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

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

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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.

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Primary Prevention of Breast Cancer − Knowledge and Attitudes of Belgian Women

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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 send 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.

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

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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 lead 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.

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Mammographic Density, Tumor Characteristics, and Prognosis

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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.

Results: Percentage mammographic density (PD) was positively associated with tumor size (p = 0.004) and grade (p = 0.033), but the relationship with grade was attenuated after adjustment for, among other variables, mode of detection (p = 0.069). Furthermore, PD was associated with both breast and locoregional recurrence even after adjustment for treatment; women with PD⩾25% had a hazards ratio (HR) of 1.96 for breast recurrence and a HR of 1.78 for locoregional recurrence compared to women with PD <25% (p = 0.032 and p = 0.017, respectively). No other associations between PD and the tumor characteristics studied (hormone receptor status, lymph node metastasis, proliferation rate, and histopathological classification) were observed, nor was PD associated with distant metastasis and survival.

Conclusion: Density may be viewed as fertile soil; increasing both risk of primary breast cancer, independent of subtype, and risk of recurrence. Thus, density should not only be taken into consideration in the screening setting, but also when making decisions on adjuvant therapy and follow-up regimes.

132   Poster
Recent Trends in Breast Cancer Incidence and Mortality Rates in South-Eastern European Countries

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Background: Breast cancer is the most frequent cancer in women across Europe, as well as worldwide. Incidence is increasing as a result from a variety of secular and exogenous influences. Studying the trends in incidence and mortality can serve the planning of breast cancer prevention policies at individual and collective level. The focus of this study is on South-Eastern European countries which have been underreporting, but may also show rapid changes. The EU FP7 EUROCOURSE project (www.eurocourse.org) aims to tackle problems of cancer registries in this part of Europe.

Materials and Methods: Within a broader project we analysed data from cancer registries in eight South-Eastern European countries, from Slovenia to Cyprus and Malta, also including Turkey. Age standardized (world standard − ASRW) incidence and mortality rates for 2008 were calculated for these countries based on the corresponding regional or national cancer registries. Average annual percent change (AAPC) with 95% confidence intervals of rates observed during 1999–2008 was calculated using joinpoint regression.

Results: Incident breast cancers comprised between 23% and 39% of all incident female cancers. Incidence rates (ASRW) varied from 35 to 82 per 100,000 women and were increasing with 1 to 4% in most of them, annually. Deaths due to breast cancer comprised between 13% and 25% of all female cancer deaths. Mortality rates (ASRW) varied between 7 and 20 per 100,000 women. In contrast to incidence, mortality was decreasing in most of the countries with 1 to 5% annually.

Conclusion: This geographical area, sharing common socioeconomic and demographic changes i.e. increased longevity, age at childbirth and decreased fertility rates, showed clear variation in breast cancer incidence and mortality. There were also effects of earlier detection through mass screening in a few countries, and as elsewhere improvements in adjuvant therapy.

133   Poster
Improved Survival of Bulgarian Breast Cancer Patients, Diagnosed in 2006–2009 Compared to Patients From an Earlier Period

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Background: Two important events, aiming improved quality of care for Bulgarian breast cancer patients took place in 2006 − an updated National standard for complex treatment of breast cancer was introduced and the National Health Insurance Fund (NHIF) requested establishment of specialized oncology committees in each hospital dealing with cancer patients. The function of those committees was to take decision about the best available individual treatment plan for all cancer patients.

The purpose is to study the impact on survival in relation to application of the National standard and requirements of NHIF.

Materials and Methods: We examined the data from the Bulgarian National Cancer Registry for female breast cancers, diagnosed in 2001–2009 and followed up to death or to the end of 2010. Characteristics of the patients − age, stage, grade, morphology and place of surgical treatment were compared between two periods − 2001–2005 and 2006–2009. Chi-square test, Kaplan–Meier method, Log-rank test and Cox regression method were used.

Results: There were 32546 female breast cancer cases, diagnosed in 2001–2009. We found statistically significant dependency (P < 0.0001) between period of diagnosis and each one of the examined factors. For the period 2006–2009, the proportions of patients younger than 40 years and older than 60 and of those, diagnosed in the first stage of the disease, were higher than the earlier period. There were improvements in morphological verification of the tumors − fewer patients with unknown grade and morphology were observed for the period 2006–2009. The proportion of patients, surgically treated in the National Hospital of Oncology was higher in 2006–2009. Five years survival was 63.7% and 70.0% for the periods 2001–2005 and 2006–2009, respectively (p < 0.0001). The risk of death was with 12% lower (Hazard ratio = 0.88, p < 0.0001) for the patients, diagnosed in 2006–2009, compared to the earlier period, after adjusting for age, stage, grade and place of surgical treatment.

Conclusions: The observed improvement of prognosis for breast cancer patients is possible to be explained with the strict application, required by NHIF, of the National standard for complex treatment in all hospitals where cancer patients were diagnosed and treated. Probably the increasing qualification of oncologists, introduction of more sensitive diagnostic techniques and improving health awareness of the women also attributed to better prognosis in recent years in a situation of preparation of population breast cancer screening program.

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Clinical and Histological Features of Breast Cancer After in Vitro Fertilization

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Background: The role of in vitro fertilization (IVF) in the induction of breast cancer remains unclear. It is very interesting to examine if this type of breast cancer has some distinctive features regarding pathology or clinical characteristics.

Materials and Methods: A research of distinctive histological, clinical and epidemiological features in cases of invasive breast cancer following in vitro fertilization in our department. Thirty four (34) cases of invasive breast cancer were analyzed. Patient characteristics were extracted from their medical records and the breast cancer data bank of our department. The registered data concerned age, initial presentation, medical and family history, the histological features of the neoplasms and the TNM staging.

Results: The main findings are the following: 7(21%) patients were under 40 years old and the other 27(79%) were older, 27(79%) women were pre-menopausal and 12(35%) had positive family history. The great majority of patients 27(79%) were diagnosed with infiltrating ductal carcinoma and the grade was I in 10(29%), II in 14(42%) and III in 10(29%). Regarding the status of lymphnodes in 17(50%) was N_0, in 4(11%) N_x, in 3(9%) N_1, in 5(15%) N_2 and in 5(15%) N_3, as far as the stage of disease is concerned in 11(32%) was I, in 9(26%) II, in 10(30%) III and in 4(12%) IV. Finally regarding the status of ER, PgR and HER2 in 20(59%) was ER(+), in 17(50%) was PgR(+) and in 12(35%) was HER2(+).

Conclusions: Even though the sample was small, a large percentage of patients had a positive family history. It's worth mentioning that many cases presented in pre-menopausal women, relatively soon after in vitro fertilization. More data are needed in order to evaluate the role of IVF in the induction of breast cancer as well as to define the high-risk sub-groups. Patients with positive family history for breast cancer are considered to be a high-risk sub-group.

135   Poster
Preliminary Results of a Medical Unit for Prevention-consultation of Familial and Hereditary Breast Cancer

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Background: Most breast cancers are sporadic and not associated with any clear familial genetic predisposition. However, approximately 10% of