

Future studies for our cohorts will be performed to investigate the ethnic differences influencing the genetic alterations related to *BRCA* mutations.

# 128 **Birth Cohort Correlates with Breast Cancer Risk in European BRCA-2 Mutation Carriers**

Poster

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**Background:** Mutations in the *BRCA*-1 and *BRCA*-2 gene lead to an elevated risk of developing breast (BC) and ovarian cancer (OC). However, risk estimates vary, depending on the study population. Furthermore, there are indications that the birth cohort can influence the cancer risk. We investigated the risks for BC and OC associated with *BRCA*-2 mutations in a cohort of female mutation carriers of a genetically heterogeneous central European population who were identified by molecular genetic testing.

**Patients and Methods:** This study included 171 women who underwent genetic counseling and where molecular genetic examination identified a mutation in the *BRCA*-2 gene at the Medical University of Vienna, Division of Senology, in Austria. A total of 57 healthy and 114 affected *BRCA*-2-carriers were detected. The risk was estimated using the product limit method. The log rank test was used to compare different strata.

**Results:** The risk of developing cancer to age 70 was found to be 85% for BC (95% CI 77–93%) and 31% for OC (95% CI 16–46%). Female *BRCA*-2-carriers born in 1958 or later were at a significantly higher risk of developing BC ( $p < 0.001$ ; 88% vs. 46% to age 40) but not of OC ( $P$  is not significant; 0% vs. 2% to age 40) compared to mutation carriers born earlier.

**Conclusion:** We conclude that female *BRCA*-2 mutation carriers should also be counseled about their cohort-dependent cancer risk, especially for breast cancer. Further research about variables that may affect cancer risk (e.g. lifestyle-related factors) should be considered.

# 129 **Primary Prevention of Breast Cancer – Knowledge and Attitudes of Belgian Women**

Poster

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**Introduction:** The accuracy of a woman's knowledge of her risk of developing breast cancer (BC) has gained importance as more options for prevention have become available including life style modifications, chemoprevention and risk reduction surgeries for those at increased risk. Furthermore according to several theoretical models in health promotion, knowledge is one of the first steps for informed decisions regarding prevention options.

**Aim:** To assess knowledge of information typically included in preventive consultation for BC.

**Methods and Results:** The studied population included 1000 consecutive women who attended our breast unit in 2009. Women were assessed using a validated 63-items questionnaire divided into five dimensions including: (1) women's screening habits and satisfaction in attending the breast clinic, (2) sociodemographic and epidemiologic data, (3) women's knowledge of risk factors, (4) personal BC risk estimation, (5) attitude towards BC prevention, and (6) willingness to participate in a BC prevention trial. The age of the respondents ranged from 16y to 88y (mean: 51y); most of women attended the breast unit for more than 1y (64%); 89.9% had a past mammography; 60% have been sent by a gynecologist. Surveyed women were mainly Belgium natives (67.6%), have been graduated (51.2%), and had a job (59.8%). A family history of BC was mentioned by 38% of the respondents and 326 (33%) had a past breast surgery. Among them, 170 have been operated on for BC. Less than half of respondents had knowledge of modifiable risk factors of BC (table).

Modifiable risk factors	Correct answer	Do not know	Incorrect answer
Overweight/Obesity	42.6%	44.6%	12.8%
Physical Activity	45.5%	33.5%	21.3%
Alcohol	46.4%	42.9%	10.7%
Diet	42.4%	36%	21%
Late pregnancy >35y	13.5%	64.7%	21.5%
Hormone Replacement Therapy	43.2%	48.2%	8.5%
Pill	15.1%	47.9%	37.1%
Tobacco	7.5%	31.1%	61.4%

Only 12% of respondents estimated correctly their life time risk of BC; 31% of them overestimated it and 57% did not know. Knowledge was not

improved in women sent by gynecologists neither general practitioners. Willingness to consider chemoprevention was declared by 23.8% of the surveyed population but in case of hypothetical medical advice, this risk reduction option was stated by 57.1%. One woman out of two mentioned an interest in preventive clinical research even if of no direct personal benefit (47%) and most women mentioned interest if potential individual benefit (61%). Most of the respondents wanted more information on methods aimed at decreasing BC risk (81.6%).

**Conclusion:** Despite women's interest, there is still a significantly unmet demand for information and decision making support in the context of BC primary prevention in Belgium.

# 130 **Over-diagnosis and the Natural History of 'Early' Breast Cancer**

Poster

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Breast screening programmes have provided us with a natural experiment of the greatest historical importance, not because of their success in reducing breast cancer mortality, but because of the observations concerning the over-diagnosis of the disease. I would therefore like to argue that some of these earliest stages of 'cancer' if left unperturbed, would not progress to a disease with lethal potential. These pathological entities might have microscopic similarity to true cancers but these appearances alone are insufficient to predict a life threatening disease. Conventional mathematical models of cancer growth are linear or logarithmic; predicting transition from in-situ phases to early invasive and from early invasive to late invasive over time. Most natural biological mechanisms are non-linear. Prolonged latency followed by catastrophe should not be all that surprising. We accept the case for prostate cancer, as we know that most elderly men will die with prostate cancer in situ and not of prostate cancer. Further support for this contention comes from other sources.

- There has been an epidemic of bilateral mastectomies in the USA following the uncontrolled proliferation of MRI scans in the routine work up of women presenting with a single focus of early breast cancer. The MRI scan is guilty of unveiling not only latent foci of pseudo-cancers outside the index quadrant but also latent foci in the contra-lateral breast.
- Contrary to all predictions, the increased rate of detection of duct carcinoma in situ (DCIS) has led to an **increase** in the mastectomy rate for the screened population. Up to 45% of screen detected cases of DCIS end up having mastectomy because of the multi-centricity of the disease. Yet the paradoxically clinically detected multi-centric invasive breast cancer is relatively uncommon.
- The TARGIT trial of intra-operative radiotherapy, demonstrated non-inferiority in outcome, as judged by local recurrence rates at 4-years amongst 2,232 patients. The TARGIT trial was predicated on the fact, that in spite of >60% of patients with a single clinical focus of the disease harbour other occult foci of disease outside the index quadrant, yet the vast majority of LR occur within the index quadrant. Looking upon it in another way the TARGIT trial experimental arm has now followed up more than 1,000 women, approximately 600 of whom have been harbouring untreated foci of cancer, for anything up to 10 years, with no greater hazard of relapse than those treated with whole breast radiotherapy.
- The logical consequence of these observations would be a trial of active surveillance versus conventional therapy for screen-detected cases of DCIS. Using this platform we might then learn what the clinical or biological characteristics of the disease are that allow it to leave its dormant phase and enter the transition to early invasion.

# 131 **Mammographic Density, Tumor Characteristics, and Prognosis**

Poster

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**Background:** Mammographic density is a well-established risk factor for breast cancer. However, little has been published on the association between density, tumor characteristics, and prognosis, and the studies that do exist are of conflicting results.

**Materials and Methods:** This study is an extension of a population-based case-control study where cases were all women with incident breast cancer, diagnosed 1993–1995, and aged 50–74 years. For this study we only included postmenopausal cases for whom we were able to retrieve mammograms ( $n = 1774$ ). Mammographic density was assessed using a computer-assisted thresholding technique. We used linear, logistic, and multinomial logistic regression, adjusting for possible confounders, to study density and tumor characteristics. The cox proportional hazards model was used to study recurrence and survival.