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An International Comparison of Cost-effectiveness of Breast Cancer Screening Strategies for Women at Increased Risk

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Introduction: For women with a *BRCA1* or *BRCA2* mutation or a strong family history of breast cancer (*BRCAu*), the screening strategies in the US, the UK and The Netherlands use different approaches in MRI and mammography. The US strategy is the most intensive where mammography and MRI are performed every year from age 25, the UK strategy is the least intensive where mammography and MRI are done from age 30 every year and only mammography from age 50 to 70 every 3 years, and the Dutch strategy is intermediate. In order to optimize screening, i.e. to find the most effective screening at reasonable costs, the aim of the present study is therefore to evaluate the cost-effectiveness of these screening strategies.

Method and Materials: A recently validated simulation model was applied to the current US, UK and Dutch screening strategies as proposed in their national guidelines. Main outcome were the life years gained, the costs and their ratio, the cost-effectiveness. Cost parameters included were the costs of screening, diagnostics and therapy and hospital stay. Each screening simulation was performed with 10,000 women and the simulation parameters were based on published data.

Results: For *BRCA1* and *BRCA2* mutation carriers no significant differences in cost-effectiveness were found. However, the number of life years gained and costs in the Dutch and US screening strategies were significantly higher than in the UK screening strategy. Although the US strategy had the highest costs, no improvement in life years gained was observed as compared to the Dutch screening strategy. For *BRCAu* women, the most cost effective screening scenario was the UK screening strategy and the least cost effective screening scenario was the US screening strategy ($p < 0.05$). No significant difference was found in life years gained. However, the US screening strategy showed an excessive increase in costs.

Conclusion: For women with a *BRCA1* or *BRCA2* mutation the US, UK and Dutch screening strategies are equally cost-effective, but the number of life years gained was lowest in the UK protocol. For women with only a strong family history of breast cancer the UK screening strategy is the most cost-effective and the US screening strategy is the least cost-effective.

Clinical relevance: This study provides information that can be used for optimisation of national screening guidelines for women at a hereditary or familial increased risk of breast cancer.

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Breast Cancer Incidence and Case Fatality Among 4.7 Million Women in Relation to Social and Ethnic Background: a Population-based Cohort Study

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Background: Incidence of breast cancer is increasing around the world and still it is the leading cause of cancer mortality in low- and middle-income countries. We utilized Swedish nationwide registers to study breast cancer incidence and case fatality to disentangle the effect of socioeconomic position (SEP) and immigration from the trends in native Swedes.

Materials and Methods: A nation-wide cohort of women in Sweden was followed between 1961 and 2007 and incidence rate ratio (IRR) and hazard ratio (HR) with 95% confidence intervals (CIs) were estimated using Poisson and Cox proportional regression models.

Results: Incidence continued to increase however it remained lower among immigrants (IRR = 0.88, 95% CI = 0.86 to 0.90) but not among immigrant's daughters (IRR = 0.97, 95% CI = 0.94 to 1.01) compared to native Swedes. Both cause-specific and all-cause case fatality decreased over the last decades and was similar in native Swedes and immigrants. However, cause-specific case fatality was significantly higher among immigrants if cancer was diagnosed after age 50 or in the most recent years. Women with the highest SEP had significantly 20% to 30% higher incidence but had 30% to 40% lower cause-specific case fatality compared with women with lowest SEP irrespective of country of birth. Age at immigration and duration of residence significantly modified the incidence and cause-specific case fatality.

Conclusions: Disparities found in case fatality among immigrants by age, duration of residence, age at immigration and country of birth emphasize the importance of targeting interventions on women that are not likely to attend screening or not likely to adhere to the therapy suggested by physicians.

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Comparison Between Screen-detected Invasive Breast Cancer and Symptomatic Breast Cancer According to Immunohistochemical Intrinsic Subtypes

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Background: The screening program aims to detect early breast cancer to improve survival. We investigated the clinicopathrogical characteristics, immunohistochemical intrinsic subtypes, and outcome of screen-detected invasive breast cancer (S-DIBC) compared with symptomatic invasive breast cancer (SIBC).

Material and Methods: From January 2005 to December 2010, 715 patients with invasive breast cancer who underwent surgery at our hospital were included. Among them, there were 155 S-DIBC. We retrospectively reviewed the clinical and pathologic data. Ki67 LI was categorized as low (<14%) and high (> or =15%) in IBC. Cases were classified as luminal A (ER+ and/or PR+, and HER2- and Ki67 low), luminal B (ER+ and/or PR+, and HER2+ or Ki67 high), HER2 disease (ER−, PR−, HER2+), or triple negative (ER−, PR−, HER2−). Overall survival (OS) and disease-free survival (DFS) curves were generated using the method of Kaplan and Meier. Survival comparisons were made with the log-rank test. The level of significance was taken to be 0.05. SPSS 18.0 software package was used for statistical analysis.

Results: S-DIBC was associated with smaller tumor size ($p < 0.001$), less lymph node involvement ($p < 0.001$), and earlier stage compared ($p < 0.001$) with SIBC ($p < 0.001$). Significantly more tumors were positive for hormone receptors and had a negative HER2 status in the S-DIBC group as compared to the SIBC group (ER+, 81.8% vs.74.7%, $p = 0.040$; PgR+, 69.7% vs. 50.1%, $p = 0.009$; HER2−, 89.0% vs. 85.7%, $p = 0.175$), with a greater proportion of the luminal A subtype in the S-DBC group (S-DBC: Luminal A 59.4%, Luminal B 23.9%, HER2 disease 5.2%, triple negative 11.9%; SBC group: Luminal A 46.5%, Luminal B 29.7%, HER2 disease 7.2%, triple negative 16.3%, $p < 0.04$). Patients with S-DBC had better prognosis [5-year OS: 100% (S-DBC) vs. 90.9% (SBC), $p = 0.004$, 5-year DFS: 96.1% vs. 89.7%, $p = 0.011$].

Conclusions: Screening mammography can detect early breast cancers as well as less aggressive phenotype, luminal A tumors.

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Contra-lateral Breast Cancer − A 5 Year Clinical Study

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Introduction: Breast cancer is now the commonest cancer and leading cause of cancer death in Indian women. Contralateral breast cancer is defined as the occurrence of a second, independent primary breast cancer in the other breast after the initial diagnosis of breast cancer. Current data suggest that between 2% and 11% of patients diagnosed with breast cancer have or will develop bilateral disease. The study of contralateral breast cancer is becoming public health issues and of etiological interest because of the increased incidence of primary breast cancer and improved survival.Since there is lack of universal criteria for a contralateral breast cancer,the present communication is a study to evaluate the role of various factors on the occurrence and pattern of contralateral breast cancer.

Material and Methods: The study comprised of 266 proven patients of breast cancer seen and treated with various modalities between 1st January 2002 to 31st December 2006 Department of Radiotherapy, Christian Medical College, Ludhiana. A detailed analysis in cases of contralateral breast cancer were carried out with respect to age, menopausal status, family history, disease stage, histopathology, hormonal receptor status and the use of chemotherapy or hormonal therapy.

Results and Analysis: Contralateral breast cancer was found in 3% of the patients. The timeto occurrence was 2 to 20 years,Median time being 6.5 years. Metachronous presentation was 75% in contrast to synchronous being 25%. Mean age of presentation was 43.25 years and mean parity was 3.125. Seventy five percent were premenopausal women and 25% were postmenopausal women. Family history for breast cancer was found in 37.5% of the patients. Twenty five percent patients received neoadjuvant chemotherapy and 50% patients adjuvant chemotherapy. All patients received external beam radiotherapy. Mean time duration between first and second malignancy was 9 years in ER+ & PR+ patients, 8.6 years in ER− & PR− patients and 3 years in HER−2/neu + patients. Sixty two percent of patients received tamoxifen as hormonal therapy where as 38%

of patients did not receive any hormonal therapy. Median time duration between 1st and 2nd malignancy was 12 years in patients who received adjuvant tamoxifen in contrast to 6 months in patients who did not.

Conclusion: seventy five percent patients were metachronous and 62.5% were sporadic. Strong family history and premenopausal status are high risk factors. Hormonal manipualtion associated with low risk of contralateral breast cancer. These studies may also help monitor treatments effects of radiotherapy,chemotherapy and tamoxifen therapy. Treatment effects should continue to be monitored, and future guidelines should be provided for long term surveillance of surviving cancer patients.

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The Correlation Between Recall Rate and Cancer Detection in Mammographic Screening

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Background: Positive screening mammograms leading to recalls for further assessment with negative result, is considered to be harmful in mammographic screening. The aim of our study was to analyze whether there are any correlation between recall rate and the rate of screen-detected and interval cancer in the Norwegian Breast Cancer Screening Program (NBCSP).

Materials and Methods: About 2 million mammography screening tests, 72.000 recalls and 13.000 breast cancer cases, including Ductal Carcinoma In Situ, constituted the basis for this study. The NBCSP was gradually implemented for women aged 50−69 years old in the period 1996–2005. The regression coefficient (t-value for the slope) and the R^2 between the rates of recall and cancer detection in 16 areas in the NBCSP were estimated by a two-way t-test to identify correlation between the covariates.

Results: The recall rate was 4.9% for prevalent and 2.6% for subsequent screens. The rate of screen-detected cancer (DCIS and invasive) was 0.64% and 0.53% for prevalent and subsequent screens, respectively. The interval cancer rate was 18.5 per 10.000 screens. The rate of screen-detected breast cancer increased by increasing recall rate for prevalent ($t=3.40$, $p=0.001$, $R^2=0.13$) and subsequent screening tests ($t=6.83$, $p<0.001$, $R^2=0.44$). The recall rate did not show any correlation with the interval cancer rate ($t=-0.679$, $p=0.500$, $R^2=0.010$).

Conclusion: The recall rate shows a statistically significant positive correlation with the rate of screen-detected cancers in the NBCSP. The interval cancer rate, however, does not show any statistical significant correlation with recall rate. It thus seems that a higher recall rate did not succeed in detecting the fast growing tumors leading to interval cancer.

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Surgical Procedures in Screen-detected Cancer by Tumor Size, Grade and Calendar Time

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Background: Screening mammography has led to an increasing incidence of breast cancer and subsequently more women undergo surgery for the disease. We wanted to investigate the use of mastectomy by calendar time in women diagnosed with screen-detected breast cancer with different size and grading.

Materials and Methods: About 2 million mammography screening tests, and 10.000 screen-detected breast cancer cases, including Ductal Carcinoma In Situ (DCIS), constituted the basis for this study. The NBCSP was gradually implemented for women aged 50−69 years old in the period 1996–2005 and the number of hospitals offering breast surgery decreased from about 60 to 18. The rate of mastectomy versus breast conservation therapy was studied by percentage distribution through the study period.

Results: The percentage of mastectomy decreased steadily by calendar time for DCIS and invasive cancer. Mastectomy was performed in about 80% of the DCIS and invasive cancers >20 mm in 1996 while the rate was about 50% in 2009. For DCIS <10 mm, the percentage was below 20% during the entire study period while 60% of the women with invasive cancers <10 mm had mastectomy in 1996, decreasing to 20% in 2009. A trend toward an increasing proportion of mastectomy was observed the last three years of the study period, for tumors of all sizes. For DCIS grade 2 and 3, the rate of mastectomy decreased from 60% in 1996 to 40% in 2009. For invasive cancer, mastectomy was performed in 60−70% of all tumors in 1996, decreasing to 20% for grade 1, 30% for grade 2, and 40% for grade 3 tumors.

Conclusion: Mastectomy rates have gradually decreased for screen-detected breast tumors in all size and grade during the period 1996–2009. The trend toward increase the last three years should be closely followed as its rationale is uncertain.

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Breast Cancer Clusters in Rio De Janeiro: Analysis the Existence of Spatial Dependence in the Mortality Rate for Female Population

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Background: High female breast cancer mortality rates have been reported in the State of Rio de Janeiro, Brazil. The authors investigate whether the high breast cancer mortality is evenly spread over the Rio de Janeiro, in the sense that any observed clusters of deaths can be explained by chance alone, or whether there are clusters of statistical significance.

Objectives: To analyze the existence of spatial dependence in the mortality rate for female breast cancer in the State of Rio de Janeiro in the period 2001–2006 and possible explanatory variables.

Material and Methods: Analysis of the spatial correlation of mortality rate from breast cancer was performed in two triennium 2001 to 2003 and 2004 to 2006.

To evaluate the spatial dependence was calculated the Global Moran's Index and being used as explanatory variables: age, race, marital status, educational level, the average income for adult people from the main job (per municipality), the rate of mammography unit by municipality, the Municipal Human Development Index, the Firjan's Index Municipal Development, the percentage of population covered by private health insurance system, the average number of basic care medical visits and total spending per person, per year, on health by the municipal government.

It was used the method to establish the spatial mortality rate caused by female breast cancer and recognize the main aspects of this spatial variation.

Results: The spatial dependence was found in triennium 2001–2003 (Moran I statistic standard deviate = 1,7379, p = 0,0410) (figure 1), but the same result were not found during 2004–2006 (Moran I statistic standard deviate = 0,4450, p = 0,3281). The best variable that explains spatial clusters was 'the average income for adult people from the main job' and 'the rate of mammography unit by municipality'.

Conclusion: It was detected during 2001–2003 a spatial dependence in death rate by female breast cancer.

This result may be partly explained by average income per inhabitant (related to poverty) and the rate of mammography unit by municipality.

The use of spatial analysis could allow a better comprehension of geographical distribution of mortality rate caused by female breast cancer in Rio de Janeiro.

The procedure, step by step, used in this analysis showed consistent outcomes and compatible with those of the international literature.

The selection of more explicative variables, including clinical and biological variables, could enable identify more potential factors associated with this death rate, that can provide margins to new investigations as well as subsidize decisions which might help the decline of this rate.

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Breast Cancer in Ethiopia: the Addis Ababa-Halle University Collaboration Project Studying Incidence, Mortality and Clinical Epidemiology

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Background: An increasing burden of non-communicable diseases in developing countries has so far only been marginally approached. Since 2010, more women die of breast cancer than due to pregnancy-related causes (maternal mortality). Our project is focussing on breast cancer in urban and rural settings in Ethiopia.

Materials and Methods: A collaboration between the Radiotherapy Center and Department of Public Health (University Addis Ababa/Ethiopia) and the Department of Gynecology and Institute of Clinical Epidemiology