### Supplementary Table 8. Sensitivity analysis excluding the study that has the most relative weight in subgroups.

| Subgroups                        | Effect estimates after exclusion of the most relative-weight study | Before exclusion | P-value for difference between before and after exclusion | Excluded study (Relative weight within random effect models, %) |
|----------------------------------|---------------------------------------------------------------|------------------|---------------------------------------------------------|---------------------------------------------------------------|
|                                  | No. of datasets | Sample size of cumulative meta-analysis | Incidence in control group (%) | Pooled RR (95% CIs), \( P \)-value | \( I^2 (P\)-value) | Pooled RR (95% CIs) |                                  |
| Overall                          | 22              | 78151 | 6615/57311 (11.54) | 0.708 (0.607, 0.826), <0.001 | 75.73 (<0.001) | 0.725 (0.627, 0.839) | 0.826 Coleman 2018-117mo.(7.70) |
| Study Design                     |                 |       |                   |                                   |                 |                   |                                  |
| RCTs                             | 14              | 11252 | 807/5143 (15.68)  | 0.861 (0.782, 0.948), 0.002 | 0.00 (0.756)  | 0.892 (0.829, 0.961) | 0.568 Coleman 2018-117mo.(40.48) |
| Cohorts                          | 7               | 45709 | 4644/36635 (12.68) | 0.560 (0.398, 0.787), 0.001 | 88.13 (<0.001) | 0.570 (0.436, 0.745) | 0.936 Kremer 2014-60mo.(16.74) |
| Follow-up Duration (year) (Only RCTs) |              |       |                   |                                   |                 |                   |                                  |
| Treatment duration               | 4               | 1379  | 97/698 (13.83)    | 0.723 (0.530, 0.986), 0.041 | 0.00 (0.866)  | 0.930 (0.817, 1.058) | 0.142 Coleman 2011-59.3mo.(82.62) |
| Post-treatment 1-2               | 7               | 5461  | 345/2213 (15.59)  | 0.706 (0.535, 0.930), 0.013 | 44.32 (0.096) | 0.780 (0.638, 0.954) | 0.568 Coleman 2014-84mo.(30.54) |
| Post-treatment 3-4               | 3               | 2276  | 143/1130 (12.65)  | 0.694 (0.499, 0.966), 0.031 | 41.18 (0.183) | 0.718 (0.585, 0.881) | 0.864 Powles 2006-67mo.(41.76) |
| Post-treatment >4                | 6               | 6554  | 439/3287 (13.36)  | 0.868 (0.764, 0.985), 0.028 | 0.00 (0.585)  | 0.906 (0.832, 0.987) | 0.583 Coleman 2018-117mo.(54.22) |
| Recurrence Sites                 |                 |       |                   |                                   |                 |                   |                                  |
| Bone metastases                  | 11              | 21780 | 736/11469 (6.42)  | 0.748 (0.635, 0.881), 0.001 | 43.00 (0.063) | 0.713 (0.602, 0.843) | 0.689 Kremer 2014-60mo.(15.61) |
| Nonskeletal metastases           | 8               | 17275 | 537/9217 (5.83)   | 0.841 (0.730, 0.969), 0.016 | 17.04 (0.296) | 0.883 (0.768, 1.014) | 0.630 Coleman 2018-117mo.(22.66) |
| Loco-regional recurrence         | 9               | 21293 | 408/11831 (3.45)  | 0.835 (0.698, 0.999), 0.048 | 10.15 (0.351) | 0.887 (0.771, 1.020) | 0.603 Kwan 2016-42mo.(36.02) |
| Contralateral recurrence         | 10              | 22228 | 601/12645 (4.75)  | 0.725 (0.594, 0.885), 0.002 | 0.00 (0.569)  | 0.775 (0.651, 0.922) | 0.621 Kwan 2016-42mo.(23.35) |
| Menopausal Status                |                 |       |                   |                                   |                 |                   |                                  |
| Postmenopausal                   | 11              | 23188 | 1513/18597 (8.14) | 0.752 (0.636, 0.889), 0.001 | 37.02 (0.103) | 0.737 (0.640, 0.850) | 0.857 Lipton 2017-49.2mo.(19.88) |
| Non-postmenopausal               | 5               | 3018  | 530/1949 (27.17)  | 0.903 (0.685, 1.190), 0.468 | 16.01 (0.313) | 0.992 (0.864, 1.139) | 0.551 Coleman 2018-117mo.(63.47) |
| Type of BPs (Only RCTs)           |                 |       |                   |                                   |                 |                   |                                  |
| Zoledronic acid                  | 6               | 2359  | 129/1185 (10.84)  | 0.738 (0.593, 0.920), 0.007 | 0.00 (0.978)  | 0.892 (0.805, 0.988) | 0.125 Coleman 2018-117mo.(78.15) |
| Clodronate                       | 2               | 1371  | 201/684 (29.53)   | 0.864 (0.681, 1.097), 0.231 | 43.24 (0.184) | 0.846 (0.736, 0.971) | 0.881 Paterson 2012-90.7mo.(39.46) |

Abbreviations: BPs, bisphosphonates; CI, confidence interval; RCTs, randomized controlled trials; RR, risk ratio.
Supplementary Table 9. Sensitivity analysis by including studies with high risk of bias (Saarto and Minckitz, RCT).

| Subgroups                               | No. of datasets | Pooled RR (95% CIs), $P$-value | $I^2$ ($P$-value) |
|-----------------------------------------|-----------------|---------------------------------|------------------|
| Overall                                  | 25              | 0.761 (0.657, 0.881), <0.001    | 79.99 (<0.001)   |
| Study Design                             |                 |                                 |                  |
| RCTs                                     | 17              | 0.920 (0.857, 0.987), 0.020     | 20.91 (0.210)    |
| Follow-up Duration (year) (Only RCTs)    |                 |                                 |                  |
| Treatment duration                       | 6               | 0.945 (0.838, 1.064), 0.350     | 0.00 (0.526)     |
| Post-treatment 1-2                       | 9               | 0.845 (0.668, 1.071), 0.163     | 66.75 (0.002)    |
| Post-treatment >4                        | 8               | 0.943 (0.821, 1.082), 0.403     | 46.48 (0.070)    |
| Recurrence Sites                         |                 |                                 |                  |
| Bone metastases                          | 14              | 0.769 (0.646, 0.915), 0.003     | 68.96 (<0.001)   |
| Nonskeletal metastases                   | 10              | 0.935 (0.787, 1.110), 0.443     | 60.10 (0.007)    |
| Loco-regional recurrence                 | 12              | 0.898 (0.767, 1.051), 0.180     | 28.26 (0.168)    |
| Menopausal Status                        |                 |                                 |                  |
| Postmenopausal                           | 13              | 0.743 (0.651, 0.849), <0.001    | 33.39 (0.115)    |
| Non-postmenopausal                       | 7               | 1.004 (0.894, 1.126), 0.951     | 0.00 (0.503)     |
| Type of BPs (Only RCTs)                  |                 |                                 |                  |
| Zoledronic acid                          | 8               | 0.905 (0.821, 0.998), 0.045     | 0.00 (0.634)     |
| Clodronate                               | 4               | 0.966 (0.726, 1.284), 0.811     | 74.17 (0.009)    |

*Saarto and Minckitz studies are RCTs of high risk of bias and then are excluded from the primary main analyses, in order to minimize the impact on the overall results, especially the results of some subgroup analyses. However, sensitivity analysis showed that the inclusion of these studies did not materially impact the results.

Abbreviations: BPs, bisphosphonates; CI, confidence interval; RCTs, randomized controlled trials; RR, risk ratio.

Supplementary Table 10. Sensitivity analysis by excluding the zero-event study (Hershman, RCT).

| Subgroups                               | No. of datasets | Pooled RR (95% CIs), $P$-value | $I^2$ ($P$-value) |
|-----------------------------------------|-----------------|---------------------------------|------------------|
| Overall                                  | 22              | 0.724 (0.625, 0.838), <0.001    | 79.29 (<0.001)   |
| Study Design                             |                 |                                 |                  |
| RCTs                                     | 14              | 0.892 (0.829, 0.961), 0.003     | 0.00 (0.651)     |
| Follow-up Duration (year) (Only RCTs)    |                 |                                 |                  |
| Treatment duration                       | 4               | 0.885 (0.720, 1.088), 0.247     | 20.47 (0.287)    |
| Menopausal Status                        |                 |                                 |                  |
| Non-postmenopausal                       | 5               | 0.973 (0.814, 1.161), 0.758     | 24.34 (0.259)    |
| Type of BPs (Only RCTs)                  |                 |                                 |                  |
| Zoledronic acid                          | 6               | 0.892 (0.805, 0.988), 0.029     | 0.00 (0.493)     |

*Hershman’ study is a randomized controlled trial, in which none event had been observed in both arms. The Hershman trial was only included in these analyses listed above.

Abbreviations: BPs, bisphosphonates; CI, confidence interval; RCTs, randomized controlled trials; RR, risk ratio.
**Supplementary Table 11. Sensitivity analysis by excluding studies without clear definition of post-diagnosis BPs use (Lipton and Rouach, Cohort).**

| Subgroups                  | No. of datasets | Pooled RR (95% CIs), P-value | $I^2$ (P-value) |
|---------------------------|-----------------|------------------------------|-----------------|
| Overall                   | 21              | 0.736 (0.631, 0.858), <0.001 | 78.38 (<0.001)  |
| **Study Design**          |                 |                              |                 |
| Cohorts                   | 6               | 0.568 (0.408, 0.792), 0.001  | 90.21 (<0.001)  |
| **Recurrence Sites**      |                 |                              |                 |
| Bone metastases           | 12              | 0.750 (0.642, 0.877), <0.001 | 53.04 (0.024)   |
| Nonskeletal metastases    | 8               | 0.953 (0.857, 1.059), 0.368  | 0.00 (0.480)    |
| Loco-regional recurrence  | 9               | 0.937 (0.828, 1.060), 0.302  | 0.00 (0.528)    |
| Contralateral recurrence  | 10              | 0.818 (0.681, 0.982), 0.031  | 0.00 (0.754)    |
| **Menopausal Status**     |                 |                              |                 |
| Postmenopausal            | 10              | 0.775 (0.686, 0.876), <0.001 | 8.03 (0.368)    |

*Lipton and Rouach studies are all cohort studies and are included in these analyses above, so this sensitivity analysis was conducted in such subgroup analyses listed above. Abbreviations: CI, confidence interval; RR, risk ratio.

**Supplementary Table 12. Publication bias analysis.**

| Subgroups                  | No. of datasets | P-value for                  | Pooled RR (95% CI)                      |
|---------------------------|-----------------|------------------------------|-----------------------------------------|
|                           |                 | Begg's rank correlation test | Egger's linear regression test          | Adjusted with trim and fill | Unadjusted                        |
| **Overall**               | 23              | 0.091                        | 0.259                                   | 0.796 (0.678, 0.933)         | 0.725 (0.627, 0.839)              |
| **Study Design**          |                 |                              |                                         |                           |                                   |
| RCTs                      | 15              | 0.428                        | 0.113                                   | 0.898 (0.834, 0.967)         | 0.892 (0.829, 0.961)               |
| Cohorts                   | 8               | 0.386                        | 0.251                                   | 0.687 (0.520, 0.907)         | 0.570 (0.436, 0.745)               |
| **Follow-up Duration (year) (Only RCTs)** | | | | | |
| Treatment duration        | 5               | 0.807                        | 0.369                                   | 0.936 (0.823, 1.064)         | 0.930 (0.817, 1.058)               |
| Post-treatment 1-2        | 8               | 0.548                        | 0.195                                   | 0.786 (0.672, 0.920)         | 0.780 (0.638, 0.954)               |
| Post-treatment 3-4        | 4               | 1.000                        | 0.590                                   | 0.690 (0.544, 0.875)         | 0.718 (0.585, 0.881)               |
| Post-treatment >4         | 7               | 0.711                        | 0.258                                   | 0.906 (0.820, 1.001)         | 0.906 (0.832, 0.987)               |
| **Recurrence Sites**      |                 |                              |                                         |                           |                                   |
| Bone metastases           | 12              | 0.373                        | 0.751                                   | 0.652 (0.549, 0.775)         | 0.713 (0.602, 0.843)               |
| Nonskeletal metastases    | 9               | 0.917                        | 0.352                                   | 0.931 (0.798, 1.087)         | 0.883 (0.768, 1.014)               |
| Loco-regional recurrence  | 10              | 0.074                        | 0.006                                   | 0.914 (0.801, 1.044)         | 0.887 (0.771, 1.020)               |
| Contralateral recurrence  | 11              | 1.000                        | 0.891                                   | 0.771 (0.648, 0.918)         | 0.775 (0.651, 0.922)               |
| **Menopausal Status**     |                 |                              |                                         |                           |                                   |
| Postmenopausal            | 12              | 0.193                        | 0.270                                   | 0.746 (0.633, 0.878)         | 0.737 (0.640, 0.850)               |
| Non-postmenopausal        | 6               | 0.260                        | 0.134                                   | 1.013 (0.810, 1.266)         | 0.992 (0.864, 1.139)               |
| **Type of BPs (Only RCTs)** |              |                              |                                         |                           |                                   |
| Zoledronic acid           | 7               | 1.000                        | 0.042                                   | 0.903 (0.816, 0.999)         | 0.892 (0.805, 0.988)               |
| Clodronate                | 3               | 1.000                        | 0.324                                   | 0.846 (0.736, 0.971)         | 0.846 (0.736, 0.971)               |

Abbreviations: BPs, bisphosphonates; CI, confidence interval; RCTs, randomized controlled trials; RR, risk ratio.