oping a breast cancer from which she will die within 10 years of diagnosis. For a 40 year old woman the equivalent respective risks are 30% and 10–14% up to age 50. The chance of a BRCA2 mutation carrier developing a breast cancer from which she will die within 10 years of diagnosis is approximately 3–4% from screening age 30 to 40 and 4–6% from age 40 to 50.

This series of BRCA-related breast cancers is very similar to others in the literature, even from centres that have reported cancers arising after intensive screening. Risk estimates can be useful in counselling BRCA mutation carriers.

O-39. Better survival and distinguishing pathological features of breast cancer in patients with BRCA-1 germline mutations

Sethi B, Makhija P, Sidhu RK, Hodgson S, Hamed H, D'Arrigo C. *Guy's Hospital, London*

Patients with BRCA-1 germline mutation develop breast cancer at a young age. Initial reports suggest worse prognosis for BRCA-1 cases but more recent studies report similar outcome as grade matched controls. BRCA-1 tumours are often of high grade and have distinguishing histopathological and biochemical features that may be helpful for pre-selection to increase detection rates of genetic testing.

To assess the validity of any distinguishing feature of BRCA-1 breast cancer and gain better understanding of its prognosis, we studied a cohort of 24 breast cancer patients with BRCA-1 mutation and long-term follow-up (up to 25y) and compared them to tumours matched for grade, age at presentation and year of presentation.

Very high mitotic rates (>40/10HPF), absence or small amount of DCIS, negativity for ER & PR, pushing margins and peripheral distribution of lymphoplasmacytic infiltrate distinguished BRCA-1 tumours from controls. Immunophenotyping (CK8/18, 19, 14, 5/6, S-100, myosin & SMA) showed no significant differences from controls. Metachronous contralateral primary breast cancer was common in BRCA-1 patients (50% v 9% in controls) and new primaries arose throughout follow-up. Despite this, overall survival was significantly better in BRCA-1 cases than in age and grade matched controls (92% v 57% at 5y; 83% v 53% at 10y; 66% v 45% at 15y; 53% v 35% at 20y; $p = 0.044$) or in a control group of 1911 grade III tumours treated at the Hedley Atkins Breast Unit from 1970–1999 ($p = 0.0025$).

Breast cancer in patients with BRCA-1 mutation has distinguishing histopathological features. These patients continue to develop new primary breast tumours throughout the period of follow-up but have better overall survival than patients matched for tumour grade; age at presentation and year of presentation.

O-40. Overexpression of HER-2 in lymph nodes disease is an independent prognostic factor and identifies a very poor prognosis group not identified by NPI

Rampaul RS, Pinder SE, Paish C, Mitchell MJ, Macmillan RD, Robertson JFR, Ellis IO. *Nottingham City Hospital*

Lymph node (LN) negative disease is often of sufficiently good prognosis that systemic adjuvant therapy is not needed. However, there are up to 12% who may suffer recurrence and thus candidates for additional therapy. The challenge is to identify such high risk patients. HER-2 has been shown to be a powerful independent prognostic factor in LN positive disease but not more powerful than the Nottingham Prognostic Index (NPI). Published data in LN negative studies has been inconsistent. 674 LN negative cases treated between 1975 and 1988 were analysed for HER-2 status. All cases were treated by mastectomy or breast conserving surgery (BCS) and triple node biopsy. No systemic adjuvant therapy was applied. HER-2 was determined by DAKO A0485 antibody and semi-quantitative scoring. Median follow up was 240 months. Mean age was 53.4 years. HER-2 positivity was seen in 17% ($n = 115$). In univariate analysis high grade, ER negativity and high NPI was associated with HER-2 positive disease ($p < 0.001$) as well as shortened disease free interval, distant metastasis and overall survival ($p < 0.005$). Multivariate analysis showed HER-2, size, grade and Vascular Invasion (VI) to be of independent significance.

A HER-2 prognostic index (HPI) was constructed [Size (mm) + Grade + VI + (1.5 × HER-2 score]. This was then compared to the NPI.

The HPI identified a group of patients (5.3%) with very poor prognosis (27% survival at 10 years) not seen with the NPI. These data suggest that identification of HER-2 status combined with size, grade and VI in a prognostic index may be a better prognostic discriminator than the NPI in node negative cases. These cases may also be candidates for novel HER-2 directed therapies.

O-41. Local recurrence in surgically treated screen-detected breast cancer in Wales

Osborn GD, Evans J, Monypenny IJ. *Breast Test Wales*

Reliable large scale data on local recurrence rates for screen-detected cancers in the NHSBSP has been lacking and may provide one of the best indicators of surgical quality. In Wales we have access to downloaded pathology data from all hospitals in Wales as part of breast cancer registration. We have used this to identify the incidence of local recurrence for screen-detected breast cancers.

6234 breast cancers were treated through the Breast Test Wales screening programme between 1989 and 2004. 59% had breast conserving surgery. Local recurrence rates of 3% have been found for both breast conserving surgery and mastectomy. Data on new contralateral primaries (1.6%) and distant recurrence (3%) are also available.

Multivariate analysis has been used to assess the relative contributions of prognostic factors in local recurrence following surgery for invasive cancers. There is a 50% decreased risk of local recurrence following mastectomy ($p = 0.012$), whilst node positivity and grade 3 tumours increase the risk of local recurrence by 91% ($p = 0.013$) and 95% ($p = 0.048$) respectively. The risk of recurrrence following mastectomy for DCIS is reduced by 74% ($p \geq 0.0001$) and the risk of recurrence following breast conservation for DCIS with involved margins increases by 140% ($p = 0.001$). The risk of local recurrence