Supplementary Table 7. Association between a genetic predisposition to breast cancer (separately measured using estrogen receptor negative and positive polygenic risk scores (PRS)) and mammographic density at baseline, mammographic density change/year, number of clusters of microcalcifications at baseline, and number of masses at baseline among women without breast cancer, who had information a polygenic risk score calculated (N=8,765). 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) |
| **Estrogen Receptor Positive 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) | -0.01(-0.08 to 0.06) | -0.14(-0.34 to 0.06) | -0.11(-0.30 to 0.09) | 1.05(0.88 to 1.24) | 1.06(0.89 to 1.25) | 0.92(0.82 to 1.03) | 0.89(0.79 to 1.01) |
| 40-60% | 0.03(-0.04 to 0.11) | 0.07(0.01 to 0.14) | -0.11(-0.32 to 0.09) | -0.11(-0.31 to 0.09) | 1.16(0.98 to 1.37) | 1.17(0.99 to 1.39) | 0.93 (0.83 to 1.05) | 0.90(0.80 to 1.01) |
| 60-80% | 0.08 (0.01 to 0.15) | 0.10(0.03 to 0.17) | -0.03(-0.24 to 0.17) | -0.03(-0.24 to 0.17) | 1.23(1.04 to 1.46) | 1.24(1.05 to 1.47) | 1.05(0.93 to 1.18) | 1.03(0.91 to 1.16) |
| 80-100% | 0.11(0.03 to 0.19) | 0.14(0.06 to 0.21) | -0.22(-0.44 to -0.01) | -0.20(-0.41 to 0.01) | 1.51(1.27 to 1.79) | 1.54 (1.29 to 1.82) | 1.11(0.98 to 1.26) | 1.10(0.97 to 1.24) |
| p-value linear  | 0.0002 | 0.0001 | 0.486 | 0.522 | <0.0001 | <0.0001 | 0.021 | 0.0425 |
|  |  |  |  |  |  |  |  |  |
| *PRS (Standardised continuous)* |  |  |  |  |  |  |  |
|  | 0.05(0.03 to 0.07) | 0.05 (0.03 to 0.08) | -0.04(-0.11 to 0.02) | -0.05(-0.11 to 0.01) | 1.15 (1.09 to 1.21) | 1.16(1.09 to 1.22) | 1.05(1.01 to 1.09) | 1.04(1.00 to 1.08) |
| p-value linear | <0.0001 | <0.0001 | 0.2017 | 0.1273 | <0.0001 | <0.0001 | 0.0162 | 0.0405 |
| **Estrogen Receptor Negative 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% | 0.09(0.02 to 0.17) | 0.08(0.01 to 0.15) | -0.10(-0.31 to 0.11) | -0.08(-0.28 to 0.12) | 1.10(0.93 to 1.30) | 1.11(0.93 to 1.31) | 0.96 (0.85 to 1.08) | 0.97(0.86 to 1.09) |
| 40-60% | 0.06(-0.02 to 0.13) | 0.03(-0.04 to 0.10) | -0.08(-0.29 to 0.13) | -0.03(-0.23 to 0.17) | 1.19(1.01 to 1.41) | 1.19(1.01 to 1.41) | 0.95 (0.85 to 1.07) | 0.96(0.85 to 1.08) |
| 60-80% | 0.13 (0.06 to 0.21) | 0.14(0.07 to 0.22) | -0.17(-0.38 to 0.05) | -0.10(-0.30 to 0.10) | 1.34(1.13 to 1.59) | 1.34(1.13 to 1.59) | 1.02(0.90 to 1.15) | 1.01(0.89 to 1.14) |
| 80-100% | 0.24(0.16 to 0.31) | 0.23(0.16 to 0.30) | -0.20(-0.41 to 0.02) | -0.15(-0.36 to 0.05) | 1.41(1.19 to 1.67) | 1.42 (1.20 to 1.69) | 1.11(0.98 to 1.25) | 1.11(0.98 to 1.25) |
| p-value linear | <0.0001 | <0.0001 | 0.4413 | 0.3842 | <0.0001 | <0.0001 | 0.0788 | 0.1016 |
|  |  |  |  |  |  |  |  |  |
| *PRS (Standardised continuous)* |  |  |  |  |  |  |
|  | 0.08(0.05 to 0.10) | 0.08(0.05 to 0.10) | -0.04(-0.11 to 0.02) | -0.04(-0.11 to 0.02) | 1.13 (1.08 to 1.20) | 1.14(1.08 to 1.20) | 1.04(0.99 to 1.08) | 1.03(0.99 to 1.07) |
| p-value linear  | <0.0001 | <0.0001 | 0.2037 | 0.1859 | <0.0001 | <0.0001 | 0.0693 | 0.0963 |

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