## Wednesday, 22 March 2006 14:15–16:00

EUROPA DONNA SESSION

# Management of high risk families

30 Invited

### Clinics for high risk women

B. Arver. *Karolinska University Hospital Solna, Department of oncology and pathology, Stockholm, Sweden*

A family history of breast cancer is a major risk factor for getting the disease. Women with one or two close relatives with early onset breast cancer have a two to three times higher risk than women in general. Females with mutation in one of the breast cancer genes BRCA1 or BRCA2 have up to 80% life time risk of getting breast cancer. Their risk of ovarian cancer is also elevated and early onset is common.

Women with a family history of breast cancer can consult our hereditary breast cancer clinic without a referral. The onco-genetic counsellor draws a pedigree and the diagnosis of cancer in the family is confirmed through medical files or by death certificates. Genetic analyses are offered if applicable and finally an individual risk assessment is made. Women with a very high life time risk of breast and/or ovarian cancer have two options, either prophylactic surgery or regular surveillance. Women opting for a prophylactic mastectomy with reconstruction are guided through the process by a multidisciplinary team including a geneticist, oncologist, surgeon, plastic surgeon, psychologist, gynaecologist and specially trained nurses. International studies have shown a 90% risk reduction after a prophylactic mastectomy and an evaluation of their postoperative quality of life and the sexual consequences of the operation are ongoing.

With regards to women who do not opt for a prophylactic mastectomy a follow up study including 600 women from Stockholm with an increased risk of breast cancer is also ongoing. Women with a 20 to 80% lifetime risk of breast cancer have been invited to participate after receiving onco-genetic counselling and a risk assessment. The main question of the study is to determine which method, self examination, doctors examination, mammography or ultrasound will first detect a malignant breast tumour? Mutation carriers from 25 years of age upwards have been included in the study. In addition lower risk women with a family history of breast cancer and who are at most ten years younger than their relative's age at diagnosis are also included. An upper age limit of 60 years has been applied. Other factors like breast density, reproduction, hormone use, physical activity and alcohol consumption are also being taken into account. Baseline data are now being evaluated.

31 Invited

### Training genetic counselors – what should this entail?

H. Meijers-Heijboer. *Erasmus Medical Canter, Department of Clinical Genetics, Rotterdam, The Netherlands*

The organisation of the medical care concerning inherited diseases and its financial reimbursement vary throughout the western world. Medical practitioners, medical geneticists, and/or genetic counsellors may provide these services. Genetic counsellors are health professionals with specialized graduate degrees who have experience in the areas of medical genetics and counselling. Most common specialisations are prenatal, cancer, paediatric and adult genetics. There is a growing demand for genetic counsellors in view of the expending knowledge of the inherited basis of disease. Despite this, only a handful of countries provides formal courses in genetic counselling. Admission requirements for individuals entering training programmes for genetic counsellor differ substantially between countries. Most enter the field from biology, genetics, nursing, psychology, public health and social work. Also, large differences exist between the responsibilities of genetic counsellors in daily clinical practice.

We advocate a master's level training programme specifically designed for genetic counsellors, with a list of core competencies that are shared by all training programmes of genetic counsellors throughout the world.

32 Invited

### Population studies of mutation carriers in the Israeli population

Abstract not received.

## Wednesday, 22 March 2006 16:00–16:45

POSTER SESSION

# Screening

33 Poster

### The frequency of breast cancer screening: results of a randomised trial

R. Blamey[1], S. Duffy[2]. [1]*Nottingham City Hospital, Nottingham Breast Institute, Nottingham, United Kingdom;* [2]*UK Co-ordinating Committee on Cancer Research (UKCCCR), UK*

This randomised trial in 110,000 women between 1989 and 1996 compared screening at the standard interval of 3 years (Controls – C) with screening annually (Trials – T), in women aged 50–64 who had undergone a prevalent screen.

A previous analysis used the Nottingham Prognostic Index (NPI) to predict outcomes of the invasive carcinomas diagnosed; these predictions were based on observed survivals in all cancers prior to 1988.

However survival within each NPI group has improved, due to better therapy. Recalculation is based on these new figures of outcomes within each NPI group.

1. Predicted outcomes are compared with observed outcomes at ten years in the table.

| Invasive cancer | No. diagnosed | | No. predicted surv. at 10 yrs | | No. observed surv. at 10 yrs (Act) | |
|---|---|---|---|---|---|---|
| | C | T | C | T | C | T |
| GPG | 92 | 113 | 87 | 108 | 89 | 107 |
| MPG | 87 | 96 | 68 | 76 | 66 | 82 |
| PPG | 22 | 20 | 11 | 10 | 14 | 14 |
| Total | 201 | 229 | 166 (82%) | 194 (85%) | 169 (84%) | 203 (89%) |

There is good agreement between the predicted and observed 10 year survivals. Neither show significant difference between C and T groups.

2. Predicted outcomes at 20 years: The predicted percent surviving in both groups is 73%.

**Conclusion:** 1. There is no significant advantage to annual screening over the standard 3 year interval in the NHSBSP and shortening of the screening interval would be extremely expensive

2. Although in the Trial group there were more cases in the GPG and less in the PPG, this was not large enough to significantly improve survival and the absolute difference is 3–5% (Relative Risk Reduction 16–23%) less deaths in the trial group at 10 years.

3. There were the same percentages of DCIS in the two groups.

4. The use of a predictive model for outcomes is justified, prediction to 20 years is of 73% survival in both groups.

34 Poster

### Over-diagnosis in screening by mammography: A follow-up of the Malmö Mammographic Screening Trial, MMST

J.P. Garne[1], S. Zackrisson, I. Andersson, L. Janzon, J. Manjer.
[1]*Department of surgery, Århus University Hospital, Århus, Denmark;*
[2]*Institute of clinical science Malmoe University Hospital, Malmoe, Sweden*

Over-diagnosis in breast cancer screening occurs when cases detected by screening would never have surfaced clinically in the absence of screening, either because the woman dies prematurely from causes other than breast cancer within the lead time period or by the detection at screening of biologically inert tumours that would not have surfaced clinically even within the normal lifetime of its bearer. Earlier studies on this subject have been based on estimates and statistical modelling. The present study is based on direct observations of the occurrence of breast cancer in the two arms of the MMST during the 10 years of the randomised study and for the following fifteen years.

**Methods:** MMST was a randomised controlled study of 42,283 women aged 45–69 years at entry, born 1908–32. The screening arm contained 21,088 women and the control arm 21,195. The study started in 1976 and ended in 1986. Hereafter the randomised design was maintained for women still under age 70. In 1990 service screening started through which all women in the age group 50–69 in Malmö were invited to screening. In the fifteen oldest birth cohorts (born 1908–22, 55–69 years at entry) the

control group was never invited to screening, while in the ten youngest (born 1923–32, 45–54 years at entry) the control group was invited after 1990. Incident breast cancer cases for the period 1987–2001 were identified through record linkage with the Swedish Cancer Register.

**Results:** At the end of the period of randomised design there was an excess of 24% (150 cases). In women aged 55–69 years at randomisation the excess was 32% and in women aged 45–54 it was16%. An excess number of cases of 10% (115 cases) remained in the former invited group at the end of follow-up in 2001. This includes invasive as well as in situ carcinoma. If only invasive carcinoma is considered, the over diagnosis reached a level of 7%.

**Conclusion:** Screening by mammography is associated with over diagnosis. The rate of over-diagnosis was greater in older than in younger women and it was mainly caused by invasive breast cancer. Women opting to continue screening after 70 years of age, should be informed of a substantial risk of over diagnosis.

35 Poster

## German pathologists in preparation for population based mammography screening: Results of a nation-wide training course series

T. Decker, D. Hungermann, H. Bürger, C. Kersting, W. Böcker. *University of Muenster, G. Domagk Institute of Pathology, Münster, Germany*

**Introduction:** In 2005, a population based mammography screening program for Germany based on the European guidelines has been started. Without improving the pathology service, the benefit of screening may be reduced or even lost. Especially specimens from minimal invasive diagnosis (MIB) of screened women provide pathologists with problems. To prepare pathologists who intend to participate in the German screening project the authors give courses on breast screening pathology as the first feature within an external quality assurance scheme.

**Aims:** 1. to evaluate the effect of the training courses on diagnostic performance, 2. to assess the performance of German pathologists interested in breast cancer screening, and 3. to identify the diagnostic problems.

**Methods:** From February to November 2005, 297 pathologists participated in 15 diagnostic courses, each for maximum 20 participants. Each course included 4 microscopic tutorials and 8 presentations. It started and ended with a diagnostic test using the same set of 11 slides of MIB specimens selected within broad diagnostic categories by two of us (T.D. and W.B.) with complete agreement. Participants reading the slides used a form planned as standard reporting form for the German Screening Project including the B category according to the EU Guidelines. Kappa statistics were calculated separately for the entry and the closing test. The advantage of these statistics is that kappa values are independent of the diagnosis; they simply reflect the consistency of ratings by the participants. The following limits were used for interpretation: <0.0: none, 0.0–0.2: poor, 0.21–0.4: slight, 0.41–0.6: fair, 0.61–0.8: good, 0.81–0.92: very good, and 0.93–1.0: excellent.

**Results:** 1. After the course the rate of cases with "good" and better consistency increased from 7 to 9/11 cases. 2. The overall consistency of the participants' B-categories is 0.62. 3. There are 4 features with poor to fair agreement: columnar cell change, columnar cell hyperplasia, DCIS low grade, and phyllodes tumor.

**Conclusions:** 1. The training course improved the consistency of the test results in MIB. 2. The consistence of attending German pathologists in MIB diagnosis is in general at least substantial (kappa >0.6) 3. To improve the performance, further education should focus on differential diagnosis of columnar cell lesions and non-high nuclear grade DCIS/ductal hyperplasia, respectively.

36 Poster

## Mammographic density and the size of breast cancers detected by programmatic screening

C. Nickson, A.M. Kavanagh, G.B. Byrnes. *University of Melbourne, School of Population Health, Melbourne, Australia*

We assess the effect of mammographic density on tumour size at detection in the Australian mammographic screening program, in order to examine the relative mortality benefits of mammographic screening.

**Brief description:** Firstly we examine descriptive statistics of tumour size according to density (threshold percent density or dense area) and mode of detection (screening or interval). We then use regression analyses to adjust for potential confounders and assess whether there is effect modification by mode of detection.

**Summary:** The median and mean size of cancers detected by screening generally increased with density at first and subsequent rounds. No such effect was apparent in interval cancers.

Histograms of tumour size quintile groups by density quintile groups revealed a shift in size distribution towards larger cancers with increasing density, at first (Figure 1) and subsequent rounds. Cancers detected in women with lower density tended to be smaller and screen-detected, whereas cancers detected in women with higher density tended to be larger and more often interval-detected. These differences appeared to be incremental across the five density groups.

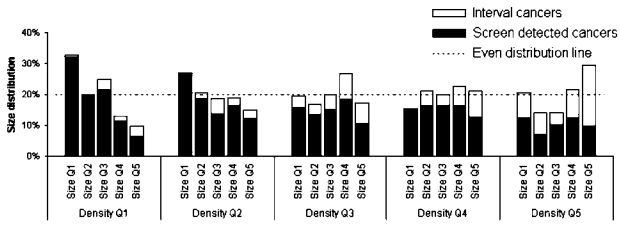


Figure 1. Distribution of tumour size by density at first round screening.

Regression showed that cancers detected in women with very high mammographic density were significantly larger than those detected in women with very low mammographic density. This effect was graded across the range of densities and was apparent both before and after adjustment for age, hormone replacement therapy (HRT) use, family history, symptomatic status and detection, however the trend was less clear in the middle range of densities after adjustment for effect modification by mode of detection. Of the factors that are potential targets for program improvement (such as age and family history), only density and HRT use were significantly associated with tumour size in the fully adjusted model. The effects at subsequent round were less clear.

Figure 2 shows the expected mean tumour size at first round screening according to density, for a 50-year-old asymptomatic woman who was not using HRT at the time of screening and had no family history of breast cancer.

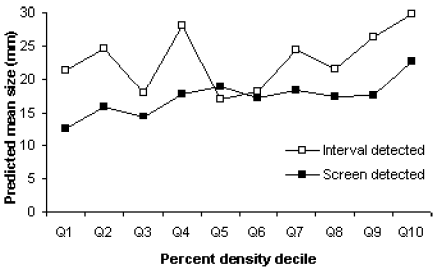


Figure 2. Expected mean tumour size at first round screening, by density.

**Conclusion:** Tumours detected in women with higher density are larger than those detected in women with lower density, and this effect is somewhat graded across the range of densities at first round screening.

37 Poster

## A multidisciplinary team approach to family history risk assessment reduced clinic attendance by half

J. Saldanha[1], R. Garret[1], M. Longmuir[3], C. Watt[3], D. George[2], C. Wilson[2], J. Doughty[2], D. Smith[1], S. Stallard[1], R. Davidson[3]. [1]*Victoria Infirmary, Breast Surgery, Glasgow, United Kingdom;* [2]*Western Infirmary, Breast Surgery, Glasgow, United Kingdom;* [3]*Yorkhill Hospital, Genetics, Glasgow, United Kingdom*

The aim of this study was to accurately assess the breast cancer risk of family history surveillance patients at 2 breast units in Glasgow utilising a multidisciplinary team approach and national guidelines. In our practise most women had been attending for family history surveillance before the introduction of Scottish guidelines that have increased awareness about the importance of accurate risk assessment in this group of women. Many had therefore never undergone a formal risk assessment or verification of their family histories and had only ever been seen by the surgical team.

Women attending for surveillance between November 2003 and February 2005 were included in this study. Genetics staff attended family history clinics and used Scottish guidelines in a 15 minute consultation to classify women already attending for annual follow up as being at low, moderate, or high risk of breast cancer. Where possible family members had their diagnoses verified through a national cancer registry. A surgical team that included specialist nurses examined all women and post consultation a summary letter including confirmation of the risk level was sent to the individual.