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.