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Screening for breast cancer in Catalonia

Which policy is to be preferred?

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Background: the effects and costs of different policies for breast cancer screening in Catalonia (Spain) were analysed, to give a basis for setting priorities and deciding on the introduction of a screening programme. Methods: the MISCAN (MIcrosimulation SCreening ANalysis) model of the natural history of breast cancer was used. The epidemiology of breast cancer in Catalonia and the demography of the Catalan population was taken into account as well as the results on mortality reduction from a Swedish overview of breast cancer screening trials. Results: the reduction in breast cancer mortality in the total female population due to a screening programme for the age group 50-64 years would be 16, 12 and 9%, with screening intervals of one, two and three years respectively. The cost-effectiveness ratios (CE ratios) for these scenarios were 924,000, 730,000 and 719,000 pesetas (P_t) per life-year gained respectively (5% discounting). The most cost-effective screening scenario is the one in which women aged 50-69 years are screened with an interval of three years with a mortality reduction of approximately 12% in the total female population (CE ratio = 694,000 P_t). Screening until the age of 69 years (two year interval) was almost as cost-effective as screening the age group 50-64 years with a two year interval, with a reduction in breast cancer mortality of 15%. Extension to under the age of 50 years resulted in diverging results depending on the assumptions for improvement in prognosis for younger women (40-49 years). Conclusion: if the extension of a two yearly screening programme for women aged 50-64 years is considered (mortality reduction of 12%), extension to older women would be more advisable, based on proven benefits and costs, than extension to younger age groups.

Key words: breast neoplasms, decision making, mass-screening, policy, prevention and control

The cost-effectiveness of breast cancer screening can vary substantially between countries, depending on, for example health care system, costs of health care, the screening programme and epidemiology of the disease. In Europe and the USA different screening policies exist and in the UK and The Netherlands these policies were in part based on cost-effectiveness analyses.[1,2]

In this study a detailed cost-effectiveness analysis was carried out for one region of Spain, Catalonia, where all relevant aspects were taken into account in as much detail as possible. In Spain, breast cancer screening activities are organized according to the regional health care organization. Pilot projects on breast cancer screening have been started in different parts of Spain.[3,4] In Catalonia, a pilot project on breast cancer screening was started for women aged 50–64 years in Molins de Rei in the metropolitan area of Barcelona in 1992.[5] The upper age limit in all pilot projects in Spain is 64 years, while the starting age is 45 or 50 years. The screening interval in these pilot projects is two years for the age group 50–64 years and one or two years for the age group 45–49 years.

In this study we show the reduction in breast cancer mortality and the cost-effectiveness ratio (CE ratio) of different screening intervals and age groups to be screened in Spain, taking into account the age-specific reductions in breast cancer mortality from a Swedish overview of screening trials.[6] Additional scenarios are examined in which screening women under the age of 50 years is as effective as for women aged 50–69 years.

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METHODS

The MISCAN model approach to assessing the benefits of screening

To predict the number of breast cancer deaths prevented for all separate screening policies, the computer simulation MISCAN (MIcrosimulation SCreening ANalysis) model of the natural history of breast cancer was used. A detailed description of the earlier MISCAN model is given by van Oortmarssen et al.[7] In the present model, breast cancer has four invasive, screen-detectable, preclinical states (≤0.5 cm, 0.5–1 cm, 1–2 cm and >2 cm) and one non-invasive state, Ductal Carcinoma In Situ (DCIS). The MISCAN model has been validated with data from the Dutch pilot screening projects from Utrecht en Nijmegen, which started in 1974 and 1975.[8,9] These data allowed an estimation of the sensitivity of mammo-

graphy in the different states and the mean duration of the screen-detectable, pre-clinical period by age.[7]

The level of mortality, underlying incidence and survival of breast cancer are important for the proportion of favourable and unfavourable effects of breast cancer screening. With the MISCAN model it is possible to take into account the demography and epidemiology of breast cancer (*table 1*). By generating individual life histories a dynamic population is simulated. The characteristics of the screening programme (attendance, interval and age groups) and the screening test (sensitivity) and assessment procedures (e.g. biopsy) are considered. The value of the improvement in prognosis by stage after detection of breast cancer by screening was determined in a separate analysis.[10] Based on the breast cancer mortality reduction reported in a Swedish overview of randomized breast cancer screening trials, the improvement in prognosis was estimated much higher in age groups over 50 years than for women aged 40–49 years (*table 2*).[6,10]

With the use of this model we were able to predict many changes resulting from the introduction of a screening programme in a population in detail. The estimates we present for the screening programmes with different age groups and intervals are for a programme starting in 1995 and carried out over a period of 27 years. This long period was chosen because of the gradual introduction of screening and the time lag between the introduction of screening and its effect on breast cancer mortality. The effects resulting from the screening programme which extend beyond the 27 years screening programme were also accounted for.

Table 1 Demography, incidence, mortality, survival and clinical stage distribution of breast cancer in Catalonia as used in the MISCAN model

Population 1991 (female)	
Total	3,096,552
Age 40–44 years	205,716
Age 45–49 years	184,291
Age 50–64 years	522,638
Age 65–69 years	160,973
Breast cancer incidence (per 100,000 person-years)	
Crude rate	75.4
Age standardized (European)	66.4
Mortality from breast cancer (per 100,000 person-years)	
Crude rate	32.8
Age standardized (European)	27.3
Five year relative survival rate	
Age <65 years	0.721
Age ≥65 years	0.693
Clinical stage distribution (%)	
DCIS	3.7
≤0.5 cm (T1a)	1.4
0.5–1 cm (T1b)	6.2
1–2 cm (T1c)	32.4
>2 cm (T2+)	56.3

DCIS: Ductal Carcinoma In Situ

Demography and epidemiology of breast cancer in Catalonia

We used the life table and female population structure to simulate the demography of the female population in Catalonia.[11] The incidence of breast cancer was used from the cancer registries in Girona and Tarragona for the years 1985–1989 (*figure 1*).[12,13] Because of small differences between rural and urban areas, the overall incidence was used. The mortality from breast cancer was based on the vital health statistics of Catalonia (*figure 1*).[11]

Table 2 Characteristics of the screening for first and subsequent screenings or different age groups

	First screening %	Subsequent screening %
Attendance rate (average)		
Age 40–49 years	75	75
Age 50–64 years	70	70
Age 50–69 years	69	69
Referral rate		
Age 50–64 years (2 year interval)	6.2	3.6
Age 50–69 years (2 year interval)	6.3	3.6
Positive predictive value (PPV) of advice for biopsy		
Age 40–49 years	21	33
Age 50–64 years	35	55
Age 50–69 years	37	58
Detection rate (per 1000 examinations at 2 year interval)[a]		
Age 40–44 years	0.7	0.7
Age 45–49 years	1.7	1.4
Age 50–54 years	2.4	1.6
Age 55–59 years	2.9	1.8
Age 60–64 years	4.5	2.7
Age 65–69 years	6.5	3.6
Age 50–64 years[b]	3.3	2.2
Age 50–69 years[b]	4.1	2.6
	Age 45–49 years[c]	Age 50–69 years
Sensitivity of screen-test[d]		
DCIS	0.32	0.40
≤0.5 cm (T1a)	0.52	0.65
0.5–1 cm (T1b)	0.64	0.80
1–2 cm (T1c)	0.72	0.90
>2 cm (T2+)	0.76	0.95
Improvement in prognosis due to screen detection[e]		
DCIS	1.000	1.000
≤0.5 cm (T1a)	0.310	0.892
0.5–1 cm (T1b)	0.230	0.814
1–2 cm (T1c)	0.070	0.567
>2 cm (T2+)	0.050	0.395

a: Note: the possibility of an increase in underlying incidence over time, as seen in some parts of Spain, is not taken into account, due to lack of data.
b: During the first five years of the programme.
c: For the age group 40–44 years the values for sensitivity were 60% of those for the age group 50–69 years.
d: Sensitivity of screen test is the probability of a positive screen result when screening a woman with screen-detectable pre-clinical cancer.
e: Improvement in prognosis is the reduction in risk of dying from breast cancer compared to a situation without screening, detected in that stage.

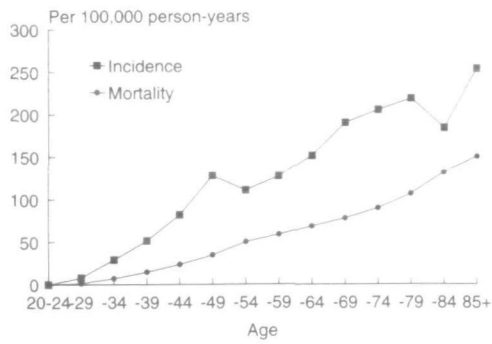

Figure 1 Breast cancer incidence and mortality in Catalonia (the MISCAN-model)

The clinical stage distribution was used to estimate the mean duration of the screen-detectable, pre-clinical phase of the different states in the model. Data on the tumour size, lymph nodes and distant metastasis (TNM stage) were available for all women hospitalized for breast cancer in Girona. These data were compared to less detailed data (local, regional and distant) of all incident cases in the Cancer Registry of Girona.[13] We used the TNM stage information of all patients that were hospitalized during 1989, because the differences were small. The age- and stage-specific survival from breast cancer as used in the model was in accordance with the five year relative survival rate from Girona for the years 1985–1989.[13] With the incidence and survival of breast cancer, the mortality of breast cancer, as found in the vital statistics, was predicted by the MISCAN model. The parameters used in the MISCAN model are shown in *table 1*.

The screening process

With regard to the screening process, we used the data of the small pilot project in Molins de Rei and the published results of a breast cancer screening programme in Navarra.[3] We assumed two-view mammography for the first screening and one-view screening for subsequent examinations. The number of women referred to the hospital for additional examinations after the first screen was 6% in Navarra, which was similar to the percentage of referrals found in Molins de Rei after a two-view examination.[5] We used a referral rate of 6.2% for the first screening and 3.6% for subsequent screening for women aged 50–64 years. The values for referral after subsequent screens and for the other age groups (50–69 and 40/45–64 years) were extrapolated using proportions of the Dutch situation, because no data for Catalonia and Navarra were available. All referred women received a clinical mammography and 12% of them also needed a biopsy. The attendance rate in Molins de Rei was 68%[5] and in Navarra 86%;[3] in the scenario of screening women aged 50–69 years with a two year interval we used an attendance rate of 70% on average. The attendance showed a slight decrease with increasing age, from 75% at age 50 years to 65% at age 70 years. The attendance rate for women aged 40–49 years was 75% for all ages. We took into account that not all women will attend the screening every round. The percentage of attenders that will attend the next screening is estimated at 88% and the percentage of women that did not attend but will attend next time is estimated at 24% for each screening round, based on the pilot project and the national screening programme in The Netherlands.[14]

The positive predictive values of an advice for biopsy were estimated to be 0.35 for the first screening and approximately 0.55 for subsequent screening examinations. The sensitivity was assumed to be as high as in The Netherlands and was dependent on the size of the tumour (T stage). The characteristics of the screening programme in Catalonia as used in the MISCAN model are summarized in the upper part of *table 2*. The age-specific detection rates were predicted by the MISCAN model given the input parameters clinical stage distribution, incidence of breast cancer and sensitivity of screening (lower part of *table 2*).

(Sensitivity) analyses

The basic scenario was screening with an interval of two years for women aged 50–64 years. In the sensitivity analyses, the age groups and intervals were changed to determine the impact on mortality reduction of breast cancer in the total female population and on the CE ratio. The intervals were varied from one to three years for the age groups 50–64 and 50–69 years. For the age groups 40–64 and 45–64 years only scenarios with a two year interval were analysed; because of the shorter pre-clinical phase for the age group 40–49 years a three year interval was assumed to be too long. We also studied the impact of a 12% lower sensitivity and an average attendance rate of 50% for women aged 50–69 years.

Recently, an updated analysis of Swedish results showed a reduction in breast cancer mortality of 23% (95% CI: 0.59–1.01) in women of 40–49 years of age at entry invited for screening compared to women not invited, which was much higher than the relative risk (RR) of 0.90 (95% CI: 0.65–1.24) in 1993.[6,15] As an optimistic variant we used an improvement in prognosis for women aged 40–49 years as high as for women aged 50 years and over.[10]

Costs

For this analysis, the Dutch cost structure was used, because extensive research on this aspect has been carried out in The Netherlands.[1,16] All costs due to the screening, assessment and treatment of breast cancer were considered.[1] We adapted this to the Spanish situation by using the gross domestic product-purchasing power parities (GDP-PPP) of 1991[17] and the most recently published correction factor for health care PPP of 1990.[18] All costs are presented in pesetas (P_t; exchange rate in 1991 100 P_t ~ \$ = 1).[17] The categories of costs for the total programme with a duration of 27 years are listed for the basic scenario in *table 3*.

The costs and effects were presented using a discounting rate of 5%, representing a time preference. Based on all

effects and costs in a screening situation compared to a non screening situation, CE ratios were calculated. For policy decisions the differences between scenarios are often expressed in marginal CE ratios. This ratio represents the extra costs to gain one extra life-year compared to the reference scenario.

RESULTS

Screening policies for women aged 50–64 years

In a Catalan screening programme for women aged 50–64 years with an interval of two years (eight invitations), the detection rates predicted by the model were 3.3 per 1,000 examinations for the first screening and 2.2 per 1,000 for subsequent screening during the first five years (lower part of *table 2*). The mortality from breast cancer in the total female population is eventually expected to be reduced by 12%, which would mean that 157 deaths from breast cancer per year would be prevented in this scenario (*table 4*). The costs per life-year gained were estimated to be 730,000 P_t (*table 4*). If the screening is carried out with a one or three year interval, the mortality reductions would be 16 and 9% and the CE ratios would be 924,000 and 719,000 P_t respectively. Intensifying the programme from a two year to a one year interval would result in an extra mortality reduction of only 33% [(16%–12%)/12%].

The scenarios were analysed with a 12% lower sensitivity or an attendance rate of 50% on average. The mortality reductions for these scenarios were 11 and 9% respectively and the CE ratios were 801,000 and 767,000 P_t respectively (*table 4*). These estimates show that a lower attendance rate would result in a proportionally lower reduction in mortality from breast cancer, but did not much influence the CE ratio.

Other screening policies

The estimates if the less intensive programme (age 50–64 years, interval three years and CE ratio 719,000 P_t) were to be extended to other age groups and/or intervals are summarized in *table 5*. A programme for women aged 50–69 years and a three yearly interval would have a CE ratio of 694,000 P_t and the marginal CE ratio would be 614,000 P_t, indicating that the costs per life-year gained for women aged 65–69 years are less than for women of 50–64 years of age. Screening with a higher frequency (50–64 years and two year interval) would result in a marginal CE ratio of 756,000 P_t. Saving an extra life-year will cost almost the same amount of money if the screening interval for the age group 50–64 years is two years instead of three years (*table 5*). A comparison of the screening scenarios 50–64 years with an interval of two years and 50–69 years with an interval of three years showed an almost equal effectiveness (mortality reduc-

Table 3 Costs due to breast cancer for the total programme (1995–2021) of screening women aged 50–64 years at an interval of two years (5% discounting)

		Costs ($\times 10^6$ P_t)				
	Average cost (P_t)	Screening	%	No screening	%	Difference (total cost)
Screening[a]	4,000	12,237	11	–	–	12,237
Assessment[b]						
Screening	454,530	3,236	3	–	–	3,236
Outside screening	324,620	21,211	19	22,861	23	–1,650
Primary treatment plus follow-up[c]	599,300	31,737	29	30,511	31	1,226
Palliative treatment	1,808,960	41,355	38	43,953	45	–2,598
Total		109,776	100	97,324	100	12,451

a: Included invitations, two-view mammography on first screening, one-view at subsequent screens and double reading by radiologists.
b Included clinical mammography and biopsy for 12% of referred women, taking into account difference in cost for biopsy of palpable and non-palpable breast cancer.
c: Consisted of breast-conserving therapy plus radiation, mastectomy, adjuvant therapy, treatment of stage IIIB/IV and cost of follow-up visits after treatment.

Table 4 Effects and costs of screening women aged 50–64 years, different policies

	Breast cancer mortality reduction (no discounting)[a]			Costs and cost-effectiveness (5% discounted)		
Scenario (age group, interval and number of invitations per woman)	%	N (per year)	Life-years gained	Total cost ($\times 10^6$ P_t)[c]	Life-years gained	CE ratio (P_t)
50(1)64 (15 invitations)[b]	15.8	207	104,505	21,121	22,864	923,800
50(2)64 (8 invitations)	12.0	157	78,593	12,451	17,049	730,300
50(3)64 (5 invitations)	8.6	112	55,088	8,627	11,991	719,500
50(2)64 (sensitivity –12%)	10.9	143	71,107	12,395	15,479	800,700
50(2)64 (attendance 50%)	8.9	116	57,854	9,637	12,570	766,700

a: Steady state after approximately 25 years from the start of the screening programme.
b: 50(1)64 is a screening programme carried out for women aged 50–64 years with a 1 year interval.
c: Refers to all costs due to breast cancer with screening minus all costs due to breast cancer without screening (see *table 3*).

tions 12 and 12.3% respectively). The marginal CE ratio for the scenario 50–64 years with an interval of two years is, however, much higher; to save an extra life-year will cost over 1 million P_t (*table 5*).

Screening with an interval of two years until the age of 69 years would result in a mortality reduction of 15% and the costs per life-year gained would be 744,000 P_t, with a marginal CE ratio of only 844,000 P_t per life-year gained (*table 5*).

The first variant of the improvement in prognosis was based on the RR of dying from breast cancer of 0.90 (95% CI: 0.65–1.24) from the Swedish overview by Nystrom et al.[6] In this scenario an extension to younger ages (45–64 years) did not much influence the mortality reduction (12.2% instead of 12.0%) and resulted in a higher CE ratio of 868,000 P_t. The marginal cost-effectiveness with the scenario 50–64 years with a two year interval as a reference shows that the costs per extra life-year saved are much less for an extension to the age group 65–69 years than for an extension to the age group 45–49 years (*table 5*). Screening from the age of 40 years would result in a high CE ratio of over 1 million P_t per life-year gained.

In the other variant, women aged 40–49 years had the same improvement in prognosis after screen detection as women aged 50–69 years (*table 5*). The CE ratio of screening women aged 45–64 will be 731,000 P_t, which is almost the same value as for the age group 50–64 years (both with two year intervals). This is also represented by the marginal CE ratio (the difference is only 6000 P_t). For a screening programme for women aged 40–64 years the CE ratio becomes less favourable (830,000 P_t) which is also shown by the marginal CE ratio. The effectiveness based on mortality reduction would be 13.8 and 15.1% for both these programmes, which is more favourable when compared to 12.2 and 12.7% with the pessimistic assumptions in improvement in prognosis.

DISCUSSION

Due to uncertainty about the effectiveness of screening women aged 40–49 years resulting in controversy about introducing screening in that age group, we have carried out an optimistic and pessimistic scenario for the effectiveness under the age of 50 years. Extension to the age of 40 years resulted even with the high improvement in prognosis in a high CE ratio, because of a lower incidence rate of breast cancer and a lower assumed sensitivity of mammography in the younger ages.

The CE ratios for screening started at the age of 45 years are not so unfavourable compared to the CE ratio of a 50–64 years programme with an interval of two years. These relatively favourable CE ratios are, however, partially explained by the high incidence peak at ages 45–49 years in Catalonia (*figure 1*), which is preceded by a high onset of pre-clinical disease and, thus, a high pre-clinical prevalence. Introducing screening for this age group would result in relatively many screen-detected cancers, although the sensitivity of mammography is lower for younger women. At age 50 years the incidence in Catalonia was relatively low, which is rather unfavourable for screening and the increase in incidence after the age of 50 years is less steep than in other European countries. These combined effects resulted in a CE ratio favourable for screening the age group 45–49 years in comparison with 50–64 years.

Under the optimistic assumptions of effectiveness under the age of 50, extending a 50–64 years programme and a two year interval to younger ages (45 years) is comparable to extending to older ages. Extension to older or younger ages was almost equally cost-effective, but the reduction in mortality from breast cancer is higher for extending to the age of 69 years (15 versus 14%). The number of life-years is, however, higher for an extension to younger ages implying that more years per life will be gained.

Table 5 Cost-effectiveness and marginal cost-effectiveness for an extension to other age groups

Scenario (age group, interval and number of invitations per woman)	Breast cancer mortality reduction[a]		Costs and cost-effectiveness (5% discounted)			
	%	N (per year)	Total costs ($\times 10^6$ P_t)	Life-years gained	CE ratio (P_t)	Marginal CE ratio (P_t)
50(3)64 (5 invitations)[b]	8.6	112	8,627	11,991	719,500	
50(3)69 (7 invitations)	12.3	161	10,926	15,734	694,400	614,200[c]
50(2)64 (8 invitations)	12.0	157	12,451	17,049	730,300	756,000[c]
50(3)69 (7 invitations)	12.3	161	10,926	15,734	694,400	
50(2)64 (8 invitations)	12.0	157	12,451	17,049	730,300	1,159,700[d]
50(2)64 (8 invitations)	12.0	157	12,451	17,049	730,300	
50(2)69 (10 invitations)	14.9	195	14,477	19,447	744,400	844,500[e]
45(2)64 (10 invitations)	12.2	159	15,240	17,559	867,900	5,468,600[e]
40(2)64 (13 invitations)	12.7	167	19,512	18,566	1,050,900	4,654,600[e]
Improvement in prognosis for women aged 40–49 years as high as for women aged 50–69 years (optimistic variant)						
45(2)64 (10 invitations)	13.8	180	14,947	20,438	731,400	736,500[e]
40(2)64 (13 invitations)	15.1	198	19,198	23,127	830,100	1,110,100[e]

a: Steady state after approximately 25 years from the start of the screening programme.
b: 50(3)64 is a screening programme carried out for women aged 50–64 years with a 3 year interval.
c: With 50 (3) 64 as a reference.
d: With 50 (3) 69 as a reference.
e: With 50 (2) 64 as a reference.

Women aged 64–69 years still have a long life expectancy and screening has been proven to be effective in the age group 60–69 years.[6] Due to the uncertainty of the effectiveness of screening younger women and the proven benefit for older women with a relatively favourable CE ratio an extension to higher ages should be preferred rather than an extension to ages under 50 years.

The mortality reductions we predicted should be regarded as estimates and some factors not taken into account in this analysis could affect these estimates. Future changes in the mortality or incidence in breast cancer were not accounted for. In the UK a decrease in mortality was shown before the screening could have had its effect on mortality.[19] The widespread use of tamoxifen during this period in the UK may be important. Another aspect not considered in this analysis is opportunistic screening, before introducing screening in the target population. These processes might also play a role in Catalonia and would probably result in less potential effectiveness of screening, although it is very difficult to quantify these effects. The numbers of the Catalonian pilot project were much too small to derive the quality of the screening programme. However, the prevalence:incidence ratio in Navarra was approximately 3.7 for the age group 45–64 years and the stage-distribution was as favourable as in the Dutch national screening programme.[3,14,20] The early indicators of efficacy in the Spanish setting seem not unfavourable.

The method used with regard to the costs may not represent the true value of resource use in the Spanish situation. Using the GDP–PPP and a correction for health care might be too approximate for the specialized field of breast cancer screening. Another aspect is that no correction was made for quality of life. From other analyses it is clear that the number of quality adjusted life-years (QALYs) lost due to screening on a national level was almost equal to the number of QALYs saved by screening.[1,21] Correction for quality of life would not change the conclusions of this analysis.

In countries where mortality from breast cancer is increasing[22,23] and the introduction of breast cancer screening is a policy priority, the diffusion of opportunistic screening is usually rapid in younger age groups where the effectiveness is less clear.[24] In that situation, the importance of the benefits of breast cancer screening in the older age group should be the incentive for policy making.

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REFERENCES

1 de Koning HJ, van Ineveld BM, van Oortmarssen GJ, et al. Breast cancer screening and cost-effectiveness: policy alternatives, quality of life considerations and the possible impact of uncertain factors. Int J Cancer 1991;49(4):531-7.

2 Forrest P. Breast cancer screening: report to the Health Ministers of England, Wales, Scotland and Northern Ireland. London: Department of Health and Social Security, 1987.

3 Ascunce N, del Moral A, Murillo A, et al. Early detection programme for breast cancer in Navarra, Spain. Eur J Cancer Prev 1994;1:41-8.

4 Servei de programmes especials. Programme of breast cancer prevention in the Valencia region (in Spanish). Valencia: Conselleria de Sanitat i Consum, 1993.

5 Marzo M. Analysis of breast cancer screening in our context (in Spanish) (doctoral thesis). Barcelona: Autonomous University of Barcelona, 1995.

6 Nystrom L, Rutqvist LE, Wall S, et al. Breast cancer screening with mammography: overview of Swedish randomised trials (see comments) (published erratum appears in Lancet 1993;342(8883):1372). Lancet 1993;341(8851):973-8.

7 van Oortmarssen GJ, Habbema JD, van der Maas PJ, et al. A model for breast cancer screening. Cancer 1990;66(7):1601-12.

8 Verbeek AL, Hendriks JH, 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;1(8388):1222-4.

9 Collette HJ, 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;1(8388):1224-6.

10 de Koning HJ, Boer R, Warmerdam PG, Beemsterboer PMM, van der Maas PJ. Quantitative interpretation of the age-specific mortality reductions from the Swedish breast cancer screening trials. J Natl Cancer Inst 1995;87(16):1217-23.

11 Servei d'Informacio Sanitaria. Analysis of mortality in Catalonia, 1991 (in Spanish). Barcelona: Departament de Sanitat i Seguretat Social, 1993.

12 Borras JA, Galceran J. Tarragona: results from the cancer registry in Tarragona (in Spanish). Registre de cancer de Tarragona, 1993.

13 Viladiu P, Izquierdo A, Beltran M, Bosch X. Epidemiology of breast and gynaecologic cancer, 1980-89 (in Spanish). Girona: Spanish Cancer Association, 1994.

14 de Koning HJ, Fracheboud J, Boer R, et al. Nation-wide breast cancer screening in The Netherlands: support for breast-cancer mortality reduction. National Evaluation Team for Breast Cancer Screening (NETB). Int J Cancer 1995;60(6):777-80.

15 Nystrom L. Update of the statistical analysis of screening women aged 40-49 in the combined Swedish trials. Congress Proceedings of the International Conference The Impact of Breast Cancer Screening with Mammography in Women Aged 40-49; Falun, Sweden, 1996.

16 de Koning HJ, van Ineveld BM, de Haes JC, van Oortmarssen GJ, Klijn JG, van der Maas PJ. Advanced breast cancer and its prevention by screening. Br J Cancer 1992;65(6):950-5.

17 OECD. Paris: Health data file. CREDES, OECD, 1992.

18 OECD. Health systems (vol II): the socio-economic environment & statistical references. Paris: CREDES, OECD, 1993.

19 Quinn M, Allen E. Changes in incidence of and mortality from breast cancer in England and Wales since introduction of screening. United Kingdom Association of Cancer Registries (see comments). BMJ 1995;311(7017):1391-5.

20 van den Akker-van Marle ME, Reep-van den Berg CMM, Boer R, Del Moral A, Ascunce N, de Koning HJ. Breast cancer screening in Navarra: interpretation of a high detection rate at the first screening round and a low rate at the second round. Int J Cancer 1997;73:464-9.

21 Beemsterboer PM, de Koning HJ, Warmerdam PG, et al. Prediction of the effects and costs of breast-cancer screening in Germany. Int J Cancer 1994;58(5):623-8.

22 La Vecchia C, Lucchini F, Negri E, Boyle P, Maisonneuve P, Levi F. Trends of cancer mortality in Europe, 1955-1989: III, Breast and genital sites. Eur J Cancer 1992;28A(4-5):927-98.

23 Sanchez V, Borras JM, Mingot M. Cancer mortality trends in Catalonia: 1975-1990 (in Spanish). Med Clin 1994;102(16):606-12.

24 Almazan C, Borras JM, de la Puente ML, Gimenez A, Granados A. Approach to the use of screening mammography in 2 health regions (in Spanish). Aten Primaria 1995;15(7):452-6.

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