attenuated after adjusting for confounders (REM – 1.50, 1.38 and 1.27).

Conclusion: We confirmed poorer BCRS in older women in our region. This was partially explained by known prognostic factors. Further research is needed to determine whether biological differences or sub-optimal management can explain the residual excess mortality.

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O-42 EARLY OPERABLE PRIMARY BREAST CANCER IN OLDER (⩾70 YEARS) WOMEN (EPCS) – BIOLOGY AND CLINICAL SIGNIFICANCE

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Introduction: Biology of breast cancer appears to change with age. Most studies are small/from multiple centres limiting their importance.

Methods: From 1973 to 2009, 2000+ EPCs were managed in Nottingham. Oestrogen receptor (ER) was assessed by immunohistochemistry (giving an H-score) on core biopsy for all patients. A total of 831 patients had primary surgery and 575 had good quality tumour samples available for tissue microarray analysis.

Results: Comparing these 831 patients with a younger (<70 years) series ($N = 1809$), expression of ER ($p < 0.001$), p53, HER4, CK14, bcl2 ($p < 0.000$) and CK 17 ($p < 0.05$) was found to increase with age, while reverse was seen with CK 7/8 ($p < 0.002$), ki67 and E-Cadherin ($p < 0.000$). No change was observed in PR, HER2, CK5/6, CK19 and MUC1 expression.

At 66-month median follow-up, for those who did not receive adjuvant systemic therapy ($N = 306$), tumour size ($p < 0.042$), grade ($p < 0.046$), axillary stage ($p < 0.000$) and PR ($p < 0.017$) were found to be independent prognostic factors.

At 49-month median follow-up, for patients with ER+ (H-score ⩾ 50) tumours, those with H-score ⩾ 250 had equivalent 5-year breast cancer specific survival (BCSS) regardless of primary treatment (surgery vs primary endocrine therapy (PET) 95% versus 93%, $p = 0.715$). For patients on PET, all those with H-score ⩾ 250 achieved clinical benefit as compared to 11 patients with H-score < 250 who progressed, at 6 months ($p < 0.03$), the former also had better BCSS ($p < 0.01$).

Conclusion: The pattern suggests a less aggressive tumour phenotype with advancing age. The ER H-score appears as an excellent surrogate for clinical outcome for ER+ EPCs. It is available at diagnosis and has a great value in guiding discussion of therapeutic options.

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O-43 A KRAS MICRORNA BINDING SITE VARIANT IS A GENETIC MARKER OF RISK FOR TRIPLE NEGATIVE BREAST CANCER

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Introduction: MiRNAs exert their regulatory effect on gene expression by binding to the 3′ untranslated region (UTR) of target mRNAs. The let-7 miRNA family are global genetic regulators critically important for controlling oncogene expression (e.g. *KRAS*). Dysregulated let-7 expression is associated with many malignancies including breast cancer, and it is hypothesized that defective interaction between let-7 and its target *KRAS* underpins this association and oncogenesis. We hypothesized that a single nucleotide polymorphism (SNP) in the *let-7*-binding site in *KRAS* disrupts *let-7* regulation of the oncogene and thus predisposes to breast cancer.

Methods: A population analysis of the association of the *KRAS* variant and breast cancer was performed on a cohort of 1010 breast cancer patients and 1497 age-matched healthy controls. Genomic DNA isolated from all participants was amplified using PCR assays designed specifically to identify the T (wild type) or G (variant) allele. Genotyping results were correlated with patients' clinicopathological parameters.

Results: The *KRAS* variant was present in 15% of all breast cancer patients, compared with baseline prevalence of <7%. In particular the *KRAS*-variant predicted a significantly increased risk of developing triple negative breast cancer in premenopausal women (OR = 4.78, CI = 1.71–13.38, $p = 0.015$), and patients with the variant allele were significantly more likely to present with advanced stage disease ($p = 0.03$).

Conclusion: These seminal findings suggest that the *KRAS*-variant acts as a genetic marker of risk for developing triple negative breast cancer. Predicting risk for this subtype is critically important, to permit early screening and intervention for 'at-risk' individuals.

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O-44 GENE–ENVIRONMENT INTERACTIONS IN 7610 WOMEN WITH BREAST CANCER: PROSPECTIVE EVIDENCE FROM THE MILLION WOMEN STUDY

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Background: Genome-wide association studies, together with analyses of specific candidate polymorphisms, have identified a number of low-penetrance breast cancer susceptibility loci. Information is scarce about the combined effects on breast cancer incidence of these genetic variants and of environmental factors (reproductive, behavioural, and anthropometric risk factors for