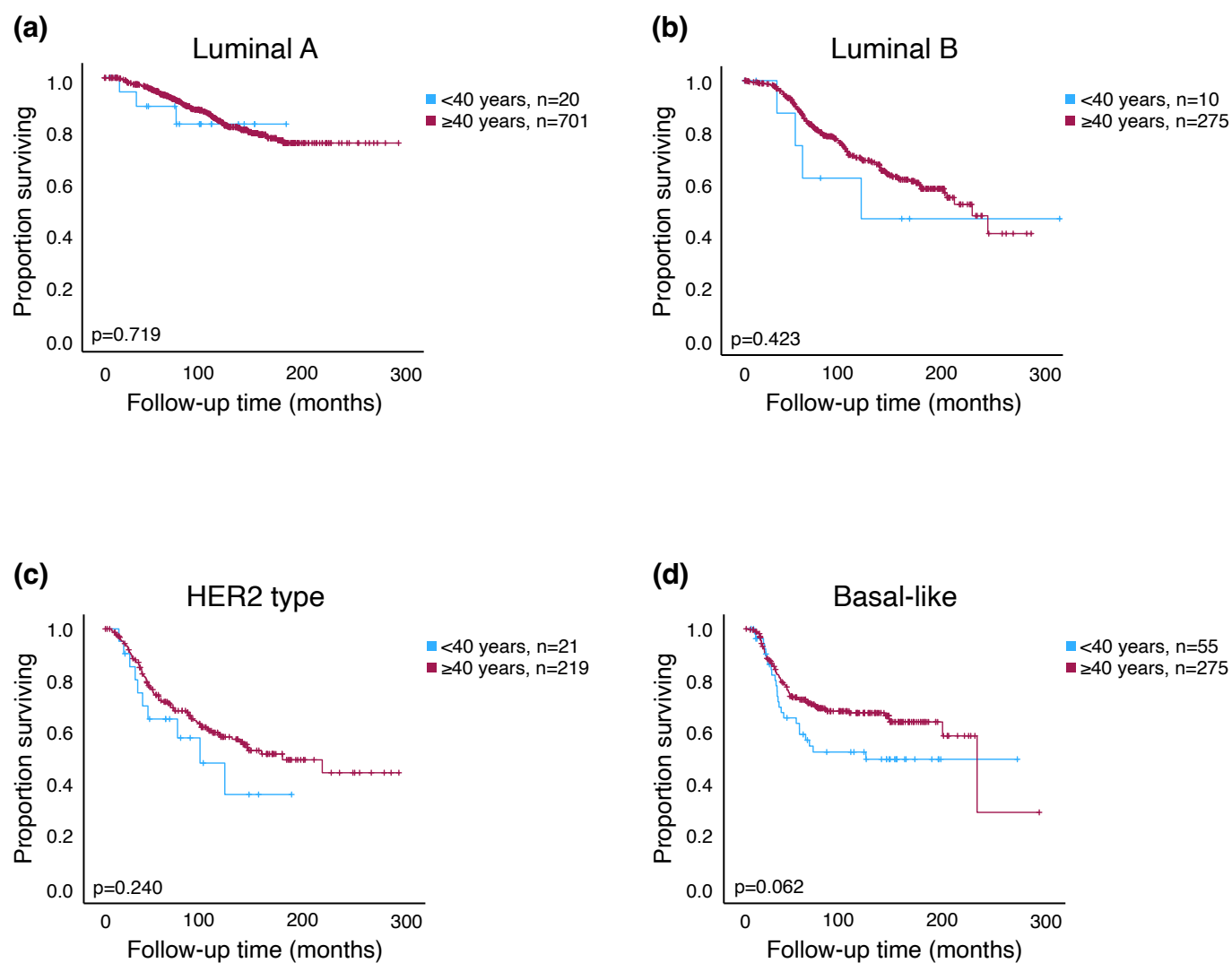


**Supplementary Table S1. Clinico-pathologic features across age groups**

|                                  | Age at diagnosis (years) |            |             | P      |
|----------------------------------|--------------------------|------------|-------------|--------|
|                                  | <40                      | 40-49      | ≥50         |        |
|                                  | n (%)                    | n (%)      | n (%)       |        |
| <b>Histological grade</b>        |                          |            |             |        |
| 1                                | 1 (0.9)                  | 25 (9.8)   | 120 (8.9)   | <0.001 |
| 2                                | 20 (18.7)                | 85 (33.2)  | 568 (42.1)  |        |
| 3                                | 86 (80.4)                | 146 (57.0) | 660 (49.0)  |        |
| <b>Tumor diameter</b>            |                          |            |             |        |
| ≤2.0 cm                          | 33 (31.4)                | 91 (35.4)  | 414 (29.4)  | 0.16   |
| >2.0 cm                          | 72 (68.6)                | 166 (64.6) | 992 (70.6)  |        |
| <b>Nodal status</b>              |                          |            |             |        |
| Negative                         | 36 (33.6)                | 136 (52.1) | 750 (53.0)  | 0.001  |
| Positive                         | 71 (66.4)                | 125 (47.9) | 666 (47.0)  |        |
| <b>ER (IHC)</b>                  |                          |            |             |        |
| Positive                         | 35 (33.0)                | 158 (61.2) | 1149 (83.0) | <0.001 |
| Negative                         | 71 (67.0)                | 100 (38.8) | 235 (17.0)  |        |
| <b>Molecular subtype (PAM50)</b> |                          |            |             |        |
| Luminal A                        | 20 (18.7)                | 108 (41.4) | 593 (41.9)  | <0.001 |
| Luminal B                        | 11 (10.3)                | 43 (16.5)  | 438 (30.9)  |        |
| HER2 type                        | 21 (19.6)                | 34 (13.0)  | 185 (13.1)  |        |
| Basal-like                       | 55 (51.4)                | 76 (29.1)  | 200 (14.1)  |        |

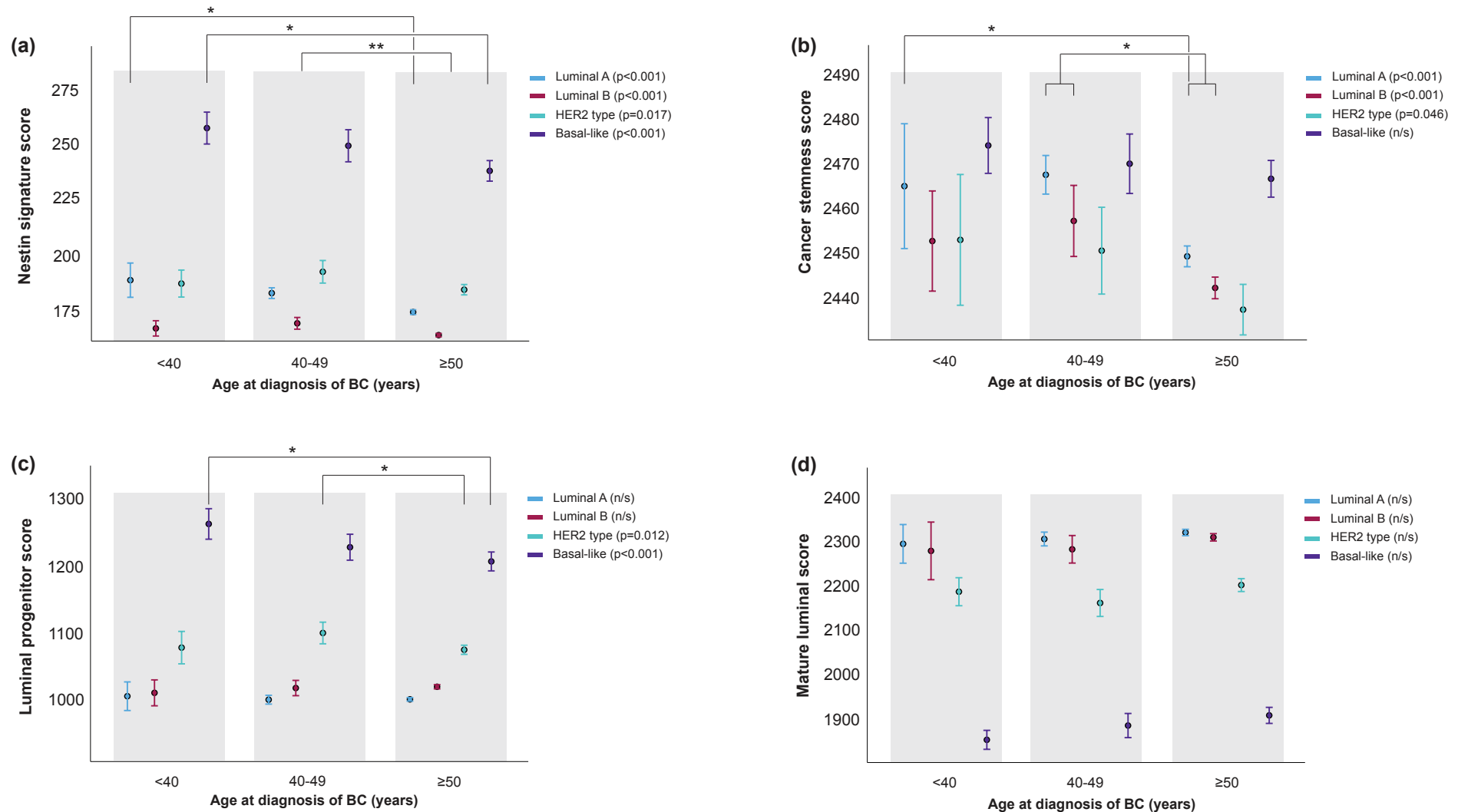
n: number of patients; P: p-values. P-values by Pearson's chi-square test. Missing data: Histologic type: n=2; histologic grade: n=73; tumor diameter: n=16; ER: n=36.

**Supplementary Figure S1.**



**Supplementary Figure S1. Kaplan-Meier breast cancer-specific survival analysis, split by molecular subgroup and across age groups.** Kaplan-Meier univariate breast cancer disease specific survival analysis according to age groups under 40 years vs 40 years and older (log-rank test for difference). Split by molecular subgroups.

**Supplementary Figure S2.**



\*  $p < 0.05$

\*\* all subgroups are significantly ( $p < 0.05$ ) different expressed

**Supplementary Figure S2. Gene expression signatures reflecting progenitor and stemness features across age groups (METABRIC combined cohorts  $n=1992$ ).** Higher scores of the signatures reflecting A-B) stemness features in breast cancer of the young; D) Luminal progenitor activation. C) Lower scores of the signature reflecting a mature luminal program in the young. Data is presented by error-bars with 95% confidence interval of the mean, p-values comparing several groups by the Kruskal-Wallis test and p-values for direct comparison by Mann-Whitney U test.

**Supplementary Table S2. Prediction of receiving chemotherapy and hormone therapy (yes/no) by multivariable logistic regression**

**(a) Chemotherapy**

| Variable                      | n (%)       | OR    | 95% CI       | P      |
|-------------------------------|-------------|-------|--------------|--------|
| <b>Age (years)</b>            |             |       |              |        |
| ≥40                           | 1593 (93.8) | 1     |              | <0.001 |
| <40                           | 105 (6.2)   | 6.11  | (3.42-10.90) |        |
| <b>Tumor size</b>             |             |       |              |        |
| ≤2.0 cm                       | 728 (42.9)  | 1     |              | 0.038  |
| >2.0 cm                       | 970 (57.1)  | 1.42  | (1.02-1.97)  |        |
| <b>Nodal status</b>           |             |       |              |        |
| Negative                      | 867 (51.1)  | 1     |              | <0.001 |
| Positive                      | 831 (48.9)  | 12.47 | (8.57-18.14) |        |
| <b>Histological grade</b>     |             |       |              |        |
| 1 and 2                       | 812 (47.8)  | 1     |              | <0.001 |
| 3                             | 886 (52.2)  | 2.59  | (1.82-3.68)  |        |
| <b>Luminal vs non-luminal</b> |             |       |              |        |
| Luminal                       | 1156 (68.1) | 1     |              | <0.001 |
| Non-luminal                   | 542 (31.9)  | 7.96  | (5.72-11.07) |        |

**(b) Hormone therapy**

| Variable                  | n (%)       | OR    | 95% CI        | p Value |
|---------------------------|-------------|-------|---------------|---------|
| <b>Age</b>                |             |       |               |         |
| ≥40                       | 1573 (93.8) | 1     |               | 0.001   |
| <40                       | 104 (6.2)   | 0.43  | (0.25-0.72)   |         |
| <b>Tumor size</b>         |             |       |               |         |
| ≤2.0 cm                   | 714 (42.6)  | 1     |               | <0.001  |
| >2.0 cm                   | 963 (57.4)  | 1.76  | (1.37-2.26)   |         |
| <b>Nodal status</b>       |             |       |               |         |
| Negative                  | 848 (50.6)  | 1     |               | <0.001  |
| Positive                  | 829 (49.4)  | 6.21  | (4.64-8.33)   |         |
| <b>Histological grade</b> |             |       |               |         |
| 1 and 2                   | 797 (47.5)  | 1     |               | <0.001  |
| 3                         | 880 (52.5)  | 1.76  | (1.33-2.33)   |         |
| <b>ER status</b>          |             |       |               |         |
| Negative                  | 395 (23.6)  | 1     |               | <0.001  |
| Positive                  | 1282 (76.4) | 25.36 | (17.44-36.86) |         |

n: number of patients; OR: odds ratio; CI: confidence interval; P: p-values; ER: estrogen receptor. All variables are categorical; Luminal includes PAM50 luminal A and B, non-luminal PAM50 HER2 and basal-like; ER status by immunohistochemistry. PAM50 normal like subgroup was excluded from the analysis. Missing cases (A) n=86 (B) n=107.