reported. 185 consecutive cases in women aged <40 compared with 477 cases aged 40–49 and 687 cases aged 50–59. Overall 10 year % survivals were 73, 80 and 82 respectively.

Table 1. Distribution of grade and NPI at presentation (%)

Age	Grade			NPI Group				
	1	2	3	EPG	GPG	MPGI	MPGII	PPG
<40	8	24	69	5	13	24	33	25
40–49	17	30	53	11	17	30	27	14
50–59	24	38	38	19	24	27	17	13

Table 2. Survival by NPI (10 year actuarial %)

	Age		
	<40	40–49	50–59
EPG	100	100	96
GPG	84	96	97
MPGI	78	78	84
MPGII	81	76	64
PPG	49	54	50

Poorer overall survival is due to more grade III and less Grade I cases in young women, placing more into the Poor Prognostic Group. Survival depends on the prognostic factors of the tumour at all ages and young age is not an independent prognostic factor.

Reference: [1] Kollias J et al. Early onset breast cancer. British J Cancer (1997) 75; 1318–23.

O-36. Prognosis after local/regional recurrence

Asgeirsson KS, Mitchell M, Lee A, Ellis IO, Blamey RW, Macmillan RD. *Nottingham City Hospital*

Both local and regional recurrence is known to be associated with a worse survival compared to patients who remain recurrence free. The study aims to quantify the effect of LR and RR on prognosis and identify the factors that influence it.

The prognosis after recurrence was analysed for 1193 patients who underwent mastectomy (Mx) and 1044 that had wide local excision (WLE) between Jan 1990 and Dec 1999. The relative reduction in survival at 10 years observed in women who had a LR or RR was calculated and a multivariate analysis of factors predicting survival after LR or RR was performed.

The relative reduction in survival observed for LR was 40.0% after Mx (48% v 80%) and 27.6% after WLE (63% v 87%). For RR it was 63.4% after Mx (30% v 82%) and 59.1% after WLE (36% v 88%). Independent predictors of survival after LR or RR were disease-free interval (DFI, $p < 0.001$), grade ($p < 0.001$), size ($p = 0.013$) and lymph node stage ($p = 0.015$). 10 year survival with no LR or RR was 86%. 10 year survival according to DFI is shown below.

DFI	LR	RR
<2 yrs	30%	35%
2–5 yrs	53%	18%
>5 yrs	86%	56%

LR and RR are associated with a large relative reduction in survival. This effect is larger for Mx patients than after WLE. Early LR or RR are both predictors of very poor survival.

O-37. Modification of the Nottingham Prognostic Index by nodal status

Macmillan RD, Mitchell M, Lee A, Ellis IO, Blamey RW. *Nottingham City Hospital*

The Nottingham Prognostic Index (NPI) has been extensively validated and is widely used to estimate prognosis and guide recommendation for adjuvant therapy. It is based on a proportional hazard (Cox) analysis.

The aim of this study was to devise a separate NPI for node +ve and node −ve cases and assess how these refined indices may impact upon treatment planning.

890 cases (ES), who had no adjuvant therapy treated between Jan 1980 and Dec 1986, and 2238 cases (LS), who had selective adjuvant therapy treated between Jan 1990 and Dec 1999 were used for multivariate analysis of factors predicting survival. In addition to size, grade and lymph node stage, this included vascular invasion (VI) and single node positivity as previous studies demonstrated that these were important prognostic factors for node −ve/node +ve cases respectively, this latter factor not being available in the early series. For 575 node −ve cases in the ES, size, grade and VI were independently and equally significant. The formula of size + grade + VI produced 4 evenly spaced prognostic groups (10-year survival 89%, 67%, 65% and 48%). Compared with the standard NPI, 73 women (13%) changed to a prognostic group that differed in 10-year survival by at least 10%.

For 784 node +ve cases in the LS, size, grade and stage (1 = single node +ve; 2 = 2 or 3 nodes +ve; 3 = 4 or more nodes positive) were independently significant factors. The weighting gave a formula of size + 4 × grade + 3 × stage which produced 5 evenly spaced significantly different prognostic groups (10-year survival 94%, 88%, 73%, 67%, 34%). Compared with the standard NPI, 298 women (38%) changed to a prognostic group that differed in 10-year survival by at least 10%.

Both of these modifications of the NPI may be useful for treatment planning.

O-38. Predicting survival in BRCA mutation carriers

Macmillan RD, Scott N, Ellis IO, Blamey RW. *Nottingham City Hospital*

The management of BRCA mutation carriers is complex but may be aided by a better understanding of risks of breast cancer death for individual women.

Of 23 BRCA1 mutation carriers presenting with breast cancer in Nottingham, 22 were grade 3, 21 were ER negative and 10 were node positive. Mean tumour size was 25 mm. Of 11 BRCA2 mutation carriers presenting with breast cancer, 4 were DCIS, 3 were grade 3, 2 were node positive and 6 were ER positive. The mean size was 30 mm.

Using penetrance data, an average Nottingham Prognostic Index score for a BRCA1 and a BRCA2 cancer and expected effects of adjuvant systemic therapy, risks can be estimated. For instance, a 30 year old woman with a BRCA1 mutation who chooses screening by mammography as her risk management option has a 20% chance of developing breast cancer over the next 10 years. There is approximately a 7–9% chance of devel-

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

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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

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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