limit, 'end'. The process stopped when all the patients reached 1 of these end-points. Results were presented as the average cost per patient. With the aid of this decision tree, an average cost of lifelong treatment and follow-up of a cohort of women with BC is calculated. Disease stage distribution is taken from the Navarre programme. An average cost was also calculated for women who do not attend screening, with stage distribution taken from the Guipuzcoa Cancer Registry. The variables remained unchanged except for stage distribution, since this is favourably affected by an earlier diagnosis. The mean survival rates associated with each stage were taken from the Guipuzcoa Cancer Registry (*table 6*). Since this offered only 10 year survival, a proportional extrapolation was made considering survival from 10 to 100 years, this latter value being 0. Distribution by stages was also taken from the Guipuzcoa Cancer Registry and from the Navarre Screening Programme (*table 6*). Non-classified cases were proportionately assigned to all stages. Moreover, a variable was introduced in both alternatives representing hospital admissions due to complications indirectly related to the disease and its treatment. These exist but are very difficult to quantify, since admissions are registered by diagnoses not related to BC. The model simulated 15 cycles. Costs associated with each stage were included in 3 categories: surgery costs, follow-up costs and associated therapies costs (*table 7*). Surgery costs are those directly related to surgical intervention, whatever procedure is performed. Follow-up costs include follow-up visits and related diagnostic tests. Associated therapies are chemotherapy, radiation therapy and hormone therapy. Since chemotherapy and hormone therapy administration depend on menopausal status, lymph node involvement and hormone receptor presence or absence, costs were weighed according to these factors and estimated for both evaluated options. Therapeutic protocols were based on current literature and an expert pannel opinion.[9,11] The basic costs calculation model was assigned a discount rate of 6% and the model which included admissions due to complications of advanced stages was assigned 3 and 6%. The latter was the one used for cost-effectiveness analysis.

Table 6 Distribution by stages and associated survival

	With programme[a] %	Without programme[b] %	5 year survival %	10 year survival %
Stage				
I	64.7	13.1	88	75
IIa	21.1	25.0	74	59
IIb	12.4	23.6	72	49
IIIa	0.7	14.4	55	43
IIIb	0.7	14.4	39	12
IV	0	9.1	15	0

a: Source: Navarre Screening Programme
b: Source: Guipuzcoa Cancer Registry.

Cost-effectiveness analysis

As already mentioned, the cost-effectiveness ratio calculation was performed with the aid of a dynamic compartmental model simulated in a computer spread sheet. It allowed the integration of the following parameters: screening costs, diagnostic costs, mammography sensitivity and specificity, health care costs, discount rate and potential efectiveness of the evaluated programme, measured by avoided deaths or saved years of life. Future costs and benefits were updated at a 6% discount rate.

The cost-effectiveness ratio is calculated as the additional or net incremental cost per life year saved or avoided

Table 7 Cost of breast cancer treatment (in ECUs)

Type	Procedures		Average cost
Surgery	Tumourectomy	5.5 day admission, 1 h. surgery room, blood count, biochemistry, biopsy, ECG, skin microscopy	1,293
Follow-up	Mastectomy	10 day admission, 2 h. surgery room, blood count, biochemistry, biopsy, ECG, mammography, chest X-ray, skin microscopy	2,459
	First year	4 out-patient visits, 3 blood counts and biochemistries, mammography, breast ultrasonogram and needle biopsy (if tumourectomy); optional CT scanning and liver or bone gammagraphy	286
	Second and third years	2 out-patient visits, blood count, biochemistry, mammography, breast ultrasonogram and needle biopsy (if tumourectomy), chest X-ray; optional CT scanning and liver or bone gammagraphy	257
	From fourth year	Yearly out-patient visit, blood count, biochemistry, mammography, breast ultrasonogram, needly biopsy (if tumourectomy), chest X-ray; optional: CT scan, bone or liver gammagraphy	247
Adjuvant therapy	With programme	Hormone therapy, chemotherapy	774
	Without programme	Hormone therapy, chemotherapy	897
Radiotherapy		25 sessions, 1% needing 8 day admission	576

Source: Jiménez Díaz Foundation analytical accounting

death with the screening programme, in comparison with the no-programme alternative. For women 45–49 years old, a marginal analysis was performed and the results are presented as marginal costs of avoiding a death or saving an extra year of life.

Sensitivity analysis

Sensitivity analysis was performed in those cases in which there was uncertainty regarding the validity of data. Since the aim of the programme was to reach an earlier diagnosis, this saved time was intended to be measured in terms of months, 1 year or 2 years. As already mentioned, a sensitivity analysis was also performed regarding this point.

Besides the basic scenario, 13 more possible scenarios are shown. In these, the following variables were changed: highest incidence and mortality associated with BC, programme compliance (60 and 85% instead of 70%), specificity (0.99 or 0.94 instead of 0.98), highest and lowest efficacy (several values depending on age groups) and a discount rate of 3%. Diagnosis costs, as stated, were extremely variable and were also subjected to sensitivity analysis. Two additional scenarios combining the highest and lowest values of several variables are presented. Results are presented both as additional cost per avoided death and saved years of life. The former is also presented both discounting and not discounting avoided deaths.

RESULTS

The biennial mammography screening programme strategy generates, in all analysed scenarios, an additional cost per avoided death as well as per life year saved when compared to the no-screening alternative. For the base scenario assumptions (*table 8*), the net cost of the programme during the 25 years it lasts would be 504 million ECUs (compliance 70%), 20% of that amount being costs associated to false-positive cases evaluation. The cost-effectiveness is 115,500 ECUs per avoided death discounted and 7,300 ECUs per life year discounted. The slight economic advantage due to the smaller costs of BC cases detected through screening mammography is outweighed by programme implementation and maintenance costs. The marginal cost stemming from the incorporation of women 45–49 years old is 229,000 ECUs per avoided death and 9,400 ECUs per saved year of life.

The programme could diagnose, with base compliance, 74,000 BC cases, with a per case cost of 7,230 ECUs. An additional 62,000 cases would escape screening. Early detection could avoid 3 deaths due to BC among every 1,000 women over the 25 years the programme lasts.

The sensitivity analysis results (*table 9*) show that the most sensitive variables are, in decreasing order, efficacy of mammography, specificity, compliance, screening costs, mortality and incidence, discount rate, diagnosis and treatment costs and sensitivity. The results for the combination of the several highest and lowest values range from 300 ECUs per life year gained in the most favourable option and without discounting, to 48,000 ECUs in the most unfavourable option and with discounted effects.

DISCUSSION

In this study, an economic evaluation using a cost-effectiveness analysis technique was performed in a breast cancer screening programme based on mammography. The aim of screening programmes is to reach an earlier diagnosis of breast cancer and, hence, to find the disease at a more limited stage which is associated with a higher chance of survival.[4] Three major techniques are currently used: self-examination, examination by health personnel and mammography. We chose to evaluate a technique whose efficacy was confirmed through controlled and randomized clinical trials.

Several studies have evaluated the impact of mammographic screening on survival. The Health Insurance Plan

Table 8 Cost-effectiveness analysis results (in thousands of ECUs)

	With screening	Without screening	Difference	Marginal analysis (women 45–49 years)
Costs				
Screening	504,021[a]		504,021	166,630
Diagnosis	35,983	42,516	–6,533	–2,126
Treatment and follow-up	202,544	227,606	–25,062	–8,155
Total	743,202	270,122	472,426	156,349
Effects				
Deaths due to breast cancer	92,490	105,810	13,320	682
Life years saved	223,751		223,751	17,344
Cost-effectiveness				
Per avoided death (not discounted)	38.4			229
Per avoided death (discounted)	115.5			
Per saved life year (not discounted)	2.1			9.4
Per saved life year (discounted)	7.3			

a: Includes false-positive cases diagnostic costs

(HIP) study,[17,18] conducted in the New York Metropolitan area, randomly assigned women to yearly mammographies during a 4 year period or to usual health care. Survival in screened women improved by 29% at the 10 year follow-up. There was an early improvement in survival for women 50–59 years old, a slight improvement for women older than 60 years and no effect for those less than 50 years.[19] The Swedish two-county study[20] evaluated screening with single-projection mammography in women 40–74 years old, performed every 2 years in women 40–49 years old and every 33 months in women older than 50 years. A reduction in mortality of 31% was shown at 5 and 9 years in the screened group, but it was restricted to women older than 50 years. The Malmö study[10] offered initial two-projection mammography followed every 18–24 months by single- or double-projection mammography to women 45–69 years old. In fact it showed an increase in mortality for screened women during the early years. Survival rates were lower for women younger than 55 years, and decreased by 20% for those older than 55 years. However, these results were biased by the high number of women from the control group who underwent mammography. The BCDDP study[21–23] lacked a control group, but compared to historic controls,[24] screened women had higher survival rates at 5 years. The main controversies regarding mammography are its efficacy on women younger than 50 years[10,23,25–27] and the optimal time interval between serial examinations.[28]

Screening costs used in this study are those corresponding to the Navarre Screening Programme. The geographic characteristics of this area made it necessary to use 2 mammography units, 1 of them itinerant and to make personal appointments with all screened women. This allows a maximal performance of both units and a high compliance with the programme.[29,30] Extrapolation of these parameters to different geographic areas can cause serious bias of the final results.

Only direct costs to the health system were taken into account and costs generated to attending women were not considered. Indirect costs such as the lack of productive capacity of women were not considered. Inclusion of indirect effects in economic evaluation is a matter of ethical controversy, since it can discriminate negatively the non-employed population and since effectiveness is measured as gained life years, a double accounting could be performed by adding up benefits of more productive years in the numerator of the cost-effectiveness ratio.

Some programme-associated costs are of great importance but very difficult to quantify and are thus named intangible costs. These include the loss in quality of life due to the mammography itself, anxiety, depression, loss of self-esteem and of body image, fear of disfiguration and sexual dysfunctions – all of which reduce the effectiveness of the programme. A wider approach such as cost-utility analysis[31] could overcome these limitations.

In addition, in the absence of screening programmes, it is likely that some mammographies would have been performed with screening and not diagnostic purposes; the related costs would have to be subtracted from the screening programme costs. Since these figures are extremely difficult to ascertain we did not make this correction; however, it is estimated that it could represent a 20% reduction in screening programme costs.[32]

A defined diagnostic and therapeutic protocol was considered, which included no indirect or intangible costs. However, no single diagnostic or therapeutic approach exists and this makes comparisons between studies more difficult. Some authors have suggested that the main determinant of treatment is the physician rather than type or stage of cancer.[31] Treatment with a screening programme is less expensive since late stages of the disease are likely to generate higher costs.

A discount rate has been applied to both the costs and results. Initially a 6% value was used, but decreasing interest types make lower rates more realistic. In this way,

Table 9 Sensitivity analysis results

Scenario	Breast cancer mortality	Breast cancer incidence	Compliance %	Costs	Specificity	Efficacy	Discount rate %	C/E (ND)	C/E (D)
Base	Average	Average	70	Average	0.98	Average	6	2.1	7.3
1	Lowest	Lowest	70	Average	0.98	Average	6	2.6	9
2	Highest	Highest	70	Average	0.98	Average	6	2	7.3
3	Average	Average	60	Average	0.98	Average	6	2.9	10
4	Average	Average	85	Average	0.98	Average	6	1.6	5.6
5	Average	Average	70	Average	0.94	Average	6	3.2	11.2
6	Average	Average	70	Average	0.99	Average	6	2	7.2
7	Average	Average	70	Average	0.98	Lowest	6	6.9	24.7
8	Average	Average	70	Average	0.98	Highest	6	1.5	5.3
9	Average	Average	70	Average	0.98	Average	3	3.2	6.9
10	Average	Average	70	Lowest	0.98	Average	6	2.3	8
11	Average	Average	70	Highest	0.98	Average	6	2.2	7.6
12	Lowest	Lowest	60	Average	0.94	Lowest	6	13.3	48
13	Highest	Highest	85	Average	0.99	Highest	6	0.3	1

C/E (ND): cost-effectiveness, effects not discounted, in thousands of ECUs
C/E (D): cost-effectiveness, effects discounted, in thousands of ECUs

a 3% rate was also analysed, the result being an important increase in programme costs of approximately 39%. However, when saved life years were updated according to the discount rate, the cost per avoided death was lower for 3% than for 6% (6,900 versus 7,300 ECUs). This can be explained by the lower decrease in the value of each death, which happens in a time horizon wider than the programme, when discounting at 3%.

The results were always more favourable for women of 50–64 years of age than for women of 45–64 years of age. The explanation is straightforward: screening costs are higher and screening effectiveness is lower for the additional group. Similar results were obtained elsewhere.[33] The marginal costs of widening the programme scope to this age group are 229,000 ECUs per avoided death and 9,400 ECUs per gained year of life, in the base scenario.

The sensitivity analysis results are similar to those obtained by Gravelle et al.[34] Efforts aimed at quality control with high standards for mammography and its interpretation, optimal performance of mammography units and high compliance, will all guarantee a higher programme efficiency. Medical diagnostic and therapeutic costs do not seem to be very determinant. The current tendencies of incidence and mortality[1] could yield a slightly better cost-effectiveness ratio, if other variables remain unchanged.

There are very few published studies on breast cancer screening programmes, and they are very difficult to compare since the design, included costs, discount rates and economic evaluation techniques are different. A recent review of 13 cost-effectiveness studies[35] showed that 1 gained year of life ranked in cost from 688 to 34,600 US dollars in 1987 (approximately 790–39,800 ECUs in 1993). Low-cost studies tended to be limited to screening and biopsy and did not consider treatment or other costs. Our study estimated that the cost per gained year of life was 7,300 ECUs as referred to 1993.

Some of these evaluations[36–38] were based upon randomized controlled studies such as the HIP and the Swedish two-county study. The studies by Van der Maas,[37] Moskowitz[38] and White et al.[39] are methodologically similar to ours. Van der Maas[37] collected data from Swedish studies and from others conducted in Utrecht and Nijmegen, The Netherlands. Women 50–70 years old were screened every 2 years. The screening cost included the time and travelling costs generated by the women. It also included diagnostic costs of true- and false-positive cases and the costs of treatment, surgery, adjuvant therapies and treatment of advanced-stage disease. Among the effects of the programme, generation of employment was considered. The length of the programme was 25 years. All costs and effects were discounted at a 5% rate, with a sensitivity analysis considering 0 and 7% rates. The results were expressed as cost ratio per gained year of life (9,700 florins or 5,200 ECUs in 1993) and per avoided death (102,000 florins or 55,000 ECUs in 1993). A recently published meta-analysis on most known randomized trials[40] has been criticized because it integrates quite heterogeneous studies, some of which include physical examination in addition to mammography.[41]

The usual care options are changing over time, in Spain as well as in many other countries and, thus, cost-effectiveness ratio values can be misleading when a wide programme time horizon is considered. It is probable that, despite all the efforts expended in assessing the efficiency of a programme such as the one we evaluated, more clinical research is needed regarding the patterns of stage distribution according to diagnostic and screening procedures before definite conclusions can be reached. The health effects generated by the Navarre programme may not be immediately attainable in the rest of Spain. Moreover, it would be desirable to better know the BC incidence rates in Spain, as if rates were lower than in North European countries, the programme might be less efficient. In Spain, health resources could be assigned to other programmes dealing with more basic needs, because the Spanish health system, at least in some areas, is not yet as developed as in other countries. In our opinion, waiting for the final results of the Navarre programme (available in a few years) would be a wise attitude before implementing a similar nation-wide programme, and would guarantee more efficient utilization of limited public health resources.

This research has been partially supported by grant number 92/0903 from the Fondo de Investigaciones Sanitarias (Health Research Fund) of the Spanish Ministry of Health for which we are very grateful.

We also wish to thank Fundación Jiménez Díaz and Navarre Department of Health, especially to Mrs. Nieves Ascunce and Mr. Angel del Moral, for kindly providing us with some of the data used in this study.

REFERENCES

1 López-Abente G, Pollan M, Ruiz M, et al. La mortalidad por cáncer en España, 1953-1986: Efecto de la edad, de la cohorte de nacimiento y del período de muerte (Cancer mortality in Spain, 1953-1986: effects of age, birth cohort and year of death). Madrid: Servicio de Epidemiología del Cáncer, Centro Nacional de Epidemiología, 1992.

2 Gorgojo L. Cáncer en España, 1986-1987 (Cancer in Spain, 1986-1987). Madrid: Dirección General de Salud Pública, Ministerio de Sanidad y Consumo, 1991.

3 Kelsey J, Gammon MD. Epidemiology of breast cancer. Epidemiol Rev 1990;12:228-40.

4 Strax P. Control of breast cancer through mass screening: from research to action. Cancer 1989;63:1881-7.

5 Baines CJ, McFarlane DV, Miller AB. Sensitivity and specificity of first screen mammography in 15 NBSS centres. Can Assoc Radiol J 1988;39:273-6.

6 Eikiden S. Mammography and palpable cancer of the breast. Cancer 1988;61:263-5.

7 Peeters PH, Verbeek AL, Hendricks JH, et al. The predictive value of positive test results in screening for breast cancer by mammography in the Nijmegen programme. Br J Cancer 1987;56:667-71.

8 Nystrom L, Rutqvist LE, Wall S, et al. Breast cancer screening with mammography: overview of Swedish randomised trials. Lancet 1993;341:973-8.

9 Ascunce N, Del Moral A. Programa de detección precoz de *cáncer de mama en Navarra (Breast cancer early detection* program in Navarre). Pamplona: Departamento de Salud, Gobierno de Navarra, 1991.

10 Andersson I, Aspegren K, Janzon L, et al. Mammographic screening and mortality from breast cancer: the Malmö mammographic screening trial. BMJ 1988;297:943-8.

11 Fernández-Cid A. Protocolos de ginecología del Instituto Dexeus. Patología mamaria maligna (Dexeus Institute Gynecology

protocols. Malignant breast diseases). Barcelona: Salvat Editores, 1991.

12 Feig SA, Ehrlich SM. Estimation of radiation risk from screening mammography: recent trends and comparisons with expected benefits. Radiology 1990;174:638-47.

13 Gohagan JK, Darby WP, Spitznagel EL, Monsees BS, Tome AE. Radiogenic breast cancer effects of mammographic screening. J Natl Cancer Inst 1986;77:71-6.

14 Hurley SF, Kaldor JM. The benefits and risks of mammographic screening for breast cancer: epidemiologic reviews. Johns Hopkins Univ School Hygiene Public Health 1992;14:101-30.

15 Doubilet P, Begg CB, Weinstein MC, Braun P, McNeil BJ. Probabilistic sensitivity analysis using Monte Carlo simulation. Med Decision Making 1985;5:157-77.

16 Beek J, Paukes SG. The Markov process in medical prognosis. Med Decision Making 1983;3:411-58.

17 Shapiro S, Strax P, Venet L. Periodic breast cancer screening in reducing mortality from breast cancer. JAMA 1971;215:1777-85.

18 Chu KC, Smart CR, Tarone RE. Analysis of breast cancer mortality and stage distribution by age for the Health Insurance Plan clinical trial. J Natl Cancer Inst 1988;80:1125-32.

19 Shapiro S, Venet W, Strax P. Ten-to-fourteen-year effect of screening on breast cancer mortality. J Natl Cancer Inst 1982;69:349-55.

20 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 Working Group of the Swedish National Board of Health and Welfare. Lancet 1985;i:829-32.

21 Baker LH. Breast Cancer Detection Demonstration Project: five-year summary report. Cancer J Clin 1982;32:194-225.

22 Morrison AS, Brisson J, Khalid N. Breast cancer incidence and mortality in the Breast Cancer Detection Demonstration Project. J Natl Cancer Inst 1988;80:1540-7.

23 Bailar JC. Mammography before age 50 years? JAMA 1988;259:1548-9.

24 Seidman H, Gelb SK, Silverberg E, et al. Survival experience in the Breast Cancer Detection Demonstration Project. Cancer 1987;37:258-90.

25 Eddy DM, Hasselblad V, McGivney W, et al. The value of mammography screening in women under age 50 years. JAMA 1988;259:1512-9.

26 Dodd GD, Taplin S. Is screening mammography routinely indicated for women between 40 and 50 years of age? J Family Pract 1988;27:313-20.

27 Verbeek ALM, Hendricks JHCL, Hollan PR, et al. Reduction of breast cancer mortality through mass screening with modern mammography: first results of the Nijmegen Project, 1975-1981. Lancet 1984;i:1222-4.

28 Tabar L, Fagerberg G, Day NE, et al. What is the optimum interval between mammographic screening examinations? An analysis based on the latest results of the Swedish two-county breast cancer screening trial. Int J Cancer 1987;55:547-51.

29 Fox SA, Murata PJ, Stein JA. The impact of physician compliance on screening mammography for older women. Arch Intern Med 1991;151:50-6.

30 Zapka JG, Stoddard AM, Constanza ME, Greene HL. Breast cancer screening by mammography: utilization and associated factors. Am J Public Hlth 1989;79:1449-502.

31 Hall J, Gerard K, Salked G, Richardson J. A cost-utility analysis of mammography screening in Australia. Soc Sci Med 1992;34:993-1004.

32 Gerard K, Salkeld G, Hall J. Counting the costs of mammography screening: first year results from the Sidney study. Med J Austral 1990;152:466-71.

33 Carter R, Glasziou P, Oortmarsen GV, et al. Cost-effectiveness of mammographic screening in Australia. Austral J Public Hlth 1993;17:42-50.

34 Gravelle HSE, Simpson PR, Chamberlain J. Breast cancer screening and health service costs. J Hlth Econ 1982;1:185-207.

35 Elixhauser A. Costs of breast cancer and the cost-effectiveness of breast cancer screening. Int J Tech Assess Hlth Care 1991;7:604-5.

36 Clarke PR, Fraser N. An economic analysis of breast cancer screening. Bath: Health Economics Study Group Meeting, University of Bath, 1986.

37 Van der Maas PJ. The costs and effects of mass screening for breast cancer. Rotterdam: Department of Public Health and Social Medicine, Erasmus University, 1988.

38 Moskowitz M. Cost of screening for breast cancer. Rad Clin North Am 1987;25:1031-7.

39 White E, Urban N, Taylor V. Mammography utilisation, public health impact and cost-effectiveness in the United States. Ann Rev Public Hlth 1993;14:605-33.

40 Simpson KN, Snyder LB. Informing the mammography coverage debate. Int J Tech Assess Hlth Care 1991;7:616-31.

41 Skrabanek P. The cost-effectiveness of breast cancer screening. Int J Tech Assess Hlth Care 1991;7:633-5.

Received 19 August 1994, accepted 7 August 1995