breast cancer). To test for evidence of gene–environment interactions, we compared genotypic relative risks for breast cancer across categories of the environmental risk factors.

Methods: We tested gene–environment interactions in 7610 women who developed breast cancer and 10,196 controls without the disease in a large UK prospective study, studying the effects of 12 polymorphisms (*FGFR2*-rs2981582, *TNRC9*-rs3803662, 2q35-rs13387042, *MAP3K1*-rs889312, 8q24-rs13281615, 2p-rs4666451, 5p12-rs981782, *CASP8*-rs1045485, *LSP1*-rs3817198, 5q-rs30099, *TGFB1*-rs1982073, and *ATM*-rs1800054) in relation to prospectively collected information about 10 established environmental risk factors (age at menarche, parity, age at first birth, breastfeeding, menopausal status, age at menopause, use of hormone replacement therapy, body-mass index, height, and alcohol consumption).

Results: We will present findings from this systematic investigation of gene–environment interactions in relation to breast cancer risk in the Million Women Study. Results from a meta-analysis of these and published data will also be shown when possible.

O-45 CHILDHOOD ADIPOSITY AND BREAST CANCER INCIDENCE IN WOMEN IN MIDDLE AGE

Benjamin J. Cairns, TienYu Owen Yang, Gillian K. Reeves, Valerie Beral, on behalf of the Million Women Study Collaborators. *Cancer Epidemiology Unit, University of Oxford, Oxford, UK*

Among 397,339 postmenopausal women, breast cancer incidence increases with increasing body mass index (BMI), while adiposity in childhood has been found to lower risk. Few epidemiological studies have been able to investigate joint effects of both childhood and adult adiposity.

In a large, prospective study of postmenopausal middle-aged women, adjusted relative risks (RR), according to BMI in middle age and relative adiposity at age 10, were estimated by Cox regression. (Analyses were confined to non-users of hormone replacement therapy, which can mask the effects of BMI on breast cancer risk.)

Among 397,339 women, there were 6189 incident breast cancers over 5.2 years mean follow-up (average age at diagnosis: 63 years). As expected, women with a high BMI in middle age had a greater breast cancer risk ($P < 0.001$). In contrast, women who were plumper than average at age 10 had a lower risk of breast cancer than women who were about average ($P < 0.001$). A similar apparently protective effect of childhood adiposity was observed at each level of women's BMI in middle age ($P = 0.08$, NS, for interaction). These relationships were not altered by height ($P = 0.9$), age at menarche ($P = 0.8$), or other reproductive and hormonal risk factors ($P > 0.1$).

Despite the increase in risk of breast cancer with increasing BMI among postmenopausal women, greater childhood adiposity lowers risk in the same women. The reason for the persistent and apparently protective effect of childhood adiposity is unclear.

O-46 MACROPHAGE INFILTRATION IS ASSOCIATED WITH POOR OUTCOME IN BREAST CANCER PATIENTS AND A REDUCED TREATMENT RESPONSE TO LETROZOLE AND ZOLEDRONATE

A. Lee, R. Lamb, H. Gregson, A. Cramer, J. Morris, L. Renshaw, M. Winter, R.E. Coleman, J.M.J. Dixon, G. Landberg, N.J. Bundred. *Breakthrough Breast Centre, Manchester, UK*

Background: Macrophage infiltration augments tumour recurrence whilst Zoledronic acid suppresses macrophage pro-tumourigenicity. In the ZO-FAST and ABCSG 12 trials, oestrogen receptor (ER) positive breast cancer patients received Zoledronate in combination with an aromatase inhibitor, Letrozole, demonstrating an increased disease-free survival. We aimed to investigate macrophage infiltration and patient prognosis and the early biological effects of adjunctive Zoledronate on patient and macrophage response to treatment in breast cancer.

Methods: Tissue microarrays from 179 breast cancer 'FasA Cohort' patients were immunohistochemically stained with CD68, a universal macrophage marker. A randomised pre-operative trial allocated ER-positive breast cancer patients ($n = 110$) to 14 days pre-operative treatment of Letrozole, Letrozole and Zoledronate, or placebo. Pre- and post-treatment specimens were collected and immunohistochemically stained for CD68 and the proliferation marker, Ki67.

Results: The FasA cohort found links between macrophage frequency and tumour grade ($P < 0.01$), size ($P < 0.05$), recurrence ($P < 0.05$) and lymph node status ($P < 0.05$). Ki67 reductions of 52% ($P < 0.001$) were seen in the aromatase inhibitor group, with no additional benefit following Zoledronate treatment. Macrophage infiltrate (Mean = 37; Range = 3–117) was positively associated with pre and post Ki67 levels ($P < 0.05$, $P < 0.01$). Additionally, low post-treatment macrophage infiltrate (Mean = 29; Range = 3–66) was associated with a greater reduction in Ki67 following aromatase inhibition ($P < 0.05$).

Conclusion: Macrophage infiltrate correlates with poor outcome in breast cancer. Aromatase inhibition but not Zoledronate lowered proliferation and macrophage infiltration in ER-positive breast cancer. For the first time we have shown novel treatment effects on the tumour stromal compartment.

O-47 THE BASO II TRIAL AT MEDIAN 15 YEARS OF FOLLOW-UP

R.W. Blamey, A. Oates, data manager, on behalf of the Contributors to BASO II. *Nottingham City Hospital, UK*

BASO II tested whether adjuvant radiotherapy or endocrine therapy were required following Wide Local Excision: Grade I/node negative/⩽2 cm diameter.

The mean endpoint was Local Recurrence (in breast) (LR).

Entry was to 4-way randomisation: RT only, Tamoxifen (TAM) only, neither, both.