Supplementary Material

Table 1. The association information of the selected SNPs with BMD of four skeletal sites

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| SNP  | EA | FA BMD | FN BMD | LS BMD | HL BMD |  |
| β(SE) | P value | β(SE) | P value | β(SE) | P value | β(SE) | P value |
| rs73186030 | T | -0.031 (0.022) | 0.180  | 0.002 (0.011) | 0.862  | -0.033 (0.012) | 0.009  | 0.006 (0.003) | 0.056  |
| rs4074995 | G | -0.024 (0.017)  | 0.171  | -0.023 (0.008) | 0.008  | -0.027 (0.010) | 0.006  | -0.004 (0.002) | 0.076  |
| rs6127099 | T | 0.013 (0.017) | 0.455  | -0.030 (0.009) | 4.90E-04 | -0.014 (0.010) | 0.171  | 0.007 (0.002) | 0.001  |
| rs219779 | G | -0.052 (0.017) | 0.004  | -0.022 (0.008) | 0.009  | -0.028 (0.010) | 0.004  | -0.010 (0.002) | 6.10E-05 |
| rs4443100 | G | -0.044 (0.018)  | 0.015  | -0.024 (0.010) | 0.017  | -0.011 (0.011) | 0.332  | -0.009 (0.002) | 8.30E-05 |

EA = effect allele; β = per allele effect on BMD; SE = standard error; P value = p-value for the genetic association.

Table 2. The association information of the selected SNPs with BMD of five age groups

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| SNP | EA | 15 or less years BMD | 15-30 years BMD | 30-45 years BMD | 45-60 years BMD | 60 or more years BMD |
| β(SE) | P value | β(SE) | P value | β(SE) | P value | β(SE) | P value | β(SE) | P value |
| rs73186030 | T | -0.008 (0.019) | 0.683  | 0.011 (0.034) | 0.747  | 0.002 (0.022) | 0.916  | -0.012 (0.016) | 0.460  | -0.025 (0.014) | 0.087  |
| rs4074995 | G | 0.010 (0.015) | 0.492  | 0.033 (0.025) | 0.189  | -0.009 (0.016) | 0.565  | -0.002 (0.012) | 0.876  | 0.005 (0.011) | 0.624  |
| rs6127099 | T | 0.006 (0.015) | 0.688  | -0.024 (0.027) | 0.366  | -0.029 (0.017) | 0.088  | -0.033 (0.013) | 0.009  | -0.010 (0.012) | 0.413  |
| rs219779 | G | 0.011 (0.015) | 0.445  | -0.050 (0.026) | 0.057  | -0.026 (0.017) | 0.127  | -0.030 (0.012) | 0.014  | -0.043 (0.011) | 9.33E-05 |
| rs4443100 | G | -0.025 (0.014) | 0.085  | -0.034 (0.025) | 0.175  | -0.052 (0.016) | 0.001  | -0.020 (0.012) | 0.089  | -0.028 (0.011) | 0.007  |

EA = effect allele; β = per allele effect on BMD; SE = standard error; P value = p-value for the genetic association.

Table 3. The association information of the selected SNPs with fracture risk of four skeletal sites

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| SNP  | EA | FA fracture | Femur fracture | LS fracture | Foot fracture |
| β(SE) | P value | β(SE) | P value | β(SE) | P value | β(SE) | P value |
| rs73186030 | T | -1.52E-04 (4.17E-04) | 0.714  | -6.46E-04 (2.53E-04) | 0.011  | 2.02E-04 (1.76E-04) | 0.249  | -1.72E-04 (1.54E-04) | 0.267  |
| rs4074995 | G | 1.83E-04 (3.14E-04) | 0.560  | -1.16E-04 (1.91E-04) | 0.543  | 1.37E-04 (1.32E-04) | 0.301  | -2.66E-05 (1.16E-04) | 0.819  |
| rs6127099 | T | 1.84E-04 (3.17E-04) | 0.561  | -5.17E-05 (1.92E-04) | 0.788  | -9.02E-05 (1.34E-04) | 0.500  | -2.70E-05 (1.17E-04) | 0.818  |
| rs219779 | G | -1.11E-04 (3.15E-04) | 0.725  | -5.88E-05 (1.91E-04) | 0.759  | 9.27E-05 (1.33E-04) | 0.485  | 1.15E-05 (1.17E-04) | 0.921  |
| rs4443100 | G | 4.41E-04 (3.03E-04) | 0.145  | -1.16E-04 (1.84E-04) | 0.530  | -4.14E-05 (1.28E-04) | 0.746  | 2.71E-04 (1.12E-04) | 0.016  |

EA = effect allele; β = per allele effect on BMD; SE = standard error; P value = p-value for the genetic association

Table 4. IVW analysis for genetic associations between serum PTH levels and fracture risk of four skeletal sites

|  |  |  |
| --- | --- | --- |
| Outcome | Effect (95% CI) | P value |
| FA fracture | 1.003 (0.996, 1.009) | 0.469  |
| Femur fracture | 0.997 (0.993, 1.001) | 0.187  |
| LS fracture | 1.001 (0.998, 1.003) | 0.730  |
| Foot fracture | 1.000 (0.998, 1.003) | 0.947  |

Effect = the combined causal effect of serum PTH levels with SD units of fracture risk; CI = confidence interval; P value = p-value of the causal estimate.

Table 5. Weighted median and MR-Egger analysis for genetic associations between serum PTH levels and BMD of four skeletal sites of bones

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Method | FA BMD | FN BMD | LS BMD | Heel BMD |
| Estimate (95% CI) | P value | Estimate (95% CI) | P value | Estimate (95% CI) | P value | Estimate (95% CI) | P value |
| Weighted median Estimate | -0.399(-0.914, 0.117) | 0.130 | -0.476(-0.684, -0.267) | 7.75E-06 | -0.441(-0.713, -0.169) | 0.002  | 0.005(-0.083, 0.092) | 0.919  |
| MR-Egger Estimate  | 1.059 (0.163, 1.956)  | 0.021 | -0.265 (-0.828, 0.297)  | 0.355 | 0.147 (-0.378, 0.671)  | 0.584 | 0.262 (-0.079, 0.603)  | 0.132 |
| MR-Egger Intercept | -0.068 (-0.106, -0.030) | 4.93E-04 | -0.010 (-0.035, 0.014) | 0.400 | -0.028 (-0.051, -0.006) | 0.014 | -0.013 (-0.027, 0.002) | 0.082 |

CI = confidence interval; P value = p-value of the causal estimate.

Table 6. Weighted median and MR-Egger analysis for genetic associations between serum PTH levels and BMD of five age groups

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Method | 15 or less years BMD | 15-30 years BMD | 30-45 years BMD | 45-60 years BMD | 60 or more years BMD |
| Estimate (95% CI) | P value | Estimate (95% CI) | P value | Estimate (95% CI) | P value | Estimate (95% CI) | P value | Estimate (95% CI) | P value |
| Weighted median Estimate | 0.134 (-0.234, 0.501) | 0.476  | -0.430 (-1.110, 0.249) | 0.215  | -0.433 (-0.846, -0.019) | 0.040  | -0.491 (-0.801, -0.181) | 0.002  | -0.365 (-0.692, -0.038) | 0.029  |
| MR-Egger Estimate  | 0.453(-0.316, 1.222) | 0.249  | -0.356 (-2.330, 1.618)  | 0.724  | 0.088 (-1.058, 1.234)  | 0.881  | -0.421 (-1.050, 0.208)  | 0.189  | 0.173 (-0.934, 1.279)  | 0.760  |
| MR-Egger Intercept | -0.018 (-0.050, 0.014) | 0.269  | -0.001 (-0.083, 0.081) | 0.979  | -0.028 (-0.077, 0.020) | 0.247  | -0.003 (-0.030, 0.023) | 0.799  | -0.026 (-0.072, 0.019) | 0.259  |

CI = confidence interval; P value = p-value of the causal estimate.

Table 7. Weighted median and MR-Egger analysis for genetic associations between serum PTH levels and fracture risk of four skeletal sites of bones

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Method | FA fracture | Femur fracture | LS fracture | Foot fracture |
| Estimate (95% CI) | P value | Estimate (95% CI) | P value | Estimate (95% CI) | P value | Estimate (95% CI) | P value |
| Weighted median Estimate | 0.002 (-0.006, 0.010) | 0.616  | -0.001 (-0.006, 0.004) | 0.634  | 1.60E-04 (-0.003, 0.003) | 0.925  | -3.22E-04 (-0.003, 0.003) | 0.824  |
| MR-Egger Estimate  | -0.003 (-0.019, 0.013)  | 0.742  | 0.003 (-0.008, 0.014)  | 0.585  | -0.003 (-0.009, 0.004)  | 0.437  | -0.004 (-0.012, 0.005)  | 0.393 |
| MR-Egger Intercept | 2.42E-04 (-4.38E-04, 0.001) | 0.485  | -2.76E-04 (-0.001, 2.01E-04) | 0.257  | 1.49E-04 (-1.38E-04, 4.36E-04) | 0.309  | 1.68E-04 (-1.73E-04, 0.001) | 0.335  |

CI = confidence interval; P value = p-value of the causal estimate.

Table 8. MR-Egger in leave-one-out analysis for genetic associations between serum PTH levels and BMD of FA and LS

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Method | Remove rs6127099 | Remove rs4074995 | Remove rs219779 | Remove rs4443100 | Remove rs73186030 |
| Estimate (95% CI) | P value | Estimate (95% CI) | P value | Estimate (95% CI) | P value | Estimate (95% CI) | P value | Estimate (95% CI) | P value |
| FA BMD |  |  |  |  |  |  |  |  |  |  |
| Estimate  | -0.411 (-2.844, 2.021) | 0.740 | 1.159 (0.163, 2.154) | 0.023 | 1.085 (0.188, 1.982) | 0.018 | 1.136 (-0.151, 2.424) | 0.084  | 1.085 (-0.008, 2.177) | 0.052  |
| Intercept | -0.026 (-0.101, 0.049) | 0.500 | -0.076 (-0.121, -0.030) | 0.001 | -0.062 (-0.101, -0.023) | 0.002 | -0.072 (-0.133, -0.012) | 0.019  | -0.070 (-0.118, -0.022) | 0.005  |
| LS BMD |  |  |  |  |  |  |  |  |  |  |
| Estimate  | -0.778 (-2.222, 0.666) | 0.291 | 0.113 (-0.519, 0.744) | 0.726 | 0.149 (-0.420, 0.719) | 0.608 | 0.403 (-0.206, 1.013) | 0.194 | 0.096 (-0.460, 0.652) | 0.734 |
| Intercept | -0.001 (-0.047, 0.045) | 0.961 | -0.026 (-0.055, 0.003) | 0.082 | -0.027 (-0.052, -0.002) | 0.037 | -0.043 (-0.071, -0.014) | 0.003 | -0.025 (-0.050, 2.12E-04) | 0.052 |

CI = confidence interval; P value = p-value of the causal estimate.