**Supplementary Table 4. GRADE quality of evidence.**

| **Certainty assessment** | **№ of patients** | **Effect** | **Quality of evidence** | **Importance** |
| --- | --- | --- | --- | --- |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Any BPs** | **Non-users** | **Relative(95% CI)** | **Absolute(95% CI)** |
| **Overall** |
| 23  | RCTs and Cohorts  | not serious  | not serious  | not serious  | not serious  | none  | 2302/22521 (10.2%)  | 7189/58989 (12.2%)  | **RR 0.725**(0.627 to 0.839)  | **34 fewer per 1,000**(from 45 fewer to 20 fewer)  | ⨁⨁⨁◯ MODERATE | CRITICAL  |
| **Subgroup by study design** |
| **RCTs** |
| 15  | RCTs  | not serious  | not serious  | not serious  | not serious  | none  | 1440/7790 (18.5%)  | 1382/6821 (20.3%)  | **RR 0.892**(0.829 to 0.961)  | **22 fewer per 1,000**(from 35 fewer to 8 fewer)  | ⨁⨁⨁⨁HIGH  | CRITICAL  |
| **Cohort Studies** |
| 8  | Cohorts  | not serious  | not serious  | not serious  | not serious  | none  | 862/14731 (5.9%)  | 5808/52168 (11.1%)  | **RR 0.570**(0.436 to 0.745)  | **48 fewer per 1,000**(from 63 fewer to 28 fewer)  | ⨁⨁⨁◯ MODERATE  | CRITICAL  |
| **Subgroup by Recurrence Sites** |
| **Bone metastases** |
| 12  | RCTs and Cohorts | not serious  | not serious  | not serious  | not serious  | none  | 770/15968 (4.8%)  | 1900/27002 (7.0%)  | **HR 0.713**(0.602 to 0.843)  | **20 fewer per 1,000**(from 27 fewer to 11 fewer)  | ⨁⨁⨁◯ MODERATE | CRITICAL  |
| **Nonskeletal metastases** |
| 9  | RCTs and Cohorts | not serious  | not serious  | not serious  | not serious  | none  | 886/9739 (9.1%)  | 897/10895 (8.2%)  | **HR 0.883**(0.768 to 1.014)  | **9 fewer per 1,000**(from 18 fewer to 1 more)  | ⨁⨁⨁◯ MODERATE | IMPORTANT  |
| **Loco-regional recurrence**  |
| 10  | RCTs and Cohorts | not serious  | not serious  | not serious  | not serious  | publication bias suspected \* | 508/12717 (4.0%)  | 2692/25357 (10.6%)  | **HR 0.887**(0.771 to 1.020)  | **11 fewer per 1,000**(from 23 fewer to 2 more)  | ⨁⨁⨁◯MODERATE  | IMPORTANT  |
| **Contralateral breast recurrence** |
| 11  | RCTs and Cohorts | not serious  | not serious  | not serious  | not serious  | none  | 225/12838 (1.8%)  | 972/26171 (3.7%)  | **HR 0.775**(0.651 to 0.922)  | **8 fewer per 1,000**(from 13 fewer to 3 fewer)  | ⨁⨁⨁◯ MODERATE | IMPORTANT  |
| **Subgroup by Menopausal Status** |
| **Postmenopausal Women** |
| 12  | RCTs and Cohorts | not serious  | not serious  | not serious  | not serious  | none  | 665/7302 (9.1%)  | 1891/23462(8.1%)  | **RR 0.737**(0.640 to 0.850)  | **21 fewer per 1,000**(from 29 fewer to 12 fewer)  | ⨁⨁⨁◯ MODERATE | CRITICAL  |
| **Non-postmenopausal Women** |
| 6  | RCTs and Cohorts | not serious  | not serious  | not serious  | not serious  | none  | 523/2231(23.4%)  | 530/1949(27.2%)  | **RR 0.992**(0.864 to 1.139)  | **2 fewer per 1,000**(from 37 fewer to 38 more)  | ⨁⨁⨁◯ MODERATE | IMPORTANT |
| **Subgroup by Follow-up Duration** |
| **Treatment Duration** |
| 5  | RCTs | not serious  | not serious  | not serious  | not serious  | none  | 446/2362(18.9%)  | 472/2376(19.9%)  | **RR 0.930**(0.817 to 1.058)  | **13 fewer per 1,000**(from 33 fewer to 10 more)  | ⨁⨁⨁⨁HIGH  | CRITICAL  |
| **Post-treatment 1-2 years** |
| 8  | RCTs | not serious  | not serious  | not serious  | not serious  | none  | 966/4929 (19.6%)  | 882/3891(22.7%)  | **RR 0.780**(0.638 to 0.954)  | **45 fewer per 1,000**(from 75 fewer to 9 fewer)  | ⨁⨁⨁⨁HIGH  | CRITICAL  |
| **Post-treatment 3-4 years** |
| 4  | RCTs | not serious  | not serious  | not serious  | not serious  | none  | 240/1676(14.3%)  | 288/1669(17.3%)  | **RR 0.718**(0.585 to 0.881)  | **45 fewer per 1,000**(from 68 fewer to 19 fewer)  | ⨁⨁⨁⨁HIGH  | CRITICAL  |
| **Post-treatment >4 years** |
| 7  | RCTs | not serious  | not serious  | not serious  | not serious  | none  | 920/4948(18.6%)  | 1014/4965(20.4%)  | **HR 0.906**(0.832 to 0.987)  | **17 fewer per 1,000**(from 31 fewer to 2 fewer)  | ⨁⨁⨁⨁HIGH  | CRITICAL  |
| **Subgroup by BP Type** |
| **Zoledronic acid** |
| 7  | RCTs | not serious  | not serious  | not serious  | not serious  | publication bias strongly suspected† | 606/2855 (21.2%)  | 666/2863(23.3%)  | **RR 0.892**(0.805 to 0.988)  | **25 fewer per 1,000**(from 45 fewer to 3 fewer)  | ⨁⨁⨁◯MODERATE  | IMPORTANT |
| **Clodronate** |
| 3  | RCTs | not serious  | not serious  | not serious  | not serious  | none  | 339/2342(14.5%)  | 387/2340(16.5%)  | **RR 0.846**(0.736 to 0.971)  | **25 fewer per 1,000**(from 44 fewer to 5 fewer)  | ⨁⨁⨁⨁HIGH  | IMPORTANT |

**GRADE quality of evidence:** **High quality:** Further research is unlikely to have an important impact on confidence in estimate of effect and is likely to change the estimate; and we are very confident that the true effect lies close to that of the estimate of the effect. **Moderate quality:** Further research is possible to have a moderate impact on confidence in estimate of effect; we are moderately confident in the effect estimate; and the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. **Low quality:** Further research is likely to have an important impact on confidence in estimate of effect and is likely to change the estimate; our confidence in the effect estimate is limited; and the true effect may be substantially different from the estimate of the effect. **Very Low quality:** We have very little confidence in the effect estimate; and the true effect is likely to be substantially different from the estimate of effect.

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

\*Possibility for publication bias according to the Egger's linear regression test (P=0.006).

†Possibility for publication bias according to the Egger's linear regression test (P=0.042).