## Working Group: Improving Standardized Measures of Breast Density and Hormone Therapy in Routinely Collected Data

Authors: The HRT and Mammography Screening Performance Working Group, ICSN

### Abstract

The effects of HRT on breast density and their subsequent impact on the outcome of breast screening have been reviewed by a working group of ICSN. The precise effect on service screening of these factors is not clear but both appear to reduce its effectiveness. At the previous meeting of ICSN in Ottawa it was decided that some information about the assessment of these factors by screening programs might be a useful starting point for discussion about their effects on screening program performance. A survey of the breast screening programs of ICSN member countries to document the recording of HRT use or breast density at mammography is described and the available results will be presented for discussion.

## Working Group: Performance Parameters Evaluation: U.S.-Norway Comparison of Interval Breast Cancers Project

Authors: BC Yankaskas, S Hofvind, J-L Bulliard, J Frauchbaud, C Klabunde

### Abstract

Background: Prior work of the International Breast Cancer Screening Network has shown that varying definitions create hurdles for comparing screening performance. Interval breast cancer rates (ICRs) are particularly affected.

Objective: To test whether variations in ICR definitions affect comparisons of ICR in Norway and North Carolina.

Methods: An interval cancer (IC) was defined as a cancer diagnosed following a negative screening mammogram in a defined follow-up period. We used data from the National Breast Cancer Screening Program in Norway and the Carolina Mammography Registry to calculate ICR for women ages 50–69, at subsequent screening, during the time period 1996–2002. ICR was defined using three different denominators (negative screens, negative final assessments, and all screens) and three different numerators (DCIS, invasive cancer, and all cancers). ICR was calculated using two methods: (1) number of ICs divided by the number of screens and (2) ICs divided by the number of women-years at risk for IC. Analysis was by chi-square tests for differences in ICR between Norway and North Carolina.

Results: There were no differences in ICR according to the definition used. In the 1–12-month follow-up period, ICRs per 1,000 for negative screens, negative final assessment, and all screens were 0.53, 0.54, and 0.54 for Norway and 1.20, 1.25, and 1.17 for North Carolina. Similar patterns were seen for 13–24 and 1–24 months follow-up as well as when women-years were used. ICR was higher in North Carolina compared with Norway under all definitions and in all follow-up time periods, regardless of calculation method.

Conclusion: For both Norway and North Carolina, the ICR did not differ by definition used. The definition had no effect on the international comparisons; however, ICRs were consistently higher in North Carolina than in Norway. There are many potential explanations for this difference.

## Discontinuing Postmenopausal Hormone Therapy (PMH) Is Associated With Increasing Mammography

Authors: DSM Buist, R Walker, W Clinton, EJA Bowles, K Kerlikowske, P Carney, T Onega, SH Taplin, DL Miglioretti

## Abstract

Background: Screening mammography rates and invasive breast cancer rates have started decreasing in the United States. Concern exists that mammography declines may be greater among women who stop using PMH than among continued and non-PMH users, which could lead to an artificial decrease in breast cancer rates.

Objective: To examine the proportion of appropriately screened women over time separately for continued, former, and non-users of estrogen+progestin (EPT) and estrogen-only (ET).

Methods: We identified a cohort of 107,005 women aged 50–79 who were enrolled between 1996 and 2006 in Group Health in western Washington State (United States). We identified PMH dispensing and screening use using electronic data. We defined appropriate screening as having a bilateral screening mammogram within the past 26 months.

Results: The percentage of women appropriately screened increased from 70.2 to 74.5% between 1999 and mid-2005 and started to fall thereafter. The lowest percentage of appropriate screening was among non-users (60–70%) and the highest among current EPT (82–84%) and ET users (79-83%). Former EPT and ET users had lower proportions of women appropriately screened than current users until late 2002, when screening rates in former users rapidly increased to the rates of current PMH users.

Conclusion: Contrary to our hypothesis, we found mammography screening rates have increased among PMH discontinuers. Higher screening rates among discontinuers may reflect a healthy user bias or increased concern over breast cancer risk among former users. Decreased mammography receipt among former PMH users is not likely to explain recent declines in breast cancer incidence.

## **Multiple Detection Modalities for Breast Cancer Screening**

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Keywords: multiple detection modalities, breast cancer screening, mixture stochastic model

## Abstract

Background: As tumour progression is dynamic, the ability of a specific screening tool to detect early breast cancers must take the time dimension into account. However, the majority of previous models only focused on solo detection modes instead of multiple detection modalities.

Objectives: The present study aimed to propose a stochastic model for the estimation of disease natural history that is superimposed with various sequential patterns detected by multiple screening tools.

Methods: We developed a mixture latent model with several multi-state models allowing different temporal sequences from the earliest time detected by various screening tools in the light of biological variation. A simulated cohort based on the Berg et al. study on the combination of ultrasonography and mammography was created and used to estimate the relevant transition parameters.

Results: The proportion of early detection for ultrasonography preceding mammography was 64%, and the opposite was 36%. The average time from the earliest time detected by ultrasonography to the earliest time detected by mammography was 2.68 years. However, from the earliest time detected by mammography to the earliest time detected by ultrasonography was very fast. The time detected by both diction modes but in the PCDP phase to clinical phase was approximately 2.5 years.

Conclusion: A mixture stochastic model was developed to elucidate the disease natural history of preclinical, screen-detectable phase characterized by the superimposition of the earliest time to detect tumor for each detection modality. It is useful for evaluation of effectiveness or cost-effectiveness of multiple detection modalities compared with a single mode.

# Comparing Organized and Opportunistic Screening Programs: Challenges and Progress

Authors: B Geller, S Hofvind, P Vacek, B Yankaskas

Key words: international comparison, mammography

#### Abstract

Background: The ICSN has attempted in the past to do country comparisons with great difficulty. Besides differences in data definitions and collection, countries also have very different procedures for the delivery of screening services, making comparison difficult.

Methods: Two sites in the United States with opportunistic screening have completed comparisons with Norway's organized program. We discovered some fundamental differences and designed methods for addressing them.

Results: In Norway, as in most European programs, the programs are evaluated as a whole as per the European guidelines, while the United States evaluates various components separately. We have learned how to dissect the organized program into components for the purpose of comparison.

Challenges: Some procedures, such as a screening mammogram, cannot be defined in exactly the same way. We do not know the background incidence rate of the different countries. Pathologists may be naming histologies differently. Double reading, CAD, and digital cannot always be identified for individual mammograms. Several women-level characteristics, such as mammographic breast density, are not routinely collected in Norway. There is no comparison for the U.S. short interval follow-up assessment in Norway.

Progress: We carefully defined each procedure and outcome to assure comparability. To address the differences in different intervals we have used women-years-at-risk and for different follow-up times we have used a life table approach for risk analyses.

Conclusion: International comparisons are complicated but feasible. Attention needs to be directed to how each measure is defined, and each data analysis needs to be carefully inspected to see if it makes sense. We run the risk of using the same words with different meanings and need to carefully check language usage to confirm that we understand each other.

## Arbitration Cancers in an Organized Population-Based Breast Screening Program Performing Independent Double Reading With Consensus

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### Abstract

Background: Several studies have analyzed the effect of different interpretation procedures on the cancer detection rate in screening mammography. However, less is known about the additional cancers detected in double versus single reading.

Aim: To compare the radiological features and histopathological findings of arbitration cancers and concordant cancers (i.e., both radiologists called it positive) diagnosed in the Norwegian Breast Cancer Screening Program.

Material and Methods: The program performs independent double reading with consensus. Arbitration cancer is thus breast cancer diagnosed after an interpretation score of 1 (negative) by one reader and 2 or higher by the second. Concordant cancers have a score of 2 or higher by both radiologists. This study includes interpretation scores from 1,033,872 screens and 5,611 breast cancers.

Results: The proportion of arbitration cancers was 24% (1,331/5,611). Calcification with no associated tumor mass was more common in arbitration cancers compared with concordant cancers (25% versus 17%, p<0.001), as well as poorly defined masses (15% versus 9%, p<0.001). Invasive arbitration cancers had a mean tumor size of 12.9mm versus 15.0mm (p<0.001) in concordant cancers. Grading and lymph node involvement were prognostically favorable in arbitration compared with concordant cancers. The OR of detecting an arbitration cancer increased by mammographic density (OR 0.82, 95% CI: 0.50–0.80) in a regression model adjusting for age and screening history (i.e., prevalent versus subsequent screen).

Conclusion: Independent double reading increased the detection rate of small invasive cancers associated with calcification and poorly defined masses.

# Experience Gained from Digital Mammography and MRI in Breast Cancer Screening of High-Risk Women

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#### Abstract

Objective: The demonstration of effective imaging methods (digital mammography, MRI) suitable for the most reliable identification of high-risk patients (BRCA1,2 gene mutation carriers) in breast cancer screening.

Materials and Method: At our Genetic Department, altogether 1,157 examinations were performed from May 1994 to May 2006. BRCA 1 was verified in 87 cases and BRCA2 in 25. Both gene mutations were present in one individual. The mean age of the participants was 41 years. In our Institute, breast MRI has been available since April 2000 and digital mammography since September 2005. With us, the breast screening of high-risk women is started 7 years earlier than the appearance of breast cancer with the youngest family member. Breast cancer screening also with MRI has been done with 58 women since April 2000 (age: 26–59 years). The combined examination verified the presence of BRCA1,2 gene mutations in these subjects, of whom 31 were symptom- and complaint-free and 27 underwent surgery and/or radiotherapy and chemotherapy, respectively.

Results: In 4/31 symptom- and complaint-free women MRI identified a malignant process. Mammography, however, failed to detect the pathology in the dense breast in three of them. In one subject, MRI revealed a contra-lateral lesion and in another subject, a multifocal one. In the latter case complementary, targeted US was used to identify the lesion that was verified by biopsy histology. Two years ago, 12 women with gene mutations were examined with digital mammography. With this method we experienced improved diagnostic accuracy in breasts with dense structure. The digital technique allows for post-processing methods by means of which we can reduce the number of additional shots, and the use of CAD (computer aided detection) that enhances the perception, primarily in dense breasts.

Conclusion: MRI with screening purpose is superior to the traditional mammography with women representing high risk for breast cancer. Therefore, in this special population group, we perform MR mammography annually, complementing the traditional imaging techniques as suggested by the American Cancer Society. Our experience gained from digital mammographic examination is in harmony with the results of other international teams. Many authors agree in that by means of the digital technique the sensitivity (diagnostic accuracy?) of mammography in the dense breast improves.

# Developing Guidelines for Monitoring Breast Screening Program Performance in Canada

Authors: J Onysko, on behalf of the Canadian Breast Cancer Screening Initiative's Quality Determinants Working Group

### Abstract

The Canadian approach to monitoring breast screening program performance addresses a number of the challenges associated with cross-jurisdictional evaluation. The development of performance measures in Canada has progressed under the stewardship of the Canadian Breast Cancer Screening Initiative's Quality Determinants Working Group, with the release of the second edition of the *Guidelines for Monitoring Breast Screening Performance*.

Measures were selected according to practical criteria: data availability and quality; availability of evidentiary basis; and wide recognition of the utility of the measure for regular national comparison. The development process was informed by recognized population screening principles, as well as evidence from randomized controlled trials, demonstration projects, and observational studies where possible.

Fourteen performance measures were ultimately established: participation rate, retention rate, abnormal call rate, invasive cancer detection rate, in situ cancer detection rate, diagnostic interval, positive predictive value, benign to malignant open surgical ratio, benign to malignant core biopsy rate, benign core biopsy rate, invasive cancer tumour size, node-negative rate in cases of invasive cancer, and post-screen detected invasive cancer rate. Each measure included a definition, the context in which it was relevant, method of calculation, target objectives, current results, and a record of modifications from the previous edition.

Evaluation of program performance has been published (retrospectively and ongoing) from 1996, with screening in 2003–04 currently under evaluation. Observed interactions among the measures, varied interpretations of data definitions, and evolving diagnostic practices have informed the ongoing development of breast screening program performance measures in Canada.