Supplementary Table 6. Association between a genetic predisposition to breast cancer (measured using family history of breast cancer and polygenic risk score) and mammographic density at baseline, mammographic density change/year, number of clusters of microcalcifications at baseline, and number of masses at baseline among women who did not go on to develop breast cancer, who also had information on family history of breast cancer and all four outcomes (N=48,654). The breast cancer polygenic risk score (PRS) sub-population includes 8,765 women. Odds ratios (OR) and beta coefficients (β) presented with 95% confidence intervals, with p-values provided for tests of linear trends.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **(log) Mammographic density (cm2)** | | **Mammographic density change (cm2)/yr** | | **Microcalcifications** | | **Masses** | |
|  | Model 1a  β (95% CI) | Model 2a  β (95% CI) | Model 1b  β (95% CI) | Model 2b  β (95% CI) | Model 1a  OR (95% CI) | Model 2a  OR (95% CI) | Model 1a  OR (95% CI) | Model 2a  OR (95% CI) |
| *Family history of breast cancer* | | |  |  |  |  |  |  |
| No | 0.00 (Ref) | 0.00 (Ref) | 0.00 (Ref) | 0.00 (Ref) | 1.00 (Ref) | 1.00 (Ref) | 1.00 (Ref) | 1.00 (Ref) |
| Yes | 0.07  (0.04 to 0.10) | 0.07  (0.04 to 0.10) | -0.12  (-0.22 to -0.03) | -0.12  (-0.22 to -0.02) | 1.14  (1.06 to 1.22) | 1.14  (1.06 to 1.22) | 0.99  (0.94 to 1.04) | 0.99  (0.95 to 1.04) |
|  |  |  |  |  |  |  |  |  |
| *Overall breast cancer PRS -percentiles* | | |  |  |  |  |  |  |
| 0-20% | 0.00 (Ref) | 0.00 (Ref) | 0.00 (Ref) | 0.00 (Ref) | 1.00 (Ref) | 1.00 (Ref) | 1.00 (Ref) | 1.00 (Ref) |
| 20-40% | -0.04  (-0.12 to 0.03) | -0.02  (-0.09 to 0.05) | -0.02  (-0.22 to 0.18) | 0.03  (-0.16 to 0.22) | 1.05  (0.88 to 1.25) | 1.06  (0.89 to 1.27) | 0.88  (0.78 to 0.99) | 0.87  (0.77 to 0.98) |
| 40-60% | 0.03  (-0.05 to 0.11) | 0.05  (-0.02 to 0.12) | -0.19  (-0.39 to 0.02) | -0.14  (-0.34 to 0.05) | 1.16  (0.97 to 1.38) | 1.17  (0.98 to 1.39) | 0.89  (0.79 to 1.00) | 0.87  (0.77 to 0.98) |
| 60-80% | 0.06  (-0.02 to 0.14) | 0.07  (-0.01 to 0.14) | 0.03  (-0.17 to 0.24) | 0.06  (-0.14 to 0.26) | 1.22  (1.02 to 1.46) | 1.23  (1.03 to 1.47) | 0.99  (0.88 to 1.12) | 0.98  (0.86 to 1.10) |
| 80-100% | 0.12  (0.04 to 0.21) | 0.13  (0.06 to 0.21) | -0.07  (-0.29 to 0.15) | -0.01  (-0.22 to 0.21) | 1.48  (1.23 to 1.77) | 1.49  (1.24 to 1.79) | 1.03  (0.90 to 1.17) | 1.02  (0.89 to 1.16) |
|  |  |  |  |  |  |  |  |  |
| p-value linear | <0.0001 | <0.0001 | 0.9729 | 0.9044 | <0.0001 | <0.0001 | 0.3541 | 0.4384 |
|  |  |  |  |  |  |  |  |  |
| *PRS (Standardised continuous)* | | |  |  |  |  |  |  |
|  | 0.05  (0.03 to 0.08) | 0.05  (0.03 to 0.08) | -0.01  (-0.07 to 0.06) | -0.01  (-0.07 to 0.06) | 1.13  (1.06 to 1.19) | 1.13  (1.07 to 1.20) | 1.03  (0.99 to 1.07) | 1.02  (0.98 to 1.06) |
| p-value linear | <0.0001 | <0.0001 | 0.9487 | 0.8205 | <0.0001 | <0.0001 | 0.2271 | 0.3443 |

Model 1a - adjusted for age at mammogram

Model 2a– Model 1 + adjusted for postmenopausal (no; yes), BMI, HRT status (former/non; current), previous benign breast disorder (no, yes), reproductive history (parity x age at first birth)

Model 1b - adjusted for sampling type and age at first mammogram

Model 2b– Model 1 + adjusted for postmenopausal (no; yes), BMI, age at last mammogram