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Original Paper

Screening for Breast Cancer in Ghent, Belgium: First Results of a Programme Involving the Existing Health Services

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In 1992, a population-based breast cancer screening programme was initiated in the municipality of Ghent: all women aged 40–69 years were personally invited to attend a local radiology unit for a mammogram, after being examined by a general practitioner or gynaecologist of their choice. The results of history taking, clinical breast examination, first and second reading, further investigation and primary treatment were registered. In total, 24.3% of the eligible population was screened in the period 1992–1994. The recall and biopsy rates were 2.9% and 1.4%, respectively. The cancer detection rate was 8.1 per 1000 women screened. Of all cancers detected, 88.0% (66/75) were invasive. Of these, 35.9% (23/64) measured 10 mm or less in diameter. The benign to malignant biopsy ratio was 0.7. Apart from the low participation, these results suggest that the programme is effective, compared with reference standards and the results of other studies. © **1998 Elsevier Science Ltd. All rights reserved.**

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INTRODUCTION

In Belgium, as in many other Western countries, breast cancer is the most frequently occurring cancer in women. In 1991, approximately 100 new breast cancer cases per 100 000 women were diagnosed (age-standardised, Belgian population, or 66.8 per 100 000, world population) [1]. Of all types of cancer, breast cancer is also the leading cause of death. In the same year, the age-standardised mortality rate (Belgian population) was 48.2 per 100 000 women (or 26.1 per 100 000, world population) [2].

Primary prevention of breast cancer is not possible. Survival, however, can be improved by detecting the cancer at an earlier, more curable stage. Controlled trials conducted over the past 30 years (e.g. the HIP-trial [3], the Swedish two-county trial [4]) have demonstrated that mammographic screening, with proper quality assurance, can reduce mortality from breast cancer by 20–40%. Belgium does not yet have a coherent policy for secondary prevention, resulting mainly in 'opportunistic' screening (i.e. screening recommended on the basis of a known risk factor, during a routine medical consultation or consultation for an unrelated condition), offered only to a fraction of the population.

In 1989, the first systematic breast cancer screening programme was set up in the northeastern part of the country by the University of Louvain, in the framework of the 'Europe against Cancer' programme [5]. The project principally targeted rural to semirural areas, and, therefore, screening was carried out with mobile mammographic units. In 1992, the Centre for Prevention and Early Detection of Cancer (CPEDC) of the University of Ghent launched a project in the municipality of Ghent, an urban area (1600 inhabitants/km^2) with a high and geographically equal distribution of physicians and radiology units. The main objective of this project was to evaluate the effectiveness of a screening programme integrated within the existing healthcare delivery system. This paper presents the results of the first screening round (1992–1994).

PATIENTS AND METHODS

Prior to the invitation of the population, the CPEDC informed all private ($n = 5$) and hospital-based radiology units ($n = 9$) about the project by mail, as well as general practitioners (GPs) ($n = 346$), gynaecologists ($n = 60$) and

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surgeons ($n = 27$) of the area. In addition, for those interested, a series of workshops were held to familiarise them with the procedures. One (hospital-based) radiology unit (7.1%) decided not to take part in the project. It can be assumed that 81 GPs and seven gynaecologists (21.7% in total) also refused to collaborate, since, in the course of the first round, they did not pass any data on their patients to the CPEDC.

To ensure high quality mammography screening, a joining radiology unit had to meet the following requirements: the performance of a daily sensito/densitometry, a phantom image quality evaluation once a month, a check-up of the equipment twice a year, mediolateral oblique and craniocaudal view mammography per breast, blind double reading of all mammograms carried out within the programme and the dedication of at least one radiologist specifically trained in mammography screening. Of the remaining 13 candidates, 12 (all private and seven hospital–based units) complied with these conditions (92.3%).

The target population was all female residents of the municipality of Ghent, aged 40–69 years at the start of the project ($n = 41\,585$). Names and addresses were extracted from the National Population Register. Each woman received a letter of invitation accompanied by an information leaflet, a reply card and registration forms to be filled in by the physicians. In addition, posters were displayed in the surgeries of the physicians, pharmacies and sociocultural organisations, encouraging women to participate. To avoid overcrowding, invitations were spread over the 2-year period. Women not intending to participate were asked to inform the CPEDC of the reason, using the reply card or by telephone. Non-responders were sent a reminder after 6 months.

Participants had to consult their GP or gynaecologist (or other specialist) first, in accordance with Belgian law. The results of the investigation (history taking and clinical breast examination) had to be sent to the CPEDC. Irrespective of the findings, the women were then referred to (preferably) one of the 12 collaborating radiology units for a screening mammogram. Again, results (first reading) and films had to be sent to the CPEDC, where the second reading was done daily, in rotation, by radiologists from the 12 units.

Feedback from the radiology unit to the referring physician was given only after the second reading, via the usual written protocol. All further diagnostic assessment was administered by the referring physician. In case of a 'positive' mammogram (suspicious or malignant finding) and in all other cases in which the radiologist had recommended further investigation, the CPEDC monitored the follow-up procedure and registered the findings. If a surgical intervention was carried out, a copy of the histopathological protocol was requested.

RESULTS

Table 1 presents participation in the programme per 5-year age group. The target population is the number of women invited for screening, adjusted for migration and death. The eligible population is the target population minus the women with previous breast cancer and women having had a mammogram (screening, diagnostic or follow-up) less than 1 year before the time of invitation. Overall, 9215 (24.3%) of the eligible women ($n = 37\,920$) attended the first round (participation rate).

Table 2 shows the number of women recalled to the screening unit for further investigation, i.e. repeat or other radiological view, ultrasound, magnetic resonance imaging or fine needle aspiration cytology (FNAC), the number of biopsies performed and the outcome per age group. Of the 9215 women screened, 263 (2.9%) were recalled (recall rate). Compliance with recall was almost complete (98.5%).

In 129 cases (1.4% of all women screened), a biopsy was carried out (biopsy rate). The 2 cases (1 woman in the age category 60–64 years and 1 in the category 65–69 years), in which a biopsy was not recommended turned out to be 'false negative'. Of the 129 biopsies performed, 75 cancers (58.1%) were detected (Table 2). This represents an overall cancer detection rate (CDR) of 8.1 per 1000 women screened and a benign/malignant (B/M) biopsy ratio of 0.7.

In total, 26 FNACs (10.0% of all additional investigation) were performed. For one FNAC (3.8% of all cases), the result was unknown. In 16 cases (64.0% of all cases, the FNAC with an inadequate result excluded), FNAC did not show any abnormality. In 5 of these cases (31.3%), a biopsy was performed and breast cancer was diagnosed (false negative). In the remaining 11 cases, no histopathological examination was carried out (and no malignancy reported in the following 2 years). Of the 9 cases in which the FNAC indicated a malignant process, 2 (22.2%) were 'false positive'. These findings correspond to a sensitivity and specificity of FNAC of 58.3% and 84.6%, respectively.

Tumour size per age group is presented in Table 3. Of all cancer cases, 66 (88.0%) were invasive. Of these invasive cancers (those without information on diameter excluded), 23 (35.9%) were 10 mm or less in diameter.

Axillary lymph node status, histological type and degree of differentiation for invasive cancers are shown in Table 4. Of all women in whom axillary nodes were sampled ($n = 65$), 44 (67.7%) were node negative (Table 4). Of the 64 cases with information on histological type, 5 (7.8%) were lobular and 54 (84.4%) were ductal cancers. Of all cancers (lobular type cancers excluded) with information on differentiation ($n = 57$), 32 (56.1%) were moderately differentiated (grade 2) and 15 (26.3%) were poorly differentiated (Grade 3).

Table 1. *Invitation and mammographic screening by age group*

Age group (years)	Target population (*n*)*	Previous breast cancer (*n*)	Recent mammogram† (*n*)	Eligible population (*n*)	Screened on invitation (*n*)
40–44	7119	31	531	6557	1645
45–49	7047	48	556	6443	1599
50–54	6017	60	409	5548	1475
55–59	6664	92	355	6217	1675
60–64	7018	89	268	6661	1554
65–69	6803	92	217	6494	1267
Total	40 668	412	2336	37 920	9215

*Adjusted for migration and death. †Screened less than 1 year before the time of invitation.

Table 2. Further examination and outcome by age group

	Additional investigation on recall		Biopsy		
Age group (years)	Recommended (*n*)	Performed (*n*)	Recommended (*n*)	Performed	Cancer detected (*n*)
40–44	20	19	5	4	3
45–49	38	38	19	18	11
50–54	53	52	24	24	12
55–59	55	54	24	24	13
60–64	56	56	39	40*	22
65–69	41	40	18	19*	14
Total	263	259	129	129	75

*In 2 cases, biopsy was not recommended, but was carried out anyway, and was false negative.

Table 3. Primary tumour size by age group

		Invasive cancer					
Age group (years)	Carcinoma *in situ* (*n*)	pT1a-b (*n*)	PT1c (*n*)	pT2-T3 (*n*)	Unknown (*n*)	Total (*n*)	Total (*n*)
40–44	0	1	1	1	0	3	3
45–49	3	2	5	1	0	8	11
50–54	1	6	2	1	2	11	12
56–59	2	3	7	1	0	11	13
60–64	2	6	9	5	0	20	22
65–69	1	5	6	2	0	13	14
Total	9	23	30	11	2	66	75

pT1a-b, tumour ≤ 10 mm in largest diameter; pT1c, tumour ≤ 20 mm in largest diameter; pT2-T3, tumour > 20 mm in largest diameter (TNM classification).

Table 4. Axillary node status, histology and differentiation for invasive breast cancers by age group

	Status				Type					Grade†				
Age group (years)	pN^- (*n*)	pN^+ (*n*)	Unknown (*n*)	Total (*n*)	Lobular (*n*)	Ductal (*n*)	Other* (*n*)	Unknown (*n*)	Total (*n*)	1 (*n*)	2 (*n*)	3 (*n*)	Unknown (*n*)	Total (*n*)
40–44	1	2	0	3	0	3	0	0	3	0	2	1	0	3
45–49	5	2	1	8	0	7	1	0	8	4	3	0	1	8
50–54	9	2	0	11	0	9	1	1	11	1	4	4	1	10
55–59	4	7	0	11	0	9	2	0	11	4	5	2	0	11
60–64	16	4	0	20	4	14	1	1	20	0	10	5	0	15
65–69	9	4	0	13	1	12	0	0	13	1	8	3	0	12
Total	44	21	1	66	5	54	5	2	66	10	32	15	2	59

pN^-, node negative; pN^+, node positive (TNM classification); Grade 1, well differentiated; grade 2; moderately differentiated; grade 3, poorly differentiated (Bloom and Richardson grading method [6]). *Medullar, tubular and mixed types. †Lobular type excluded.

In 44 (58.7%) of all cancer cases, breast-conserving surgery was performed (Table 5).

16 new cancer cases occurred within 24 months after previous screening, corresponding to an interval cancer rate of 1.7 per 1000 women screened. 6 (37.5%) of these were classified as 'true' interval cancers, 2 (12.5%) as 'radiographically occult' ('negative' mammogram on presentation), 6 (37.5%) as 'minimal signs present' and the remaining 2 cases (1 25%) as 'missed', i.e. they were, in the opinion of the radiologist, insufficiently suggestive of malignancy. All interval cancers were invasive, of which 3 (18.8%) were lobular type and the remainder were ductal type. In total, 5 (31.3%) of the interval cancers were 10 mm or less in diameter; 10 (62.5%) were node negative. Of the ductal type cancers, 5 (38.5%) were classified as grade 2 and 6 (46.2%) as grade 3. None of these distributions differed significantly from the corresponding distributions for the screen-detected cancers (Fisher's exact test, $P > 0.05$).

Table 5. Primary treatment by age group

	Treatment		
Age group (years)	Conservative (*n*)	Mastectomy (*n*)	Total (*n*)
40–44	1	2	3
45–49	7	4	11
50–54	7	5	12
55–59	8	5	13
60–64	12	10	22
65–69	9	5	14
Total	44	31	75

DISCUSSION

Mortality, of course, is the ultimate criterion in evaluating a breast cancer screening programme [7]. However, since changes in mortality cannot be assessed for many years,

information on participation, further investigation, outcome and treatment procedures can be used as 'surrogate' indicators of effectiveness. The results of the Ghent project will be compared with the reference standards provided by the European Commission [8] and the results of other breast cancer screening projects. Unless stated otherwise, EC standards and results refer to women aged 50–64 years.

Participation in the programme is substantially lower than the European reference standard of 60% for a prevalent screening round. However, a survey of a random sample of 360 women conducted by the CPEDC in 1995 (report in preparation) showed that approximately 20% of the target population (women aged 50–64 years) was recently screened at the time of invitation. This is approximately four times the number calculated on the basis of the registered information, i.e. from the reply cards and telephone calls from non-participants (5.2%). The results of the survey also indicated that approximately 25% of the eligible women were screened within the period of the first round, but not registered (follow-up examinations not counted). Taking both of these findings into account, the 'adjusted' participation rate is approximately 50%, which is on the same level as that found in most Europe against Cancer projects, such as the French ADEMAS programme, 49.7% [9], the project in southern Greece, 51.4% [10] and the Florence programme, Italy, 58.9% [11].

The proportion of women recalled for further investigation was much lower than the EC standard (< 7%). Apart from the quality assurance measures taken into account (regular technical check-up, the use of two-view mammography, blind double reading, etc.), the low recall rate might be due to the high number of ultrasounds performed at the time of screening ($n = 300$). The CDR was approximately five times the national incidence rate (IR) of 2.1 per 1000 women (age 50–64 years, 1991) [1]. This is considerably higher than the recommended $> 3 \times$IR. The B/M biopsy ratio was also favourable, according to the reference standard of < 2 to 1.

Despite the promotion of the use of FNAC by the CPEDC, the number of FNACs carried out by the radiologists was low when compared with the Florence programme, 37.1% of all additional investigations carried out [11], and the Eccles programme, 36.3% [12]. As long as FNAC is not made compulsory in Belgium, its frequency (and diagnostic value) will remain low, since the technique is unpopular with gynaecologists and surgeons.

The proportion of invasive lesions ≤ 10 mm in diameter exceeds the minimum found (25%). The proportion of carcinoma *in situ* found was somewhat lower than the European standard of > 15%. However, since many such lesions will never develop into a clinically manifest tumour [13], it could be stated that the low number of carcinoma *in situ* detected reduces the risk of 'overdiagnosis'. The relatively large number of more aggressive, poorly differentiated invasive cancers (grade 3) detected suggests no 'length-time bias', i.e. the tendency for slow-growing tumours to be over-represented among the screen-detected cases [14].

The proportion of women treated with breast-conserving surgery was high compared with the Eccles programme, 37% [12], but did not achieve the level observed in the ADEMAS programme, 76.6 [9] and the Florence programme, 80.0% [11].

The interval cancer rate was similar to that reported in the Stockholm trial, 1.8 per 1000 per 24 months (women aged 40–69 years) [15] and the Kopparberg study, 1.8 per 1000 per 24 months for women aged 40–49 years and 33 months for the age group 50–69 years [16]. Although the characteristics of the interval cancers hardly differed from the screen-detected cancers, they tended to be less differentiated, which could be seen as an indication of screening effectiveness.

It is tempting to conclude from these results that the first round of the screening programme in Ghent was effective, despite the low participation rate. However, it may be that performance indicators were positively modified by the high number of 'opportunistic' screened women in the period of the first round (25%). This group is proportionally much larger (approximately half the total women screened) than the proportion of GPs and gynaecologists who did not collaborate in the project (21.7%). Assuming that the co-operating physicians did not register all their patients, it is possible that some of the 'obvious' cases were not registered. An analysis of the results of the clinical examination seems to confirm this hypothesis: in more than 90% of the participating women no clinical abnormality was found, which is higher than expected (in the absence of screening, approximately 30% of the women are asymptomatic). Therefore, for the subsequent rounds, greater efforts are to be made, not only to encourage the women to participate, but also to convince the physicians to report fully on their screening activities.

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