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 1aβ (95% CI) | Model 2aβ (95% CI) | Model 1bβ (95% CI) | Model 2bβ (95% CI) | Model 1a OR (95% CI) | Model 2aOR (95% CI) | Model 1aOR (95% CI) | Model 2aOR (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