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 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) |
| **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