**Supplement.**

**Supplemental Figure S1.** Post-Diagnosis Weight Change and Breast Cancer-Specific Mortality.

**Supplemental Table S1.**Category of Weight Change and All-cause Mortality by Follow-Up Period.

**Supplemental Table S2.** Average Association of Post-Diagnosis Weight Change and All-cause and Breast Cancer-Specific Mortality by Subgroup.

**Supplemental Table S3.** Average Association of Post-Diagnosis Weight Change and Breast Cancer-Specific and All-cause Mortality by Immunohistochemistry.

Supplemental Figure S1. Post-Diagnosis Weight Change and Breast Cancer-Specific Mortality (n=12,590; breast cancer deaths=503)



Losses in bodyweight of 5% (HR 1.24; 95% CI: 1.11, 1.39), 10% (HR 1.68; 95%CI: 1.32, 2.15), 15% (HR 2.14; 95% CI: 1.63, 2.81), and 25% (HR 3.17; 95% CI: 2.10, 4.77) were associated with breast cancer-specific death. Meanwhile, gains in bodyweight of 5% (HR 0.98; 95% CI: 0.85, 1.13), 10% (HR 1.09; 95%CI: 0.81, 1.45), and 15% (HR 1.24; 95% CI: 0.89, 1.74), were not significantly associated with breast cancer-specific death, while gains of 25% (HR 1.62; 95% CI: 1.00, 2.63) were.

Model adjusted for age at diagnosis (continuous), race, smoking status, alcohol intake, stage (in BMI subgroup), grade, comorbidities, tumor characteristics, receipt of chemotherapy (yes/no), receipt of radiation therapy (yes/no), and pre-diagnosis BMI

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Supplemental Table S1. Category of Weight Change and All-cause Mortality by Follow-Up Period | | | | | | | | | | | |
|  | Large Loss | | Modest Loss | | Stable | | Modest Gain | | | Large Gain | |
| (>10%) | | (>5-<10%) | | (within 5%) | | (>5-<10%) | | | (>10%) | |
|  | Events /  At Risk | HR (95% CI) | Events /  At Risk | HR (95% CI) | Events /  At Risk |  | | Events /  At Risk | HR (95% CI) | Events /  At Risk | HR (95% CI) |
|  | *Earlier, <3 years of follow-up* | | | | | | | | | | |
| Body mass index |  |  |  |  |  |  | |  |  |  |  |
| Obese, >30 kg/m2 | 52 / 223 | 2.07 (1.49, 2.88) | 50 / 322 | 1.39 (1.00, 1.94) | 124 / 1198 | Ref. | | 20 / 197 | 1.02 (0.63, 1.63) | 10 / 71 | 1.44 (0.75, 2.76) |
| Overweight, 25-<30 kg/m2 | 33 / 129 | 2.74 (1.82, 4.13) | 25 / 197 | 1.18 (0.76, 1.83) | 100 / 1056 | Ref. | | 23 / 224 | 1.08 (0.68, 1.71) | 7 / 110 | 0.66 (0.31, 1.44) |
| Normal, 18.5-<25 kg/m2 | 34 / 93 | 4.81 (3.19, 7.25) | 21 / 173 | 1.49 (0.92, 2.41) | 91 / 1177 | Ref. | | 16 / 287 | 0.83 (0.49, 1.42) | 13 / 129 | 1.01 (0.56, 1.83) |
|  |  |  |  |  |  |  | |  |  |  |  |
| Stage |  |  |  |  |  |  | |  |  |  |  |
| III | 44 / 35 | 2.53 (1.66, 3.86) | 72 / 38 | 1.99 (1.33, 2.96) | 254 / 72 | Ref. | | 45 / 13 | 1.00 (0.55, 1.83) | 24 / 14 | 1.67 (0.94, 2.99) |
| II | 49 / 171 | 2.84 (2.04, 3.95) | 41 / 252 | 1.38 (0.97, 1.97) | 132 / 1136 | Ref. | | 24 / 253 | 0.85 (0.55, 1.31) | 9 / 122 | 0.56 (0.29, 1.11) |
| I | 35 / 195 | 2.93 (1.99, 4.32) | 20 / 336 | 0.85 (0.53, 1.37) | 113 / 1996 | Ref. | | 22 / 409 | 1.04 (0.65, 1.64) | 8 / 162 | 1.02 (0.49, 2.09) |
|  |  |  |  |  |  |  | |  |  |  |  |
|  | *Later, >3 years of follow-up* | | | | | | | | | | |
| Body mass index |  |  |  |  |  |  | |  |  |  |  |
| Obese, >30 kg/m2 | 23 / 225 | 1.60 (1.01, 2.53) | 20 / 391 | 0.82 (0.51, 1.34) | 90 / 1507 | Ref. | | 11 / 261 | 0.62 (0.33, 1.16) | 2 / 94 | 0.36 (0.09, 1.47) |
| Overweight, 25-<30 kg/m2 | 11 / 105 | 1.80 (0.93, 3.46) | 6 / 250 | 0.57 (0.24, 1.32) | 56 / 1395 | Ref. | | 21 / 307 | 1.69 (1.01, 2.81) | 10 / 145 | 1.52 (0.77, 3.01) |
| Normal, 18.5-<25 kg/m2 | 6 / 52 | 1.54 (0.66, 3.59) | 7 / 191 | 0.83 (0.38, 1.80) | 67 / 1431 | Ref. | | 11 / 343 | 0.75 (0.40, 1.43) | 7 / 173 | 0.92 (0.44, 1.93) |
|  |  |  |  |  |  |  | |  |  |  |  |
| Stage |  |  |  |  |  |  | |  |  |  |  |
| III | 8 / 56 | 1.42 (0.66, 3.05) | 8 / 95 | 0.96 (0.45, 2.06) | 41 / 377 | Ref. | | 6 / 75 | 0.75 (0.32, 1.79) | 5 / 45 | 1.00 (0.39, 2.54) |
| II | 17 / 153 | 1.79 (1.06, 3.02) | 12 / 317 | 0.69 (0.38, 1.27) | 88 / 1475 | Ref. | | 17 / 325 | 0.82 (0.48, 1.38) | 12 / 175 | 1.10 (0.60, 2.01) |
| I | 15 / 174 | 1.84 (1.06, 3.20) | 14 / 427 | 0.74 (0.42, 1.30) | 88 / 2529 | Ref. | | 20 / 525 | 1.11 (0.68, 1.80) | 4 / 206 | 0.66 (0.24, 1.81) |

\*Adjusted for age at diagnosis (categorical), race/ethnicity, alcohol, smoking status, comorbidities, pre-diagnosis body mass index (categorical), stage, grade, receipt of chemotherapy (yes/no), receipt of radiation therapy (yes/no), and tumor characteristics (ER, PR and HER2 status)

| Supplemental Table S2. Average Association of Post-Diagnosis Weight Change and All-cause and Breast Cancer-Specific Mortality by Subgroup | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | # Events / N | Large Loss  (>10%) | Modest Loss  (>5-<10%) | Stable  (within 5%) | Modest Gain  (>5-<10%) | Large Gain  (>10%) | P Interaction |
| Overall Death | |  | HR (95% CI) | | | | |  |
| Comorbidity at diagnosis | |  |  |  |  |  |  |  |
| None | | 654 / 10545 | 2.42 (1.93, 3.04) | 1.18 (0.94, 1.49) | Ref. | 0.88 (0.67, 1.15) | 0.89 (0.63, 1.26) | 0.12 |
| >1 | | 326 / 2045 | 1.92 (1.41, 2.61) | 0.90 (0.64, 1.26) | Ref. | 1.08 (0.76, 1.54) | 1.16 (0.70, 1.94) |  |
| Body mass index at diagnosis | |  |  |  |  |  |  |  |
| Obese, >30 kg/m2 | | 402 / 4486 | 1.88 (1.44, 2.45) | 1.16 (0.88, 1.52) | Ref. | 0.84 (0.57, 1.22) | 0.97 (0.54, 1.74) | 0.94 |
| Overweight, 25-<30 kg/m2 | | 292 / 3916 | 2.44 (1.72, 3.47) | 0.98 (0.66, 1.44) | Ref. | 1.30 (0.92, 1.84) | 0.99 (0.59, 1.64) |  |
| Normal, 18.5-24.9 kg/m2 | | 273 / 4047 | 3.59 (2.49, 5.17) | 1.25 (0.83, 1.88) | Ref. | 0.81 (0.54, 1.23) | 0.94 (0.58, 1.51) |  |
| Race/Ethnicity | |  |  |  |  |  |  |  |
| Non-Hispanic white | | 711 / 8268 | 2.03 (1.63, 2.53) | 1.17 (0.93, 1.46) | Ref. | 1.00 (0.78, 1.28) | 1.08 (0.78, 1.50) | 0.34 |
| Black | | 101 / 911 | 4.21 (2.56, 6.94) | 1.06 (0.54, 2.08) | Ref. | 0.38 (0.14, 1.05) | 0.67 (0.28, 1.59) |  |
| Hispanic | | 81 / 1264 | 2.54 (1.24, 5.21) | 1.70 (0.93, 3.10) | Ref. | 1.34 (0.64, 2.81) | 0.91 (0.28, 3.03) |  |
| Asian/Pacific Islander | | 84 / 2069 | 2.65 (1.30, 5.42) | 0.76 (0.36, 1.64) | Ref. | 0.99 (0.48, 2.03) | 1.02 (0.31, 3.37) |  |
| Chemotherapy | |  |  |  |  |  |  |  |
| No | | 499 / 6794 | 2.22 (1.70, 2.88) | 0.91 (0.68, 1.22) | Ref. | 0.89 (0.67, 1.19) | 0.90 (0.58, 1.39) | 0.35 |
| Yes | | 481 / 5796 | 2.30 (1.78, 2.96) | 1.36 (1.05, 1.75) | Ref. | 0.99 (0.72, 1.35) | 1.04 (0.71, 1.53) |  |
| Breast Cancer Death | |  |  |  |  |  |  |  |
| Comorbidity at diagnosis | |  |  |  |  |  |  |  |
| None | | 396 / 10545 | 2.27 (1.69, 3.06) | 1.27 (0.95, 1.70) | Ref. | 1.00 (0.72, 1.39) | 1.04 (0.69, 1.56) | 0.69 |
| >1 | | 107 / 2045 | 1.87 (1.10, 3.16) | 0.94 (0.53, 1.69) | Ref. | 1.26 (0.69, 2.30) | 0.76 (0.27, 2.13) |  |
| Body mass index at diagnosis | |  |  |  |  |  |  |  |
| Obese, >30 kg/m2 | | 204 / 4486 | 2.13 (1.49, 3.05) | 1.20 (0.82, 1.77) | Ref. | 0.96 (0.57, 1.61) | 0.98 (0.45, 2.12) | 0.78 |
| Overweight, 25-<30 kg/m2 | 162 / 3916 | 2.07 (1.25, 3.43) | 1.11 (0.67, 1.84) | Ref. | 1.47 (0.94, 2.30) | 0.94 (0.49, 1.80) |  |
| Normal, 18.5-24.9 kg/m2 | | 133 / 4047 | 2.20 (1.21, 3.97) | 1.42 (0.83, 2.43) | Ref. | 0.75 (0.41, 1.37) | 0.85 (0.44, 1.64) |  |
| Race/Ethnicity | |  |  |  |  |  |  |  |
| Non-Hispanic white | | 352 / 8268 | 2.00 (1.46, 2.74) | 1.35 (0.99, 1.83) | Ref. | 1.19 (0.85, 1.66) | 1.07 (0.68, 1.68) | 0.30 |
| Black | | 57 / 911 | 5.35 (2.72, 10.55) | 1.47 (0.63, 3.43) | Ref. | 0.60 (0.18, 2.03) | 0.96 (0.35, 2.64) |  |
| Hispanic | | 44 / 1264 | 1.53 (0.52, 4.55) | 1.10 (0.43, 2.79) | Ref. | 1.77 (0.70, 4.52) | 0.83 (0.19, 3.73) |  |
| Asian/Pacific Islander | | 49 / 2069 | 1.35 (0.46, 4.02) | 0.70 (0.27, 1.83) | Ref. | 0.46 (0.14, 1.52) | 1.16 (0.27, 5.04) |  |
| Chemotherapy | |  |  |  |  |  |  |  |
| No | | 167 / 6794 | 2.19 (1.38, 3.48) | 0.86 (0.50, 1.48) | Ref. | 0.89 (0.54, 1.47) | 0.73 (0.34, 1.60) | 0.34 |
| Yes | | 336 / 5796 | 2.09 (1.52, 2.87) | 1.41 (1.04, 1.91) | Ref. | 1.16 (0.81, 1.66) | 1.13 (0.73, 1.76) |  |

Adjusted for age at diagnosis (continuous), race, smoking status, alcohol intake, stage (in BMI subgroup), grade, comorbidities, tumor characteristics, receipt of chemotherapy (yes/no), receipt of radiation therapy (yes/no), and pre-diagnosis BMI; P-interaction from likelihood ratio test comparing models with and without interaction terms of weight change category and each subgroup variable

| Supplemental Table S3. Average Association of Post-Diagnosis Weight Change and Breast Cancer-Specific and All-cause Mortality by Immunohistochemistry Subtype[[1]](#footnote-1) | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | # Events / N | Large Loss  (>10%) | Modest Loss  (>5-<10%) | Stable  (within 5%) | Modest Gain  (>5-<10%) | Large Gain  (>10%) | P Interaction |
|  |  | HR (95% CI) | | | | |  |
| Overall Death |  |  |  |  |  |  | 0.20 |
| Surrogate Luminal A | 290 / 5290 | 2.28 (1.62, 3.21) | 0.97 (0.68, 1.39) | Ref. | 0.92 (0.62, 1.35) | 0.82 (0.43, 1.56) |  |
| Surrogate Luminal B | 342 / 4080 | 2.97 (2.20, 4.01) | 1.12 (0.80, 1.57) | Ref. | 1.34 (0.96, 1.87) | 0.88 (0.54, 1.46) |  |
| Her2+, endocrine negative | 37 / 539 | 3.31 (1.31, 8.37) | 0.87 (0.24, 3.17) | Ref. | 1.03 (0.30, 3.48) | 2.70 (0.82, 8.88) |  |
| Triple Negative | 201 / 1365 | 2.57 (1.69, 3.92) | 1.79 (1.23, 2.62) | Ref. | 0.80 (0.48, 1.32) | 1.11 (0.63, 1.96) |  |
|  |  |  |  |  |  |  |  |
| Breast Cancer Death |  |  |  |  |  |  | 0.22 |
| Surrogate Luminal A | 85 / 5290 | 1.40 (0.69, 2.83) | 1.03 (0.55, 1.93) | Ref. | 1.13 (0.58, 2.20) | 1.25 (0.49, 3.18) |  |
| Surrogate Luminal B | 195 / 4080 | 2.93 (1.98, 4.33) | 1.06 (0.67, 1.68) | Ref. | 1.33 (0.86, 2.07) | 0.76 (0.38, 1.52) |  |
| Her2+, endocrine negative | 28 / 539 | 3.67 (1.14, 11.75) | 1.01 (0.21, 4.95) | Ref. | 1.06 (0.26, 4.40) | 2.65 (0.72, 9.76) |  |
| Triple Negative | 141 / 1365 | 2.53 (1.51, 4.26) | 1.96 (1.26, 3.05) | Ref. | 0.93 (0.53, 1.65) | 0.90 (0.43, 1.90) |  |

N=1,316 patients did not contribute to this subtype analysis because of missing information on HER2 status.

Adjusted for age at diagnosis (continuous), race, smoking status, alcohol intake, stage (in BMI subgroup), grade, comorbidities, tumor characteristics, receipt of chemotherapy (yes/no), receipt of radiation therapy (yes/no), and pre-diagnosis BMI

P Interaction from likelihood ratio test comparing models with and without interaction terms of weight change category and each subgroup variable.

1. Definitions adapted by Prat et al from the 3-marker immunohistochemistry plus grade subtypes in the St. Gallen’s Consensus Conference we separated breast cancer into subtypes as follows: 1) Surrogate Luminal A (well or moderately differentiated and ER+ and PR+ and Her2−); 2) Surrogate Luminal B (poorly or undifferentiated ER+ or PR+ and any of PR−, Her2+); 3) HER2 positive, endocrine negative (ER−, PR−, and Her2+); and 4) Triple negative (ER−, PR−, and Her2−). [↑](#footnote-ref-1)