Results from the systematic review and meta-analysis on the correlation between the BTMs and BMD in postmenopausal women patients underegoing anti-osteoporosis therapy

***Conclusion*:** We reanalyzed the 20 eligible studies that include only postmenopausal women by excluding the other two studies that included men. The only difference between the results of the analyses on the 22 eligible studies and on the 20 eligible studies is the bone resorption marker of serum C-terminal crosslinking telopeptide of type I collagen (S-CTX). The combination of the systematic review and subgroup analysis of the 20 studies showed that the correlations between the changes in serum CTX and BMD were also moderately strong. As for the other markers we concluded form the analyses on the 22 studies including both women and men (i.e. PINP at baseline, serum bone ALP, serum osteocalcin, and urine NTX), they are all valuable in predicting long-term BMD changes. Therefore, in postmenopausal osteoporosis patients, the S-CTX could also be the candidate for future prediction of the BMD changes after drug intervention.

S4.1 Search results

S4.2 Quality assessment of eligible studies

S 4.3 Findings from the systematic review

S4.3.1 Pretreatment BTMs and BMD changes after drug intervention

S4.3.2 Changes in markers of bone formation and changes in BMD after drug intervention

S4.3.3 Changes in markers of bone resorption and changes in BMD after drug intervention

S4.4 Findings from the subgroup analyses

S4.4A Forests of subgroup analyses on the correlation between baseline BTMs and BMD changes

S4.4B Forests of subgroup analyses on the correlation between the changes in bone ALP and BMD

S4.4C Forests of subgroup analyses on the correlation between the changes in osteocalcin and BMD

S4.4D Forests of subgroup analyses on the correlation between the changes in PINPand BMD

S4.4E Forests of subgroup analyses on the correlation between the changes in S-CTX and BMD

S4.4F Forests of subgroup analyses on the correlation between the changes in U-NTX and BMD

S4.1 Search results

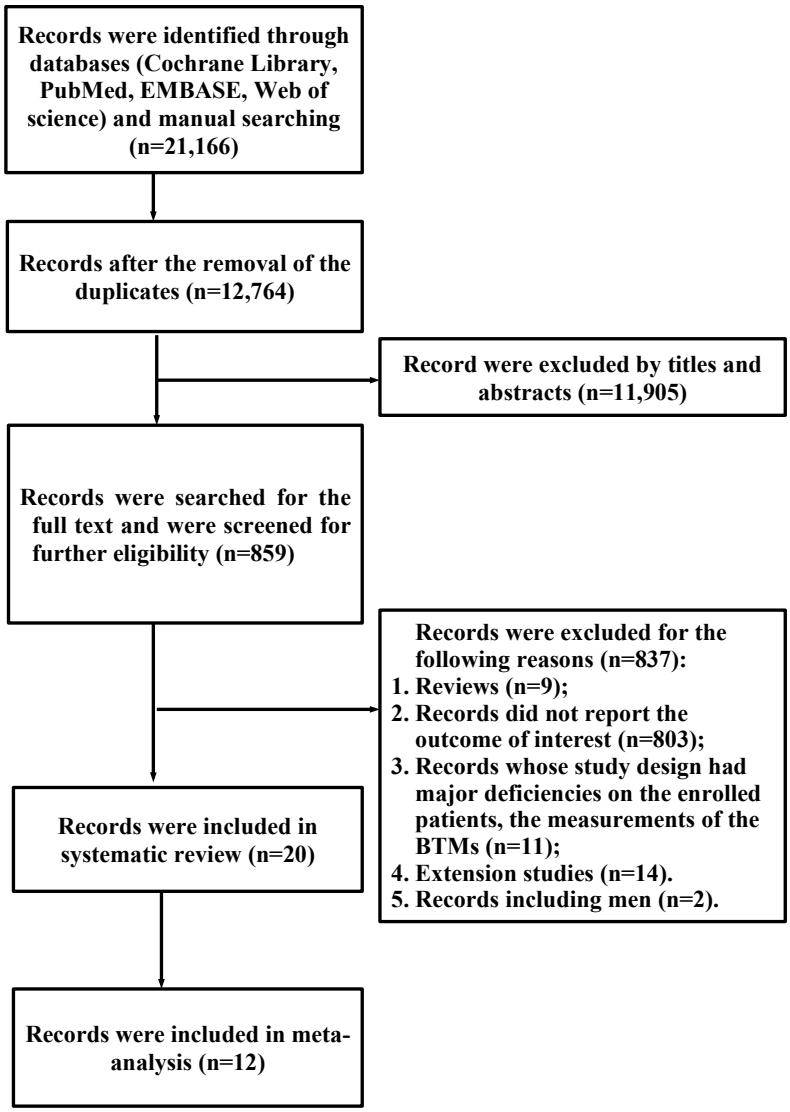
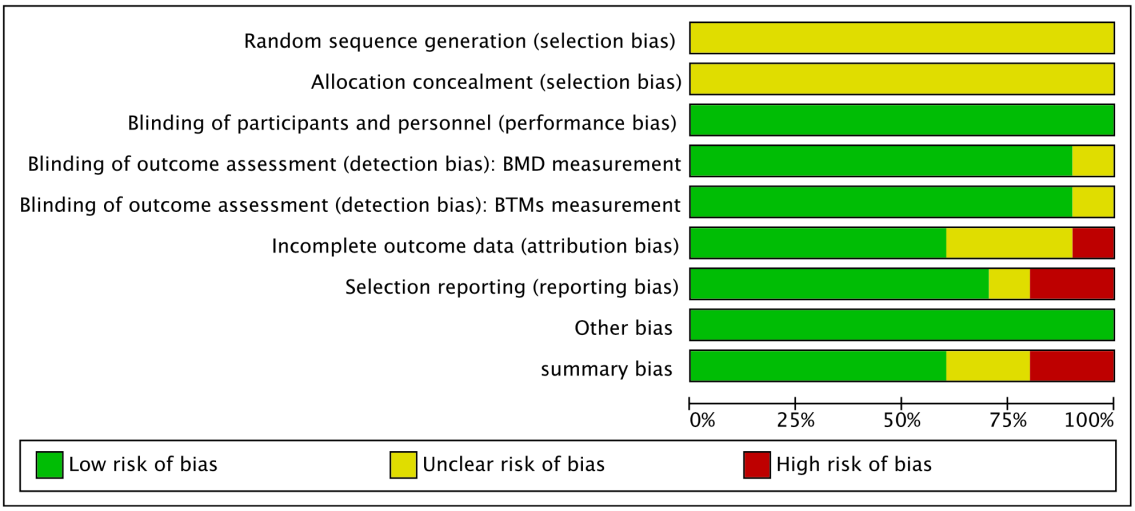
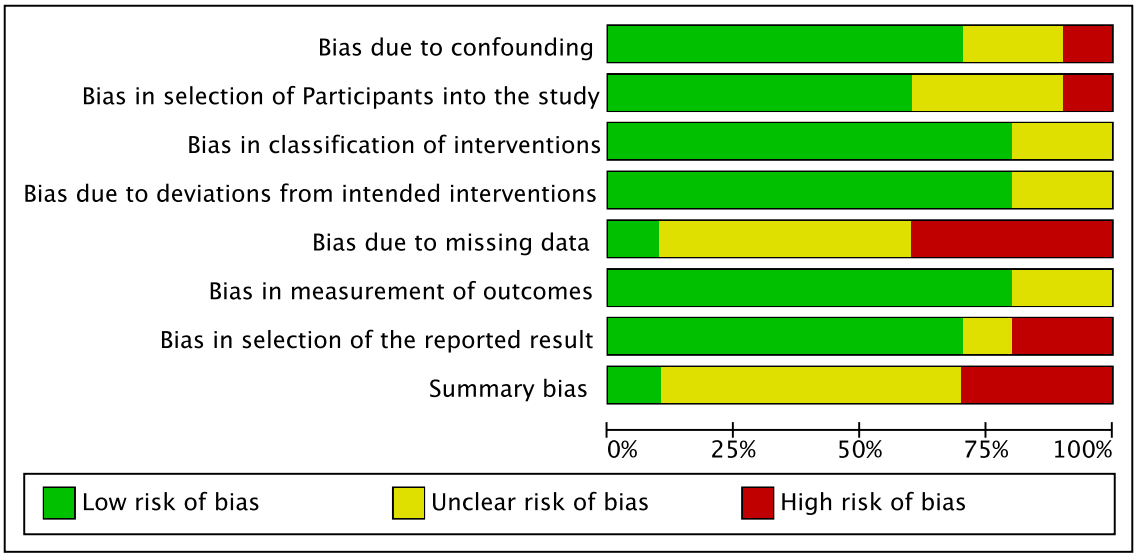


Figure 1. Flow chart of the literature search and study selection.

S4.2 Quality assessment of eligible studies



(a)



(b)

Figure 2. Quality assessment of the eligible studies. (**a**) Summary of the quality of the randomized controlled trials; (**b**) Summary of the quality of the nonrandomized trials.

S 4.3 Findings from the systematic review

S4.3.1 Pretreatment BTMs and BMD changes after drug intervention

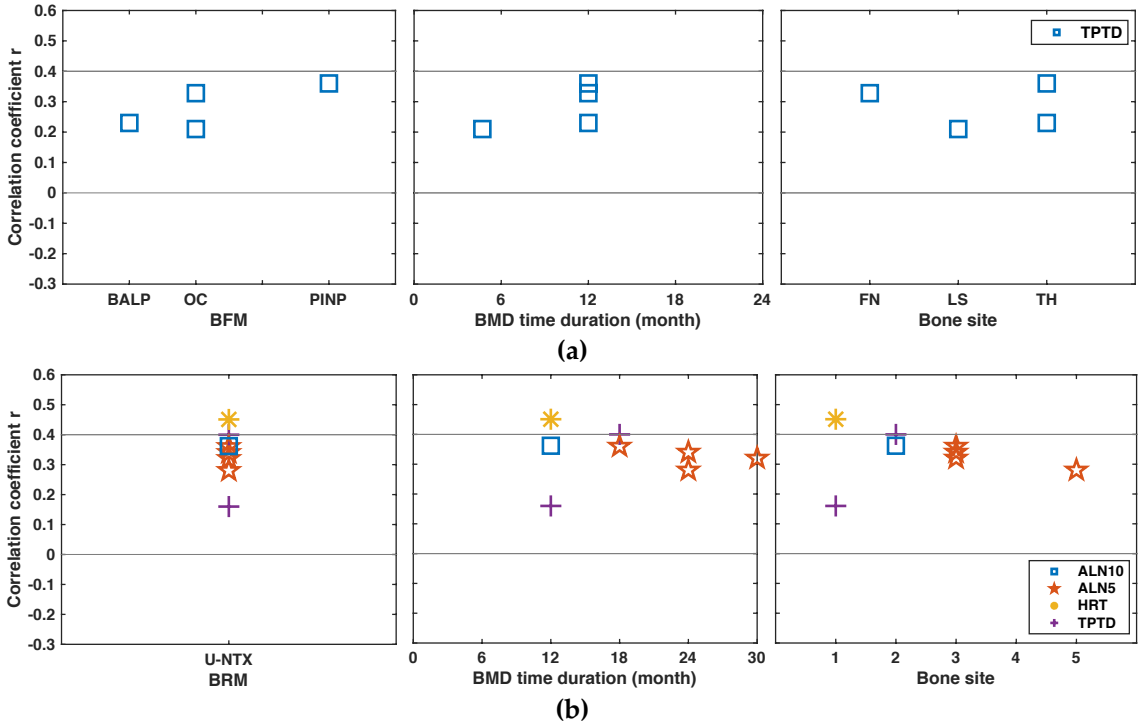


Figure 3. Significant correlations between baseline BTMs and BMD changes at different bone sites under different drug interventions over time. (a) Correlations between baseline BFMs and BMD changes from baseline at different bone sites under different drug interventions over time; (b) Correlations between baseline BRMs and BMD changes from baseline under different drug interventions over time. BFM bone formation marker, BRM, bone resorption marker, ALN alendronate, ALN5 5mg/d ALN, ALN10 10 mg/d ALN, ALN10+HRT, combination of 10 mg/d ALN and HRT, HRT hormone replacement therapy, TPTD teriparatide, FN femoral neck, LS lumbar spine, TB total body, TH total hip, TR trochanter.

S4.3.2 Changes in markers of bone formation and changes in BMD after drug intervention

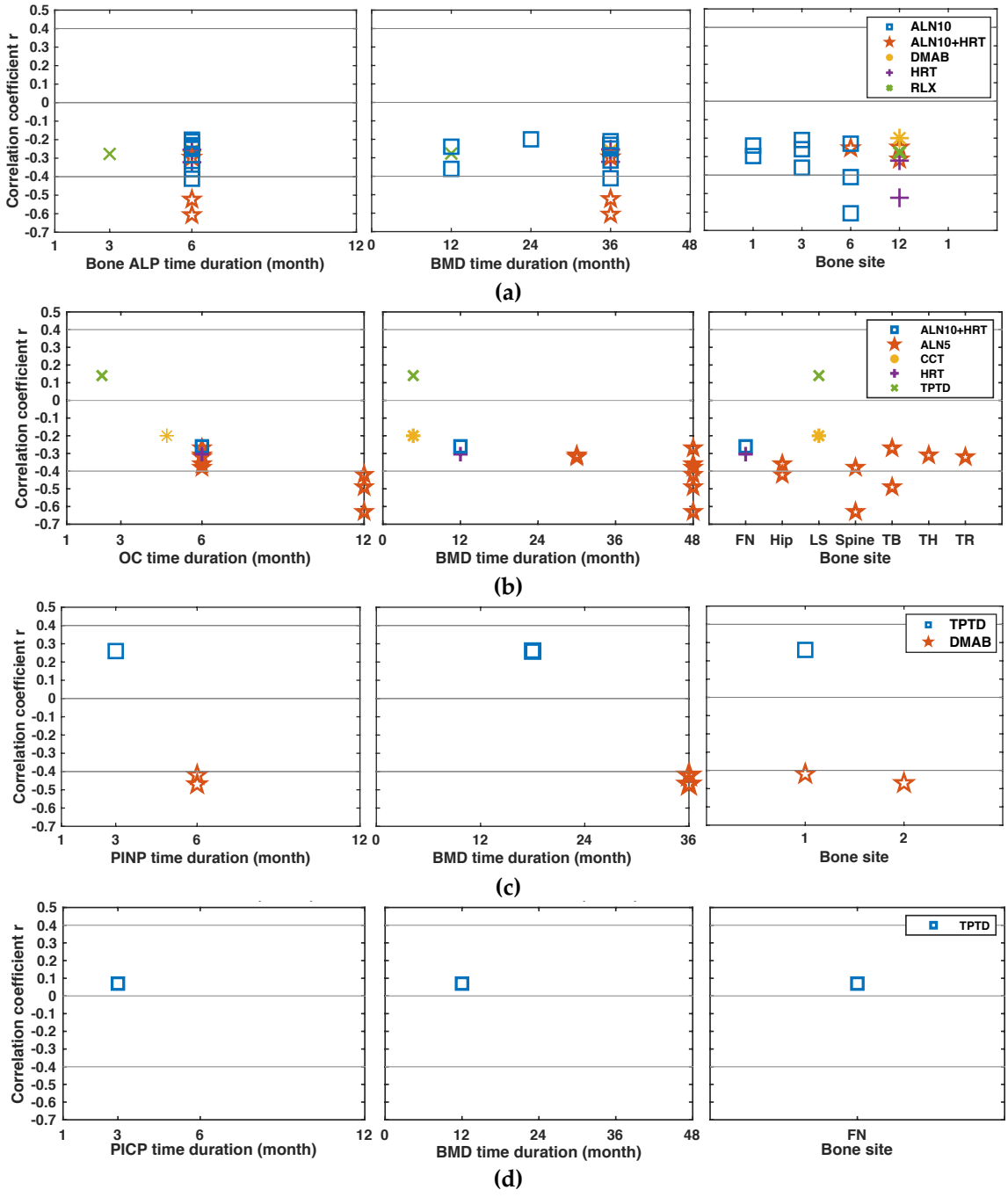


Figure 4. Significant correlations between the changes in BFMs and BMD at different bone sites under different drug interventions over time. (a) Correlations between the changes in bone ALP and BMD from baseline at different bone sites under different drug interventions over time; (b) Correlations between the changes in OC and BMD under different drug interventions over time; (c) Correlations between the changes in PINP and BMD under different drug interventions over time; (d) Correlations between the changes in PICP and BMD under different drug interventions over time. ALN alendronate, ALN5 5mg/d ALN, ALN10 10 mg/d ALN, ALN10+HRT, combination of 10 mg/d ALN and HRT, BFM bone formation marker, CCT calcitonin, DMAB denosumab, HRT hormone replacement therapy, RLX raloxifene, TPTD teriparatide, FN femoral neck, LS lumbar spine, TB total body, TH total hip, TR trochanter.

S4.3.3 Changes in markers of bone resorption and changes in BMD after drug intervention

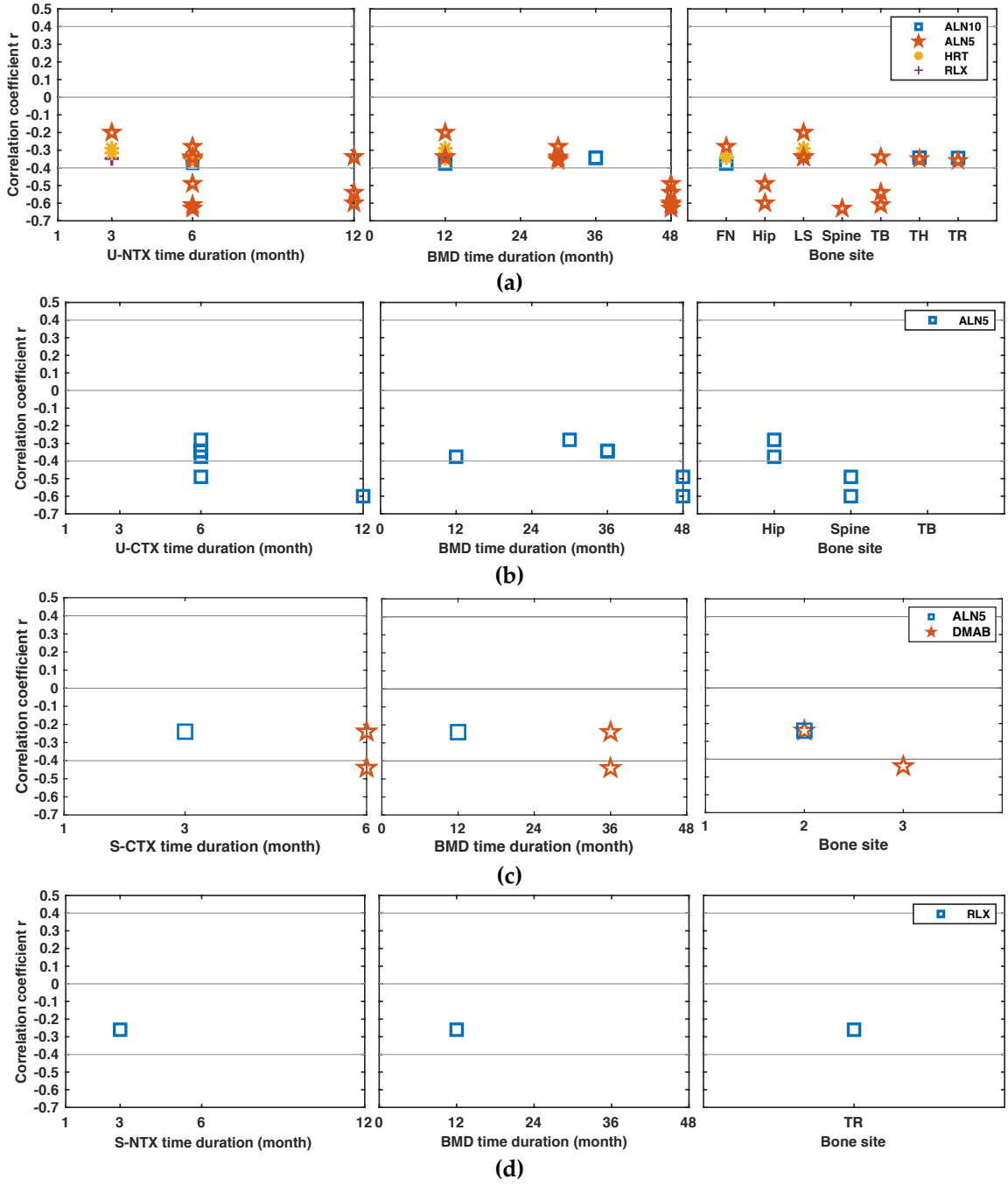


Figure 5. Significant correlations between the changes in BRMs and BMD at different bone sites under different drug interventions over time. (a) Correlations between the changes in U-NTX and BMD from baseline at different bone sites under different drug interventions over time; (b) Correlations between the changes in U-CTX and BMD under different drug interventions over time; (c) Correlations between the changes in S-CTX and BMD under different drug interventions over time; (d) Correlations between the changes in S-NTX and BMD under different drug interventions over time. ALN alendronate, ALN5 5mg/d ALN, ALN10 10 mg/d ALN, ALN10+HRT, combination of 10 mg/d ALN and HRT, BRM bone resorption marker, DMAB denosumab, HRT hormone replacement therapy, RLX raloxifene, TPTD teriparatide, FN femoral neck, LS lumbar spine, TB total body, TH total hip, TR trochanter.

S4.4 Findings from the subgroup analyses

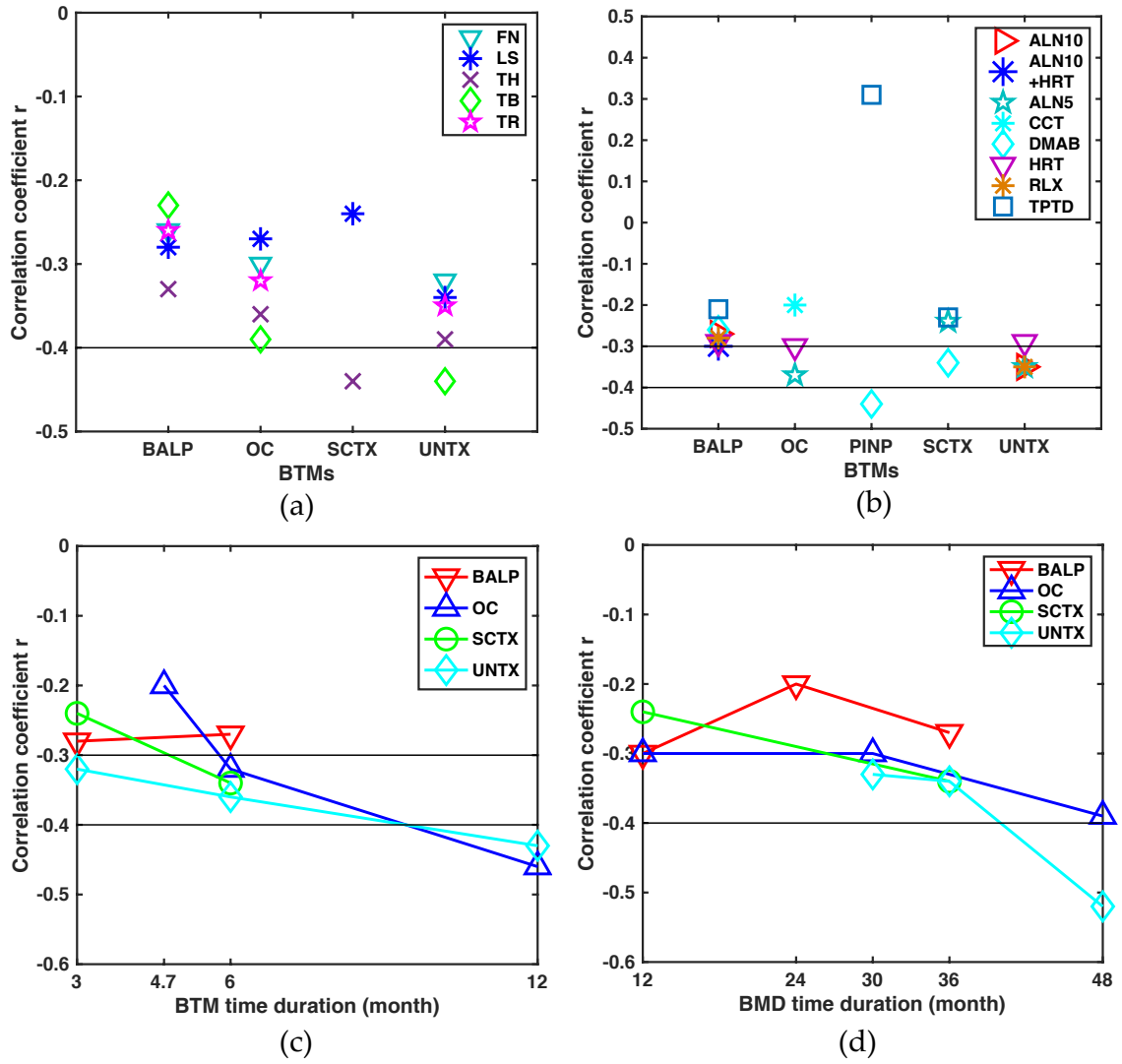


Figure 6. Assembled results of the subgroup analyses. (a) Assembled CORs between the changes in BTMs and BMD from baseline by group of bone sites; (b) Assembled CORs between the changes in BTMs and BMD from baseline by group of drug intervention; (c) Assembled CORs between the changes in BTMs and BMD from baseline by group of the time duration of BTMs measurements; (d) Assembled CORs between the changes in BTMs and BMD from baseline by group of the time duration of BMD measurements. ALN alendronate, ALN5 5mg/d ALN, ALN10 10 mg/d ALN, ALN10+HRT, combination of 10 mg/d ALN and HRT, CCT calcitonin, COR summary correlation coefficient r, DMAB denosumab, HRT hormone replacement therapy, RLX raloxifene, TPTD teriparatide, FN femoral neck, LS lumbar spine, TB total body, TH total hip, TR trochanter.

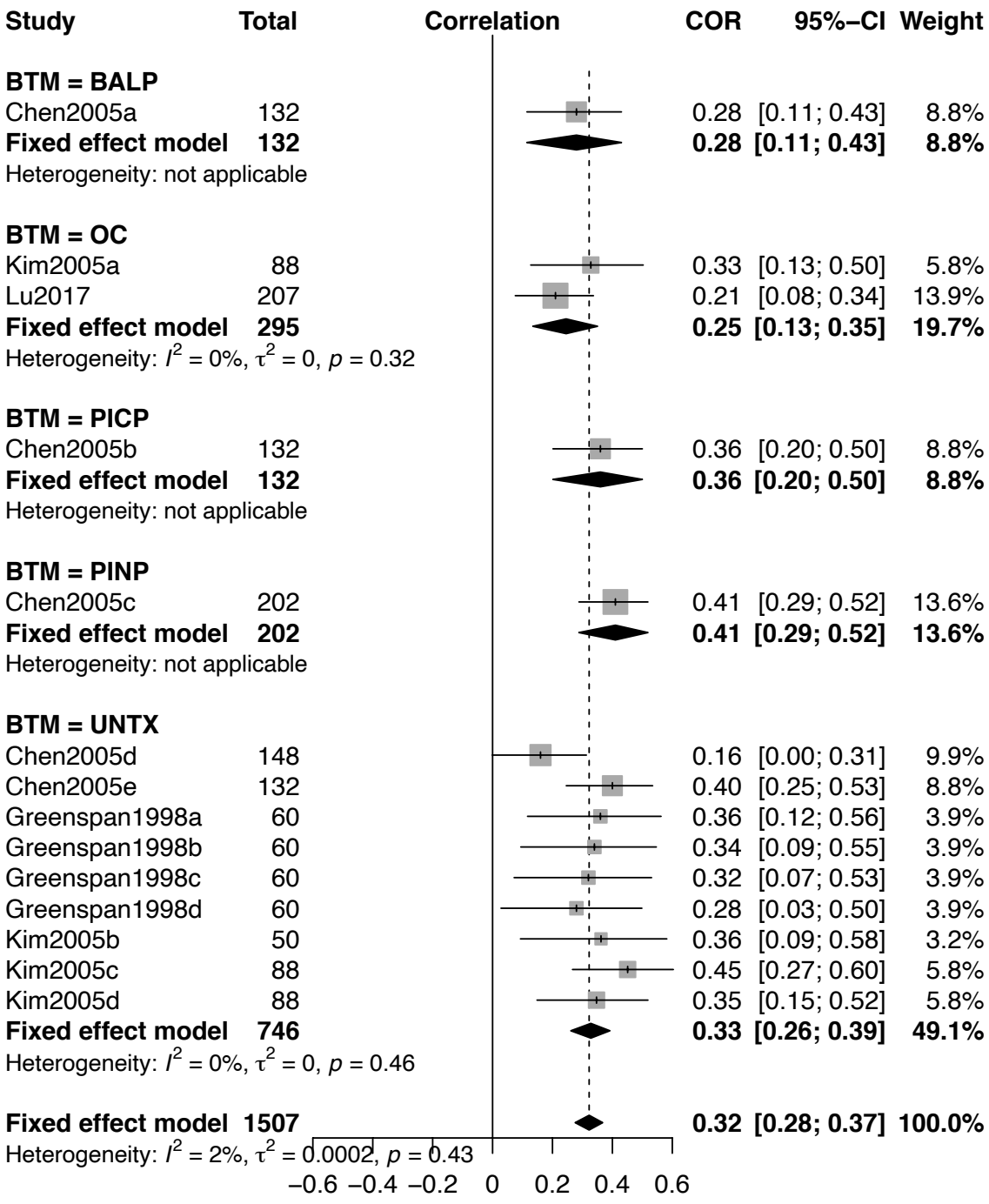


Figure S4.4A.1 Forests of subgroup analyses on the correlation between baseline BTMs and BMD changes by group of BTMs.

S4.4B Forests of subgroup analyses on the correlation between the changes in bone ALP and BMD

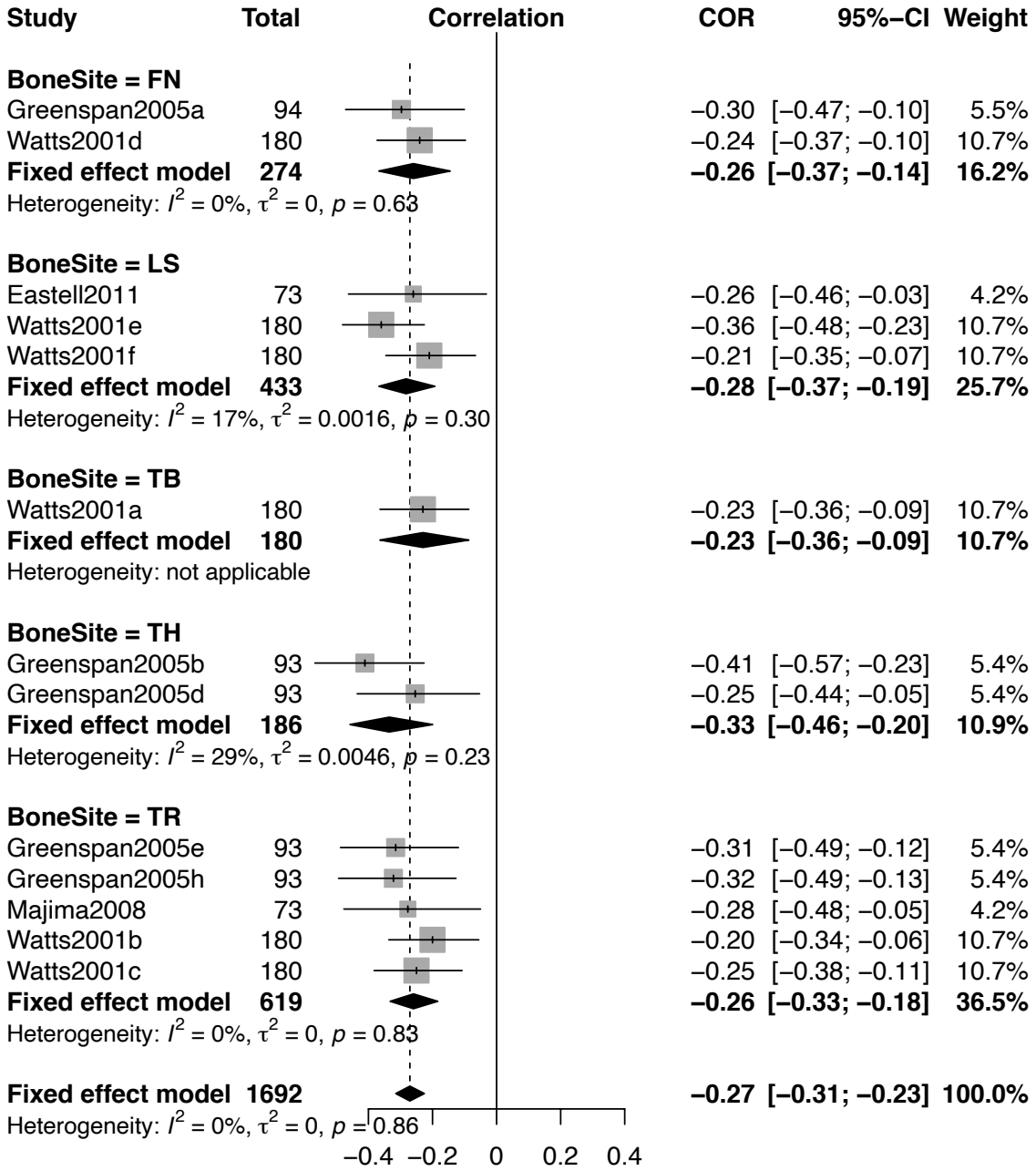


Figure S4.4B.1 Forests of subgroup analyses on the correlation between the changes in bone ALP and BMD by group of bone sites. FN femoral neck, LS lumbar spine, TB total body, TH total hip, TR trochanter.

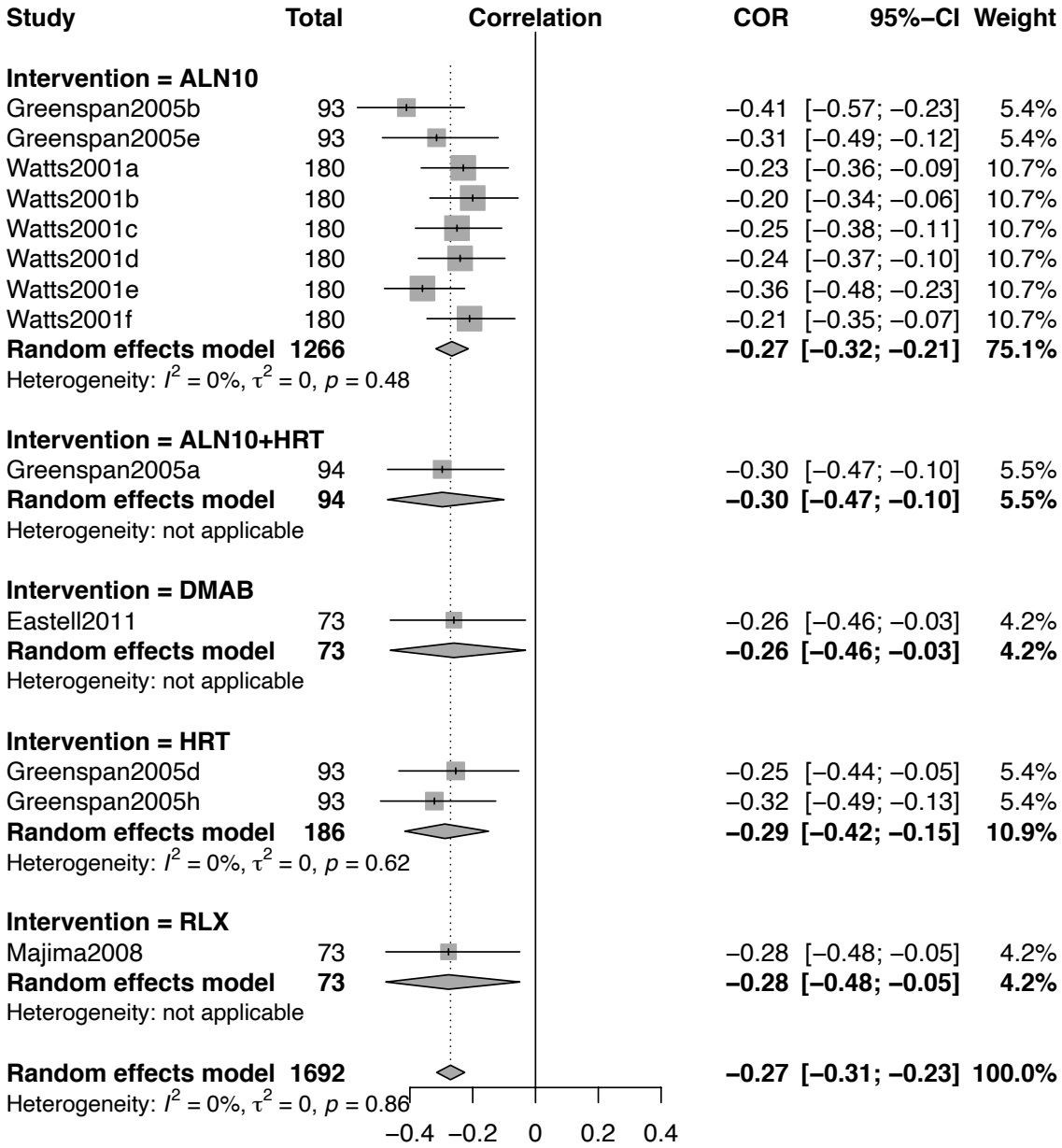


Figure S4.4B.2 Forests of subgroup analyses on the correlation between the changes in bone ALP and BMD by group of intervention. ALN10 10 mg/d Alendronate, ALN10+HRT combination of 10 mg/d Alendronate and HRT, HRT Hormone replacement therapy.

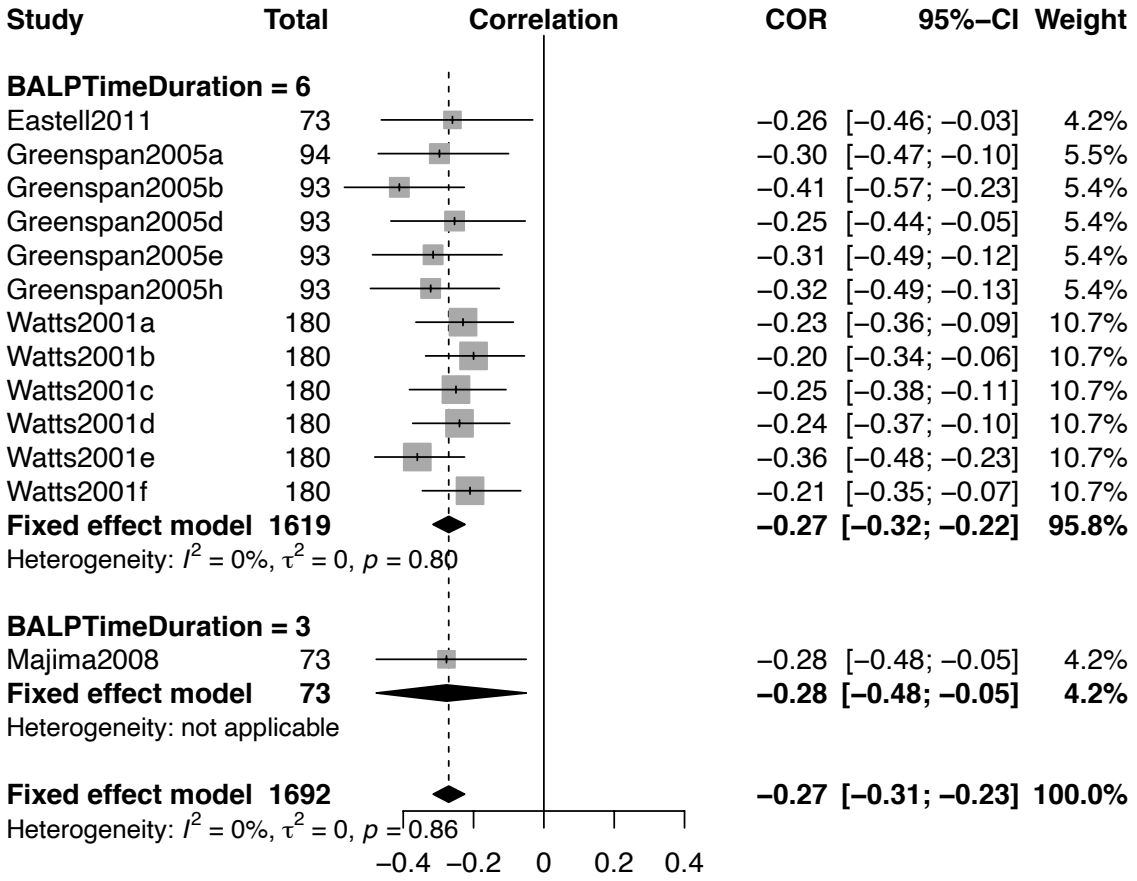


Figure S4.4B.3 Forests of subgroup analyses on the correlation between the changes in bone ALP and BMD by group of the time duration of bone ALP measurements.

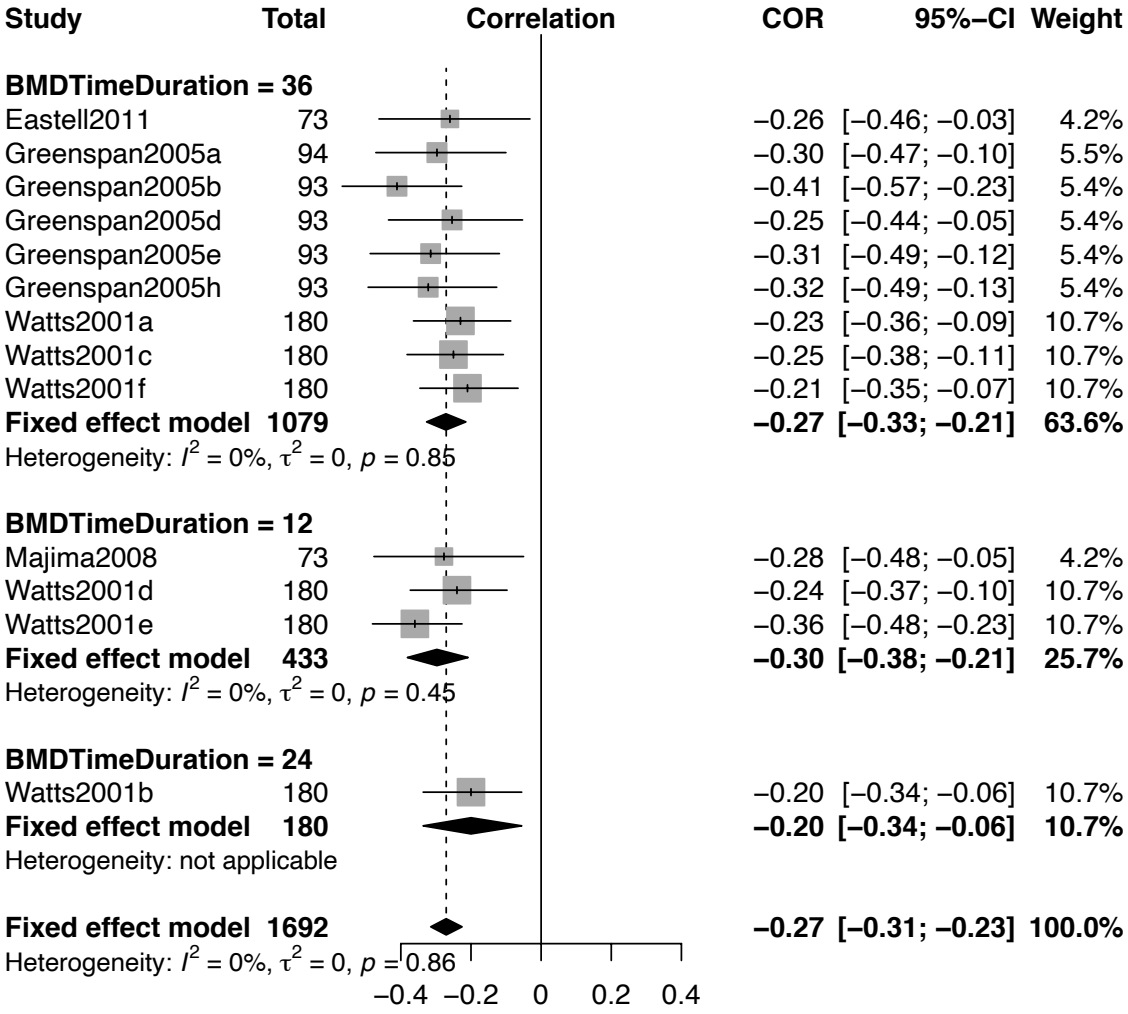


Figure S4.4B.4 Forests of subgroup analyses on the correlation between the changes in bone ALP and BMD by group of the time duration of BMD measurements.

S4.4C Forests of subgroup analyses on the correlation between the changes in osteocalcin and BMD

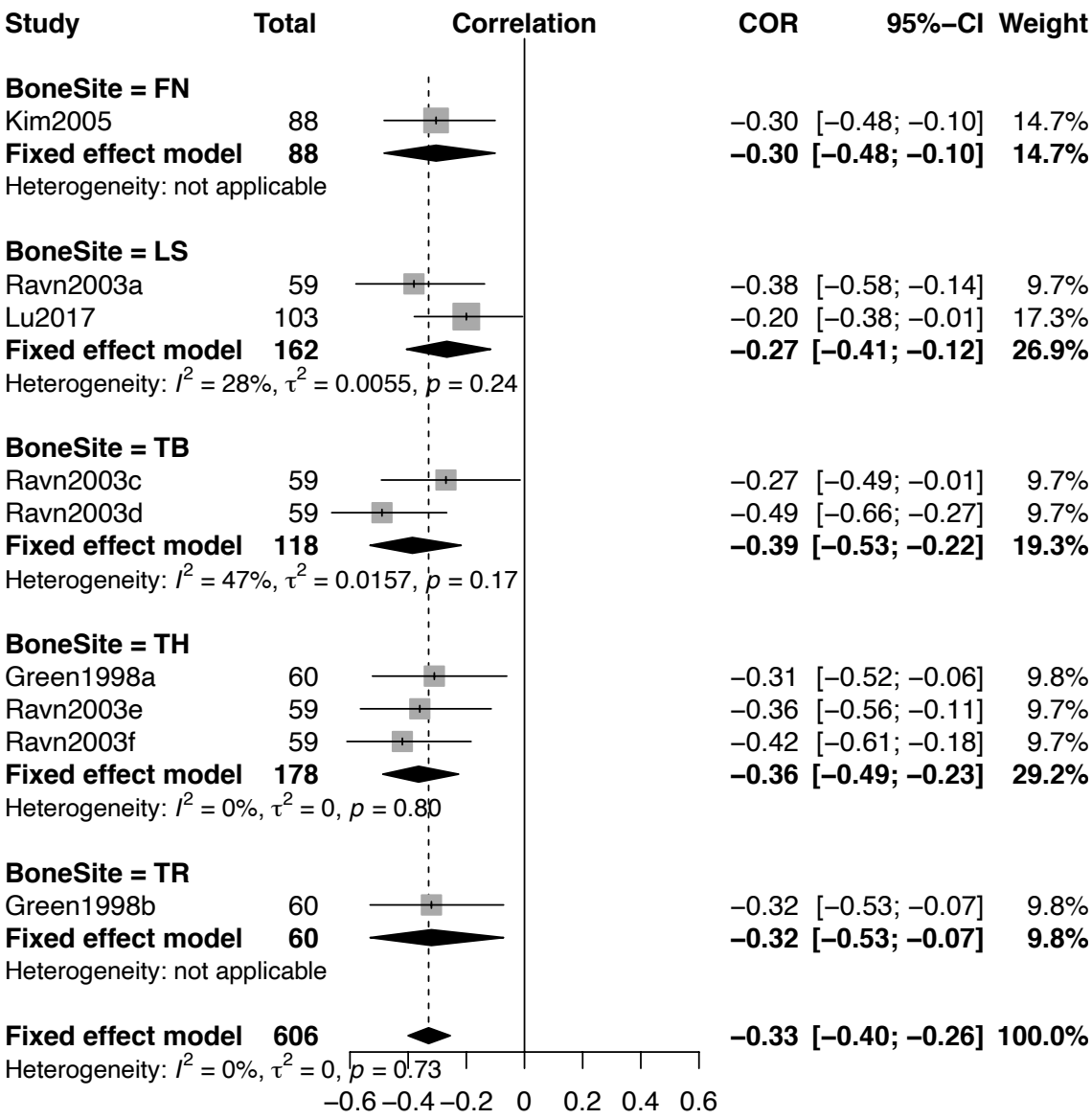


Figure S4.4C.1 Forests of subgroup analyses on the correlation between the changes in osteocalcin and BMD by group of bone sites. FN femoral neck, LS lumbar spine, TB total body, TH total hip, TR trochanter.

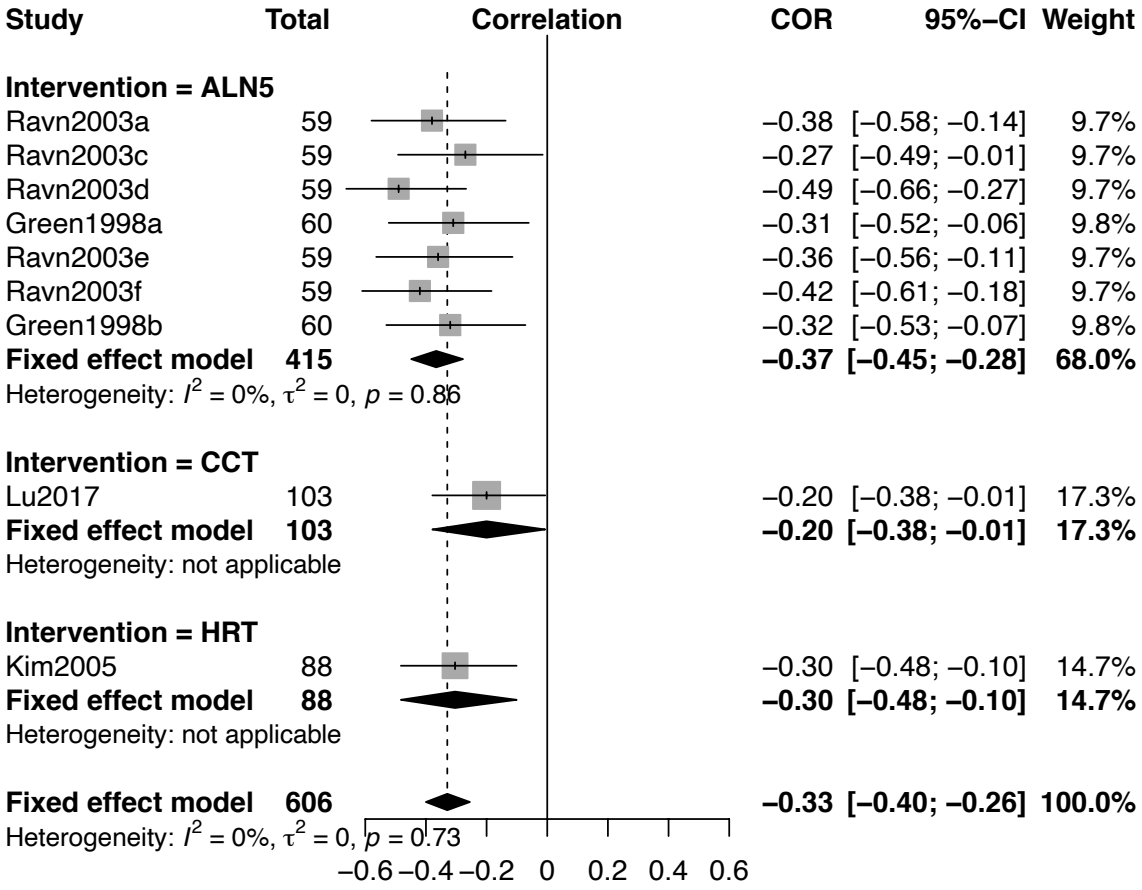


Figure S4.4C.2 Forests of subgroup analyses on the correlation between the changes in osteocalcin and BMD by group of intervention. ALN5 5 mg/d Alendronate, CCT Calcitonin, HRT Hormone replacement therapy.

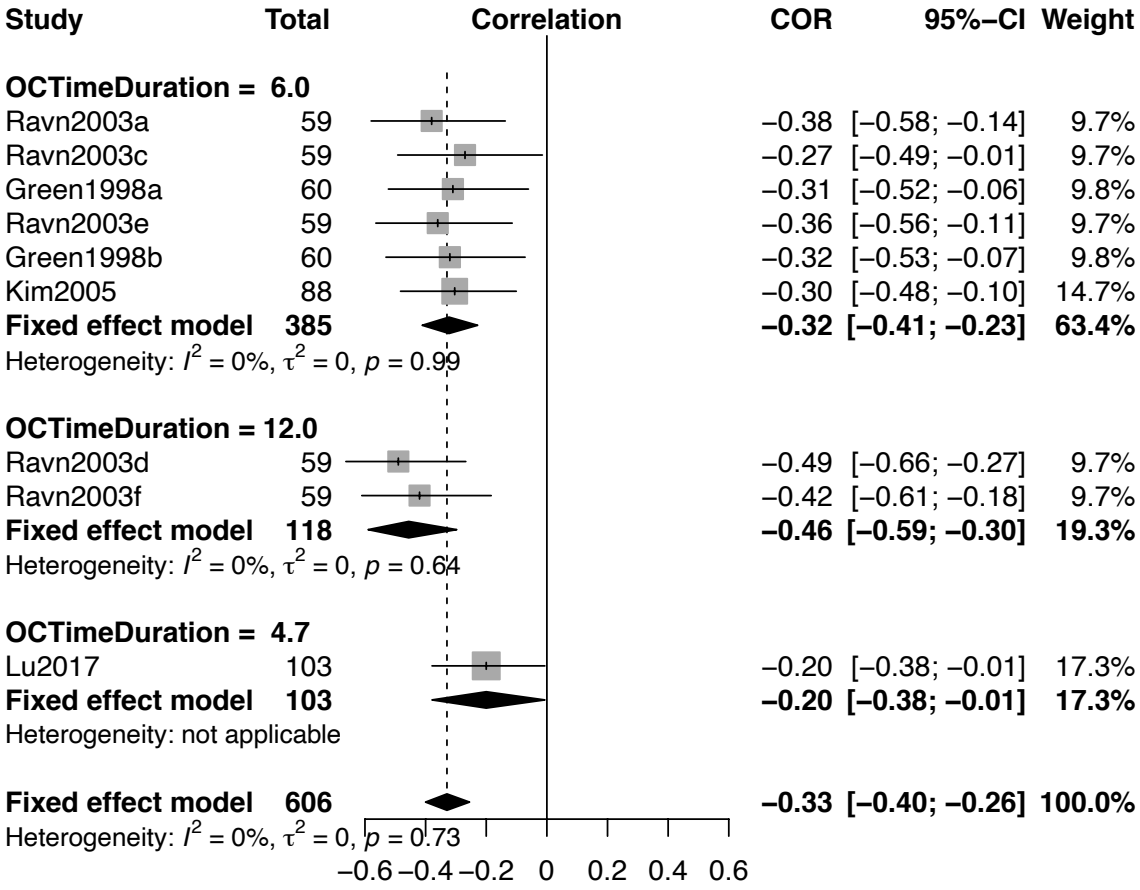


Figure S4.4C.3 Forests of subgroup analyses on the correlation between the changes in osteocalcin and BMD by group of the time duration of osteocalcin measurements.

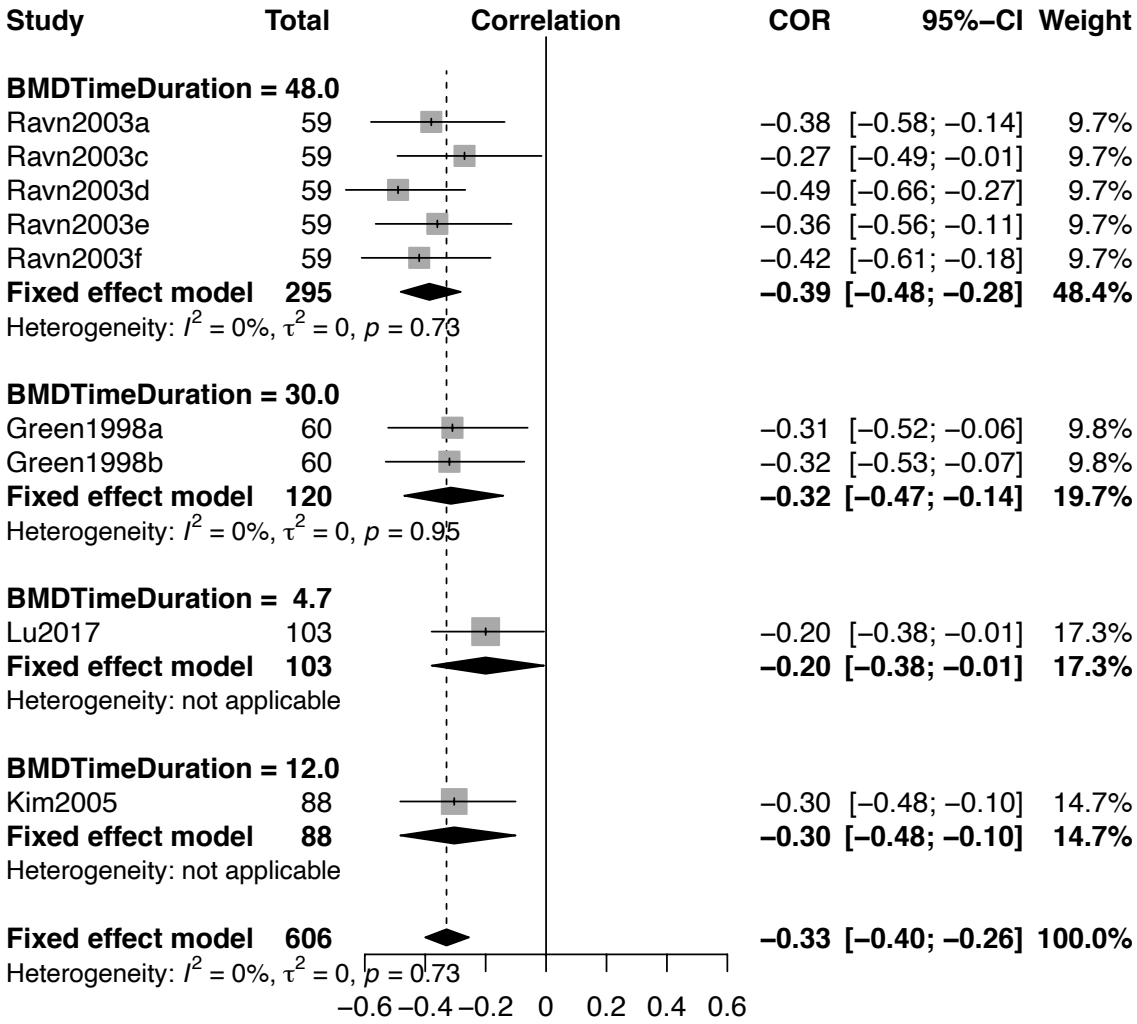


Figure S4.4C.4 Forests of subgroup analyses on the correlation between the changes in osteocalcin and BMD by group of the time duration of BMD measurements.

S4.4D Forests of subgroup analyses on the correlation between the changes in PINP and BMD

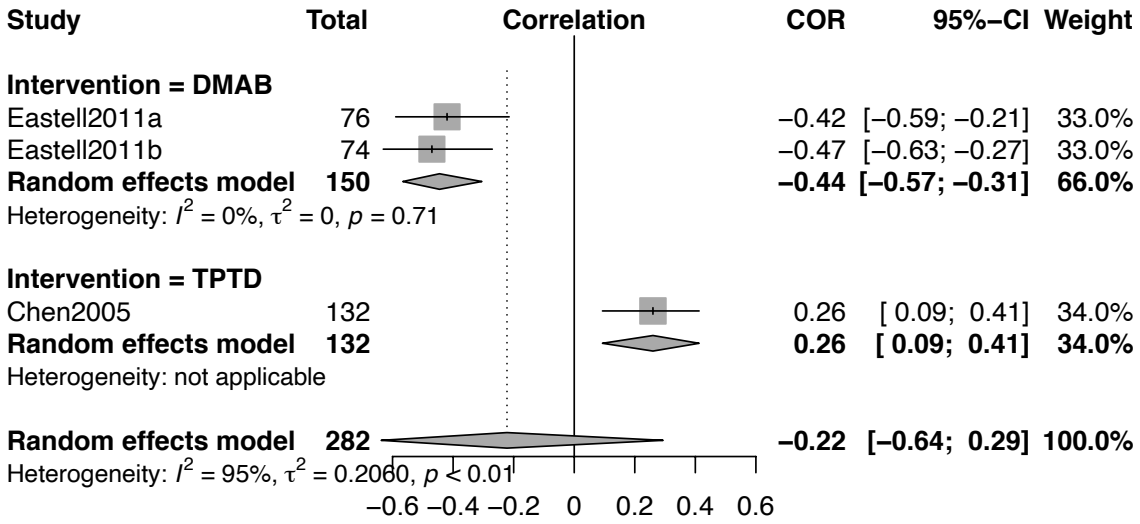


Figure S4.4D.1 Forests of subgroup analyses on the correlation between the changes in PINP and BMD by group of intervention. DMAB Denosumab, TPTD Teriparatide.

S4.4E Forests of subgroup analyses on the correlation between the changes in S-CTX and BMD

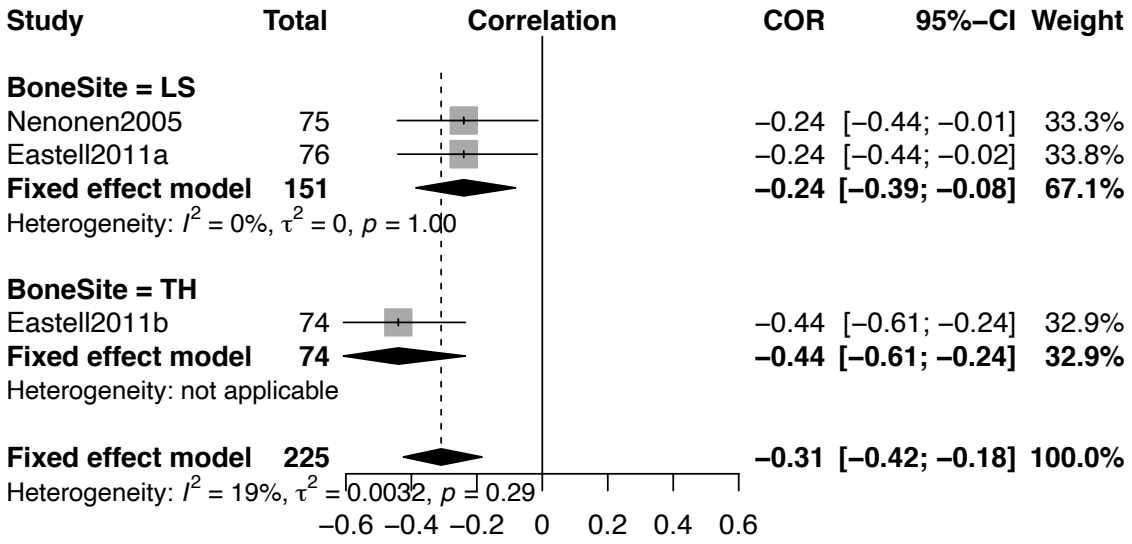


Figure S4.4E.1 Forests of subgroup analyses on the correlation between the changes in S-CTX and BMD by group of bone sites. FN femoral neck, LS lumbar spine, TH total hip.

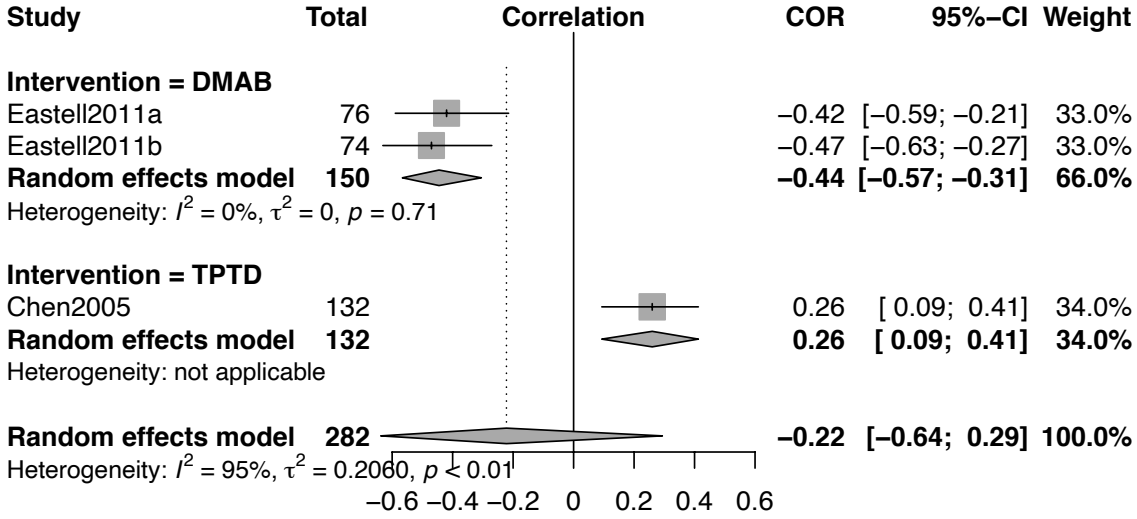


Figure S4.4E.2 Forests of subgroup analyses on the correlation between the changes in S-CTX and BMD by group of intervention. ALN5 5 mg/d Alendronate, DMAB Denosumab, TPTD Teriparatide.

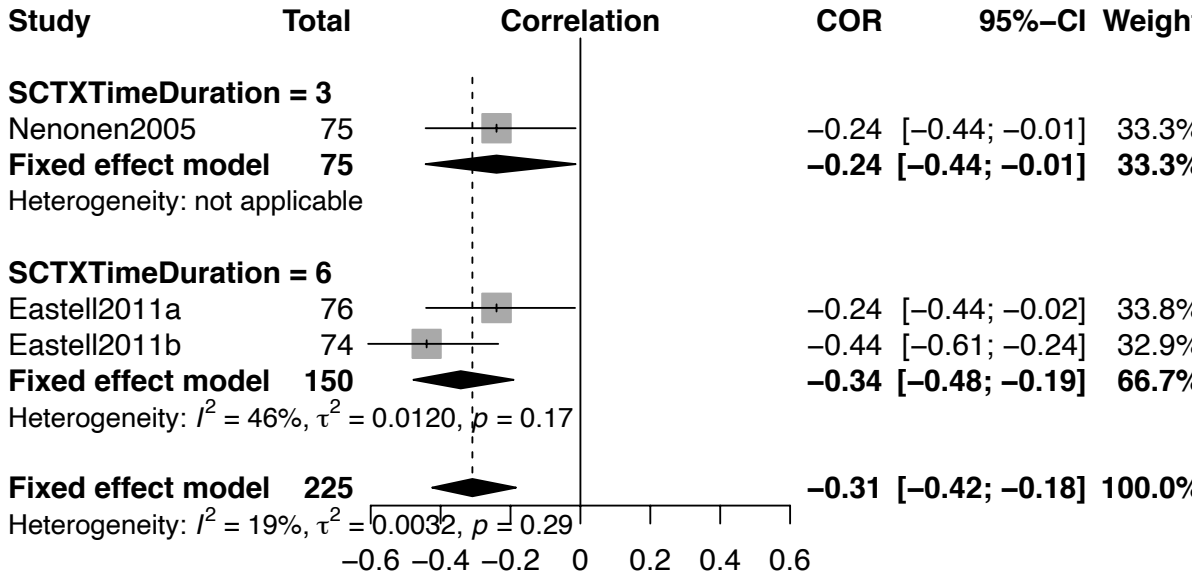


Figure S4.4E.3 Forests of subgroup analyses on the correlation between the changes in S-CTX and BMD by group of the time duration of PINP measurements.

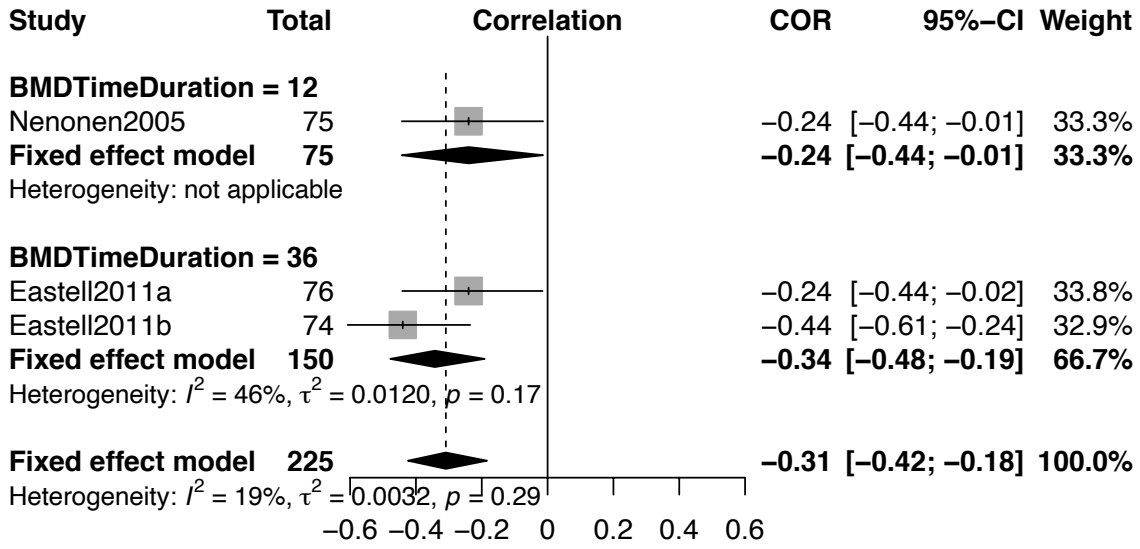


Figure S4.4E.4 Forests of subgroup analyses on the correlation between the changes in S-CTX and BMD by group of the time duration of BMD measurements.

S4.4F Forests of subgroup analyses on the correlation between the changes in U-NTX and BMD

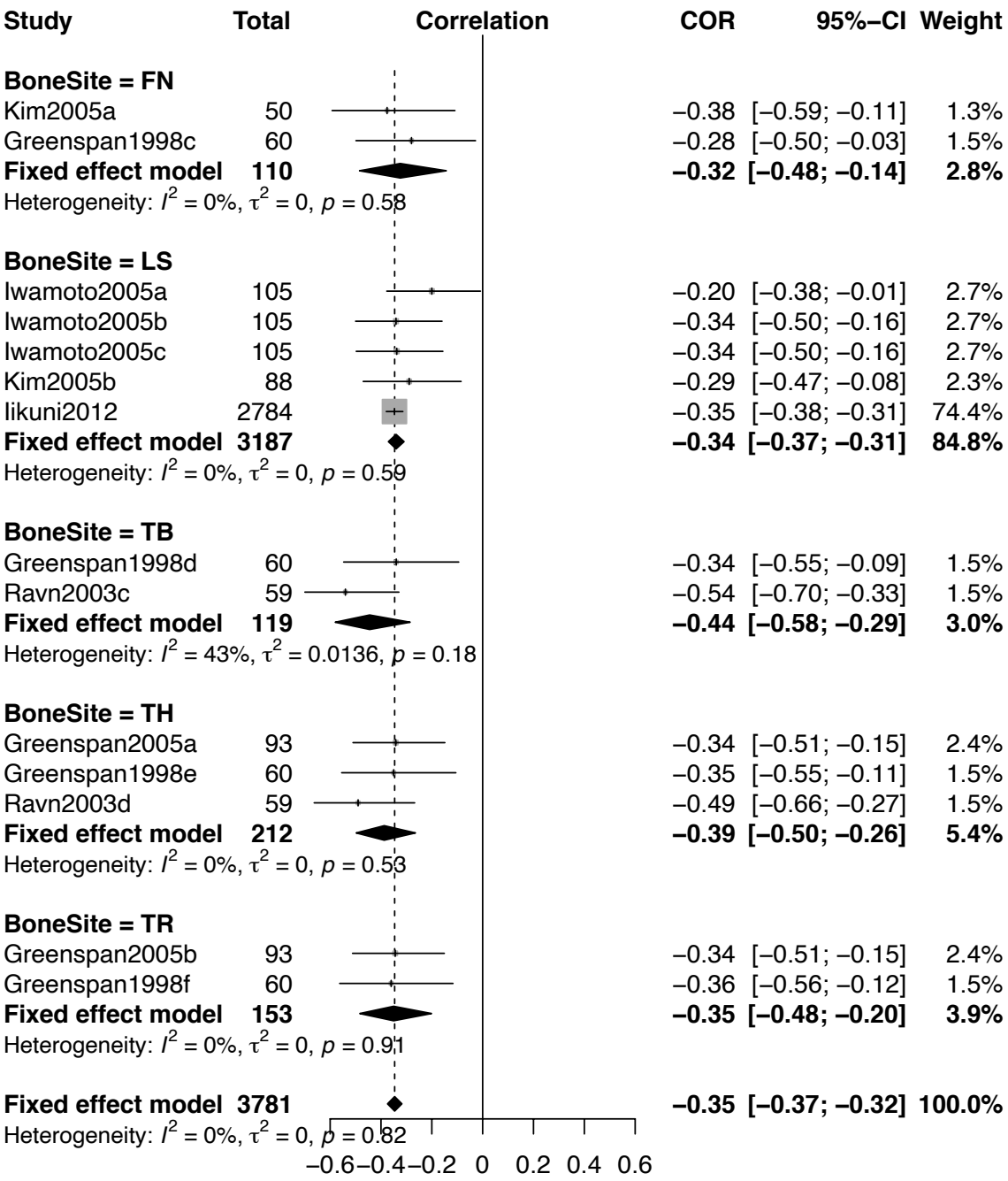


Figure S4.4F.1 Forests of subgroup analyses on the correlation between the changes in U-NTX and BMD by group of bone sites. FN femoral neck, LS lumbar spine, TB total body, TH total hip, TR trochanter.

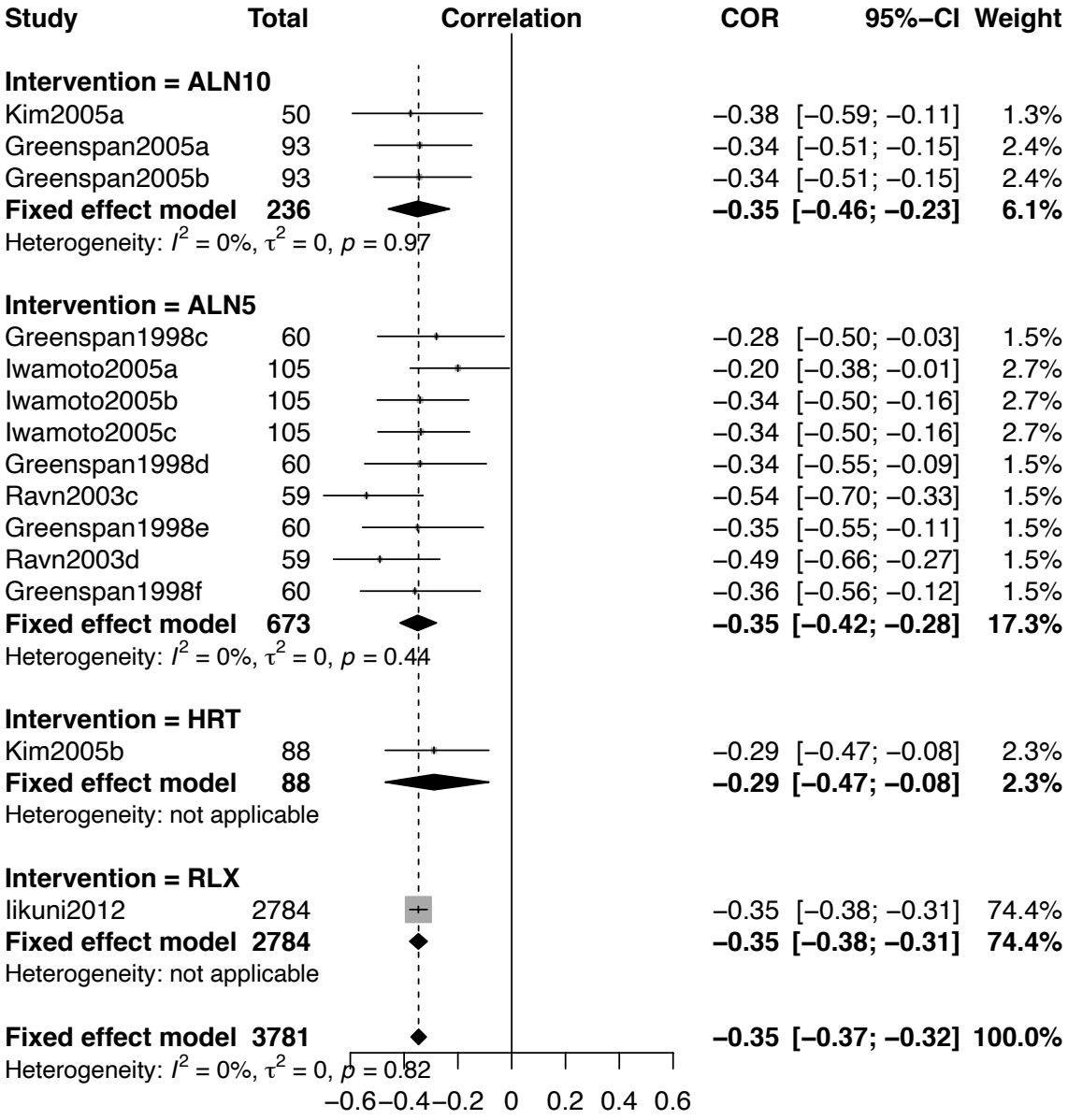


Figure S4.4F.2 Forests of subgroup analyses on the correlation between the changes in U-NTX and BMD by group of intervention. ALN10 10 mg/d Alendronate, ALN5 5 mg/d Alendronate, HRT Hormone replacement, RLX Raloxifene.

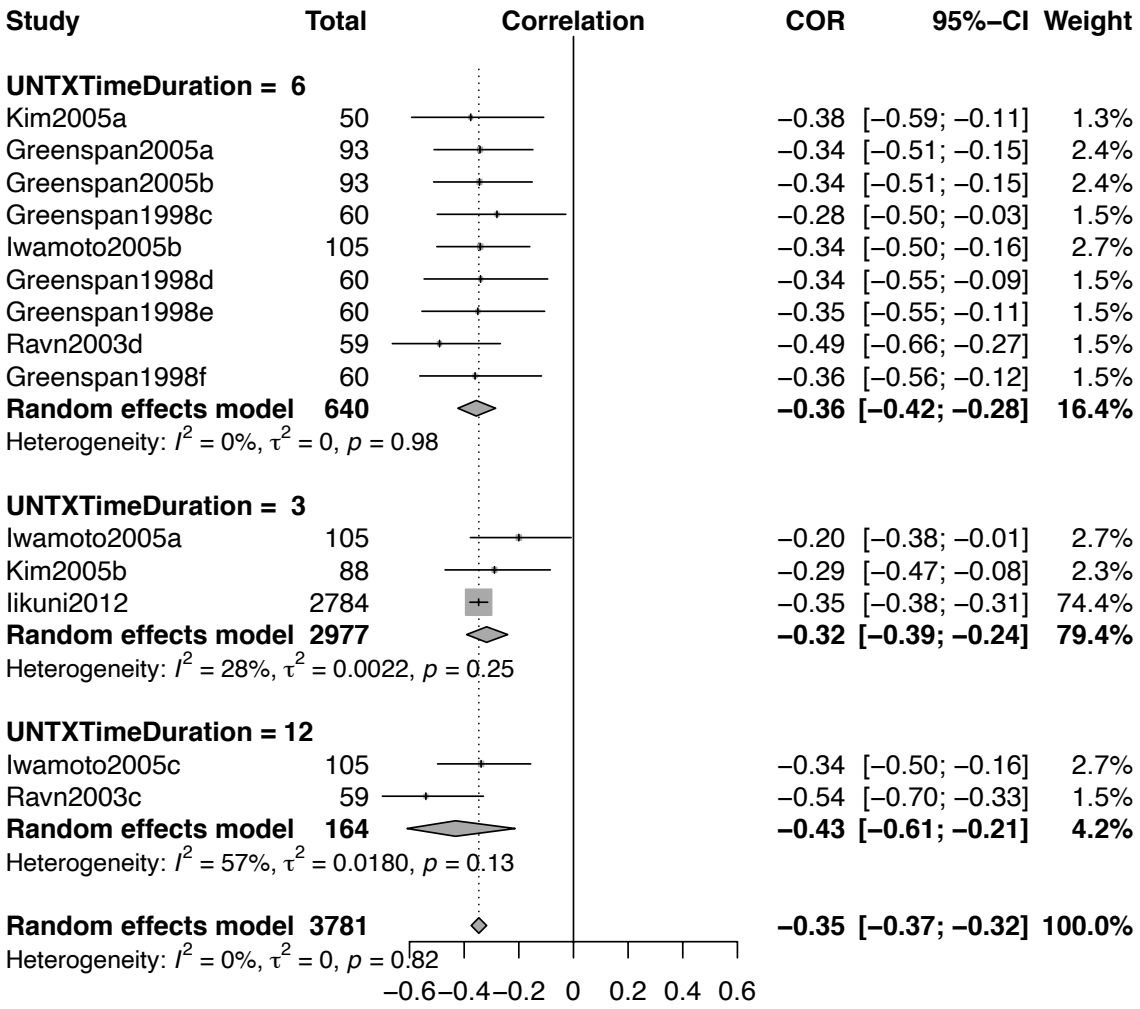


Figure S4.4F.3 Forests of subgroup analyses on the correlation between the changes in U-NTX and BMD by group of the time duration of U-NTX measurements.

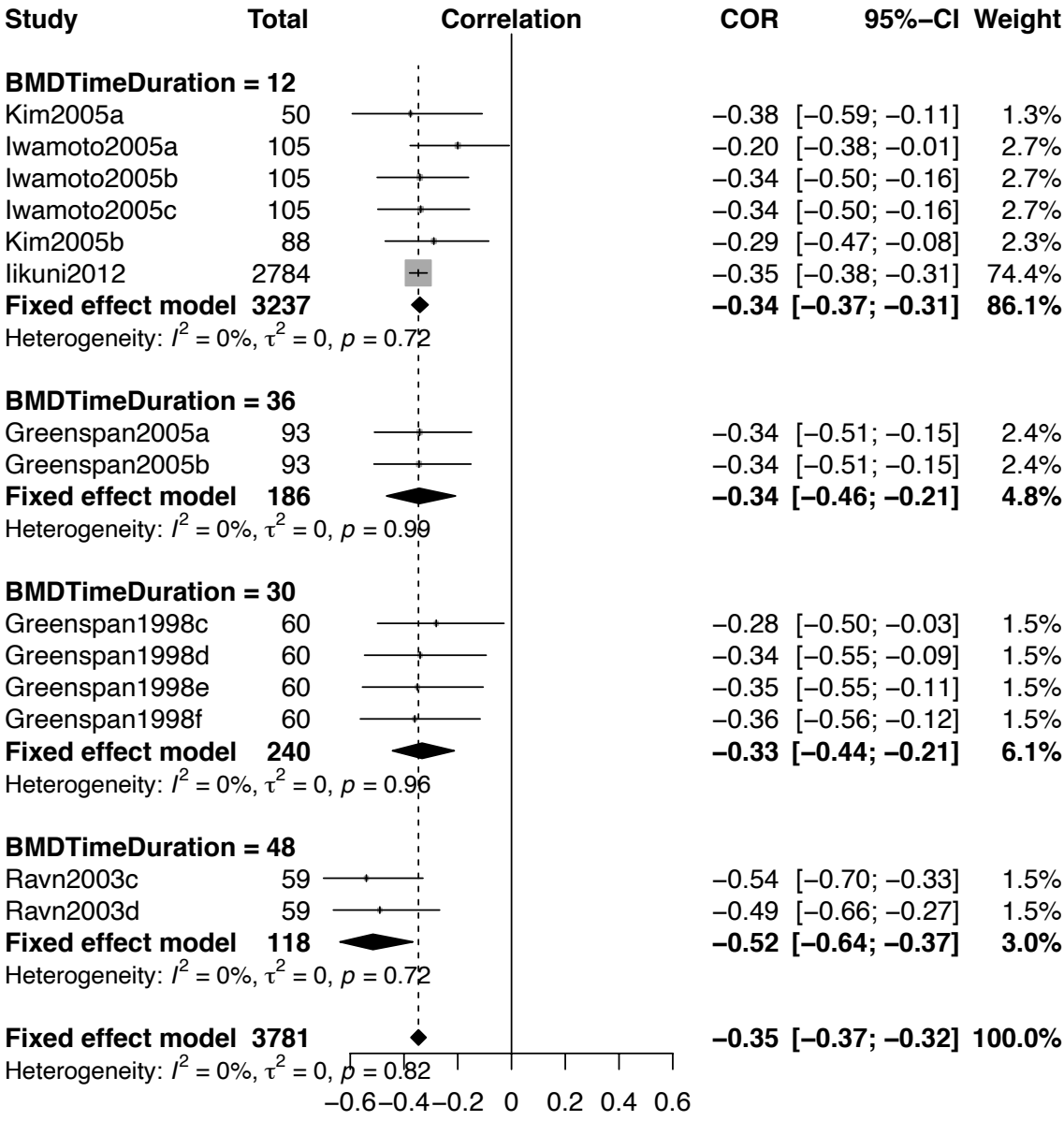


Figure S4.4F.4 Forests of subgroup analyses on the correlation between the changes in U-NTX and BMD by group of the time duration of BMD measurements.