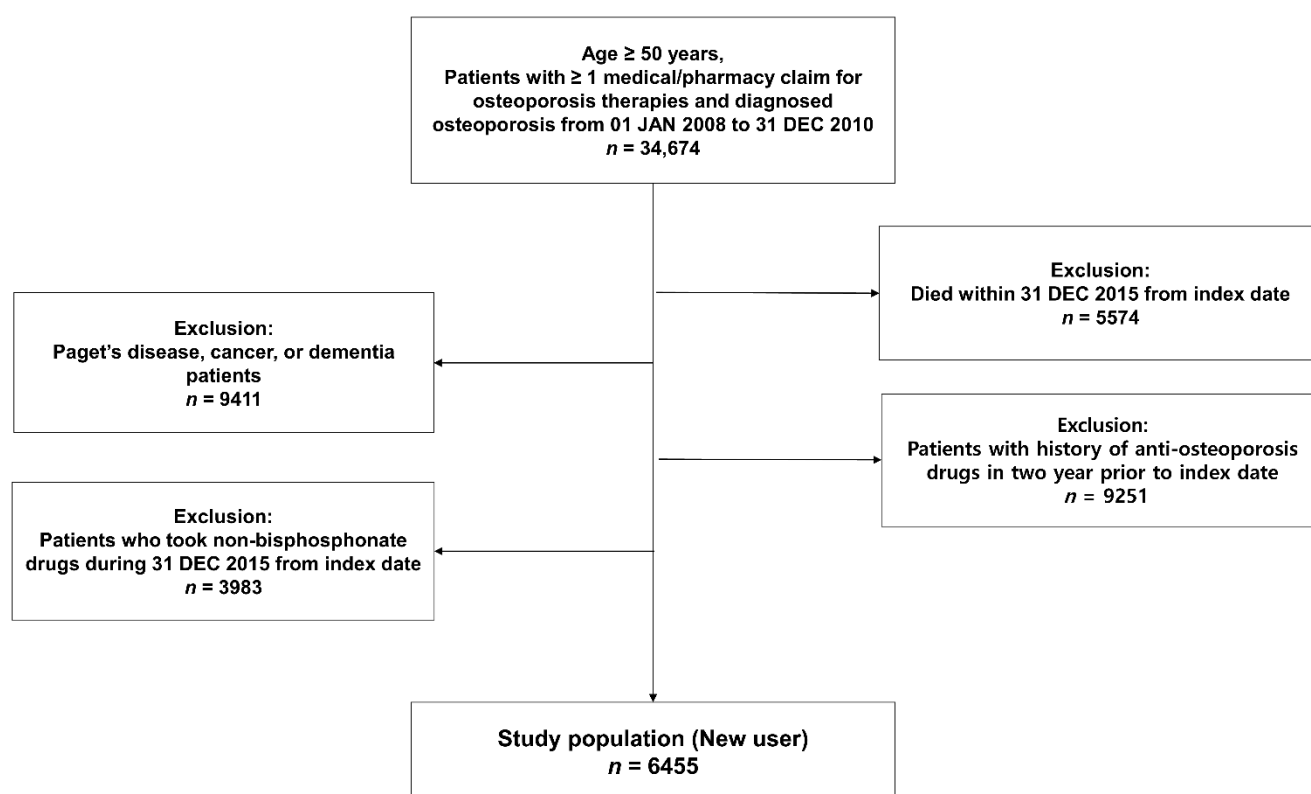


Supplementary Figure S1. Description of study period in extended version: We recruited patients diagnosed with osteoporosis from January 2008 to January 2011. Two years prior to index period (from January 2006 to January 2008) were used as wash-out period. We selected patients who were diagnosed with osteoporosis and prescribed bisphosphonates between 01 January 2008 and 31 December 2010. The first date of bisphosphonate prescription during this period was set as the index date. Only the patients whose data were available until 31 December 2015 were included.



Supplementary Figure S2. Study population of longer-version study: Initial enrollment and exclusion criteria. The first date of bisphosphonate prescription during this period was set as the index-date.

Supplementary Table S1. Types and codes according to dosing interval of bisphosphonate drug.

| Dosing Interval | ATC | HIRA General Name Code | Type |
|-----------------|---------|------------------------|----------------------------|
| Daily | M05BA01 | 147401ATB | Disodium etidronate 200 mg |

| | | | | |
|-----------|--|---------|-----------|---|
| | | M05BA04 | 228301ATB | Alendronate sodium 10 mg |
| | | M05BA04 | 228302ATB | Alendronate sodium 5 mg |
| | | M05BA07 | 442301ATB | Risedronate sodium 5 mg |
| | | M05BB03 | 468000ATE | Alendronate sodium 5 mg |
| | | | | Calcitriol 0.5µg |
| Weekly | | M05BA04 | 228303ATB | Alendronate sodium 91.37 mg |
| | | M05BA04 | 228305ATB | Alendronate sodium trihydrate 91.37 mg |
| | | M05BA07 | 442302ATB | Risedronate sodium 35 mg |
| | | M05BB03 | 481100ATB | Alendronate sodium 91.37 mg |
| | | | | Cholecalciferol concentrated 26.67 mg |
| | | M05BB03 | 500200ATB | Alendronate sodium 91.37 mg |
| | | | | Cholecalciferol concentrated 53.33 mg |
| | | M05BB07 | 511200ATB | Risedronate sodium 35 mg |
| | | | | Cholecalciferol 56 mg |
| Monthly | | M05BA07 | 442303ATB | Risedronate sodium 75 mg |
| | | M05BA06 | 480304ATB | Ibandronate sodium monohydrate 168.75 mg |
| | | | | Risedronate sodium 2.5hydrate 172.1 mg |
| | | M05BB07 | 518400ATB | Cholecalciferol 0.75 mg |
| | | | | Ibandronate sodium monohydrate 168.75 mg |
| | | M05BB | 523900ATB | Cholecalciferol concentrated granule 240 mg |
| | | M05BA07 | 442330ATB | Risedronate sodium 150 mg |
| | | M05BA07 | 500901ATB | Risedronate sodium 150 mg |
| 3 Monthly | | M05BA03 | 207930BIJ | Pamidronate Disodium 15 mg |
| | | M05BA06 | 480330BIJ | Ibandronate sodium monohydrate 3.375 mg |
| | | M05BA06 | 641201BIJ | Ibandronate sodium monohydrate 3.375 mg |
| | | M05BA03 | 207902BIJ | Pamidronate Disodium 15 mg |
| | | M05BA06 | 480303BIJ | Ibandronate sodium monohydrate 3.375 mg |
| Yearly | | M05BA08 | 420732BIJ | Zoledronic acid monohydrate 5.33 mg |
| | | M05BA08 | 420702BIJ | Zoledronic acid monohydrate 5.33 mg |

ATC: Anatomical Therapeutic Chemical Classification System; HIRA: Health Insurance and Review Assessment.

Supplementary Table S2. Patient demographic characteristics according to dosing interval of bisphosphonate drug.

| | | Total <i>n</i> (%) | Daily <i>n</i> (%) | Weekly <i>n</i> (%) | Monthly <i>n</i> (%) | 3 Monthly <i>n</i> (%) | Switch <i>n</i> (%) |
|-------------------|------------|--------------------|--------------------|---------------------|----------------------|------------------------|---------------------|
| | | 281,996 (100) | 4367 (1.55) | 123,405 (43.76) | 40,878 (14.5) | 68,575 (24.32) | 44,771 (15.88) |
| Age, y | 50–59 | 51,850 (100) | 745 (1.44) | 26,636 (51.37) | 7371 (14.22) | 10,202 (19.68) | 6896 (13.3) |
| | 60–69 | 100,048 (100) | 1367 (1.37) | 44,597 (44.58) | 15,317 (15.31) | 22,699 (22.69) | 16,068 (16.06) |
| | 70–79 | 90,796 (100) | 1407 (1.55) | 36,763 (40.49) | 12,775 (14.07) | 24,164 (26.61) | 15,687 (17.28) |
| | ≥80 | 39,302 (100) | 848 (2.16) | 15,409 (39.21) | 5415 (13.78) | 11,510 (29.29) | 6120 (15.57) |
| Gender | Men | 23,142 (100) | 813 (3.51) | 18,952 (81.89) | 420 (1.81) | 1242 (5.37) | 1715 (7.41) |
| | Women | 258,854 (100) | 3554 (1.37) | 104,453 (40.35) | 40,458 (15.63) | 67,333 (26.01) | 43,056 (16.63) |
| Area of residence | Metropolis | 110,198 (100) | 1806 (1.64) | 50,717 (46.02) | 16,239 (14.74%) | 24,738 (22.45) | 16,698 (15.15) |
| | Cities | 127,923 (100) | 1862 (1.46) | 55,974 (43.76) | 18,254 (14.27) | 32,067 (25.07) | 19,766 (15.45) |
| | Rural area | 43,871 (100) | 699 (1.59) | 16,711 (38.09) | 6385 (14.55) | 11,769 (26.83) | 8307 (18.94) |

| | | | | | | | |
|-------------------------|------------------------|---------------|-------------|-----------------|----------------|----------------|----------------|
| Insurance fee | 1–5q | 77,547 (100) | 1157 (1.49) | 33,490 (43.2) | 11,114 (14.33) | 18,934 (24.42) | 12,852 (16.57) |
| | 6–10q | 42,310 (100) | 637 (1.51) | 19,029 (44.98) | 6138 (14.51) | 10,052 (23.76) | 6454 (15.25) |
| | 11–15q | 60,400 (100) | 936 (1.55) | 26,647 (44.12) | 8846 (14.65) | 14,587 (24.15) | 9384 (15.54) |
| | 16–20q | 101,739 (100) | 1637 (1.61) | 44,239 (43.48) | 14,780 (14.53) | 25,002 (24.57) | 16,081 (15.81) |
| Fracture history | Yes | 30,303 (100) | 647 (2.14) | 11,940 (39.4) | 3610 (11.91) | 8701 (28.71) | 5405 (17.84) |
| | No | 251,693 (100) | 3720 (1.48) | 111,465 (44.29) | 37,268 (14.81) | 59,874 (23.79) | 39,366 (15.64) |
| Fracture | Forearm | 5571 (100) | 89 (1.6) | 2236 (40.14) | 796 (14.29) | 1548 (27.79) | 902 (16.19) |
| | Hip | 2532 (100) | 95 (3.75) | 1051 (41.51) | 328 (12.95) | 701 (27.69) | 357 (14.1) |
| | Humerus | 896 (100) | 18 (2.01) | 372 (41.52) | 102 (11.38) | 260 (29.02) | 144 (16.07) |
| | Spine | 13,908 (100) | 288 (2.07) | 5451 (39.19) | 1458 (10.48) | 4107 (29.53) | 2604 (18.72) |
| | Others | 2945 (100) | 59 (2) | 1090 (37.01) | 401 (13.62) | 802 (27.23) | 573 (19.46) |
| | Multi fractures | 4471 (100) | 98 (2.19) | 1740 (38.92) | 525 (11.74) | 1283 (28.7) | 825 (18.45) |
| Surgery history | Yes | 7865 (100) | 209 (2.66) | 3306 (42.03) | 1026 (13.05) | 2070 (26.32) | 1254 (15.94) |
| | No | 274,131 (100) | 4158 (1.52) | 120,099 (43.81) | 39,852 (14.54) | 66,505 (24.26) | 43,517 (15.87) |
| Surgery | Forearm | 2134 (100) | 29 (1.36) | 877 (41.1) | 293 (13.73) | 603 (28.26) | 332 (15.56) |
| | Hip | 2172 (100) | 89 (4.1) | 986 (45.4) | 276 (12.71) | 501 (23.07) | 320 (14.73) |
| | Humerus | 525 (100) | 11 (2.1) | 210 (40) | 75 (14.29) | 140 (26.67) | 89 (16.95) |
| | Spine | 2913 (100) | 73 (2.51) | 1194 (40.99) | 364 (12.5) | 793 (27.22) | 489 (16.79) |
| | Multi fractures | 121 (100) | 7 (5.79) | 39 (32.23) | 18 (14.88) | 33 (27.27) | 24 (19.83) |

Supplementary Table S3. MPR according to dosing interval of bisphosphonate drug and patients' demographic sub-groups.

| | | Total | | p-Value | Daily | Weekly | Monthly | 3 Monthly | Switch |
|---------------|--------------|----------------|----------------------|----------------|----------------------|----------------------|----------------------|----------------------|----------------------|
| | | N (%) # | Mean (95% CI) | | (n = 4367) | (n = 123,405) | (n = 40,878) | (n = 68,575) | (n = 44,771) |
| | | | | | Mean (95% CI) | Mean (95% CI) | Mean (95% CI) | Mean (95% CI) | Mean (95% CI) |
| Age | 50–59 | 51,850 (18.4) | 49.3 (49.0–49.6) | <0.001 * | 37.1 (36.8–37.4) | 41.3 (41.0–41.6) | 47.5 (47.2–47.8) | 56.7 (56.4–57.0) | 67.9 (67.7–68.1) |
| | 60–69 | 100,048 (35.5) | 52.7 (52.5–52.9) | | 39.8 (39.6–40.0) | 42.4 (42.2–42.6) | 51.3 (51.1–51.5) | 61.0 (60.8–61.2) | 68.1 (67.9–68.3) |
| | 70–79 | 90,796 (32.2) | 49.5 (49.3–49.7) | | 37.5 (37.3–37.7) | 37.2 (37.0–37.4) | 47.1 (46.9–47.3) | 57.3 (57.1–57.5) | 64.3 (64.1–64.5) |
| | ≥80 | 39,302 (13.9) | 42.6 (42.3–42.9) | | 32.1 (31.8–32.4) | 31.0 (30.7–31.3) | 39.3 (39.0–39.6) | 45.0 (44.7–45.3) | 60.1 (59.8–60.4) |
| Gender | Men | 23,142 (8.2) | 38.3 (37.9–38.7) | <0.001 ** | 36.2 (35.8–36.6) | 33.6 (33.2–34.0) | 18.9 (18.6–19.2) | 39.8 (39.4–40.2) | 62.0 (61.6–62.4) |
| | Women | 258,854 (91.8) | 50.7 (50.6–50.8) | | 37.3 (37.2–37.4) | 40.2 (40.1–40.3) | 48.0 (47.9–48.1) | 56.7 (56.6–56.8) | 65.8 (65.7–65.9) |

| | | | | | | | | | |
|-------------------------------|-----------------|----------------|------------------|-----------|------------------|------------------|------------------|------------------|------------------|
| Area of residence | Metropolis | 110,198 (39.1) | 50.4 (50.2–50.6) | | 38.3 (38.1–38.5) | 40.9 (40.7–41.1) | 49.4 (49.2–49.6) | 56.7 (56.5–56.9) | 66.6 (66.4–66.8) |
| | City | 127,927 (45.4) | 49.6 (49.4–49.8) | <0.001 * | 39.7 (39.5–39.9) | 39.0 (38.8–39.2) | 47.7 (47.5–47.9) | 56.5 (56.3–56.7) | 65.8 (65.6–66.0) |
| | Rural area | 43,871 (15.6) | 47.8 (47.5–48.1) | | 27.1 (26.8–27.4) | 34.4 (34.1–34.7) | 43.1 (42.8–43.4) | 55.4 (55.1–55.7) | 63.2 (62.9–63.5) |
| Insurance fee | 1–5q | 77,547 (27.5) | 49.6 (49.4–49.8) | | 36.3 (36.1–36.5) | 39.6 (39.4–39.8) | 47.2 (47.0–47.4) | 55.6 (55.4–55.8) | 65.0 (64.8–65.2) |
| | 6–10q | 42,310 (15.0) | 48.7 (48.4–49.0) | <0.001 * | 35.9 (35.6–36.2) | 38.4 (38.1–38.7) | 47.1 (46.8–47.4) | 55.6 (55.3–55.9) | 65.7 (65.4–66.0) |
| | 11–15q | 60,400 (21.4) | 49.5 (49.2–49.8) | | 36.8 (36.5–37.1) | 39.0 (38.7–39.3) | 47.8 (47.5–48.1) | 56.5 (56.2–56.8) | 66.2 (66.0–66.4) |
| | 16–20q | 101,739 (36.1) | 50.0 (49.8–50.2) | | 38.3 (38.1–38.5) | 39.2 (39.0–39.4) | 48.2 (48.0–48.4) | 57.2 (57.0–57.4) | 65.9 (65.7–66.1) |
| Fracture history [†] | Yes | 30,303 (10.7) | 51.0 (50.6–51.4) | <0.001 ** | 40.4 (40.0–40.8) | 39.9 (39.5–40.3) | 49.0 (48.6–49.4) | 53.8 (53.4–54.2) | 66.1 (65.8–66.4) |
| | No | 251,693 (89.3) | 49.4 (49.3–49.5) | | 36.5 (36.4–36.6) | 39.1 (39.0–39.2) | 47.6 (47.5–47.7) | 56.8 (56.7–56.9) | 65.6 (65.5–65.7) |
| Fracture [†] | Forearm | 5571 (18.4) | 49.7 (48.8–50.6) | <0.001 * | 47.1 (46.1–48.1) | 37.8 (36.9–38.7) | 48.2 (47.3–49.1) | 54.4 (53.6–55.2) | 65.9 (65.2–66.6) |
| | Hip | 2532 (8.4) | 50.6 (49.4–51.8) | | 48.0 (46.7–49.3) | 43.2 (41.9–44.5) | 49.2 (47.9–50.5) | 47.2 (46.0–48.4) | 66.8 (65.8–67.8) |
| | Humerus | 896 (3.0) | 50.5 (48.4–52.6) | | 40.2 (38.3–42.1) | 38.8 (36.7–40.9) | 48.9 (46.7–51.1) | 51.6 (49.6–53.6) | 65.7 (63.9–67.5) |
| | Spine | 13,908 (45.9) | 50.7 (50.1–51.3) | | 38.2 (37.6–38.8) | 39.0 (38.4–39.6) | 47.2 (46.6–47.8) | 53.6 (53.1–54.1) | 65.8 (65.3–66.3) |
| | Others | 2945 (9.7) | 55.0 (53.8–56.2) | | 38.4 (37.1–39.7) | 39.0 (37.8–40.2) | 47.2 (45.9–48.5) | 53.6 (52.4–54.8) | 65.8 (64.8–66.8) |
| | Multi fractures | 4471 (14.8) | 51.7 (50.7–52.7) | | 34.8 (33.8–35.8) | 40.7 (39.7–41.7) | 48.8 (47.8–49.8) | 54.4 (53.5–55.3) | 67.1 (66.3–67.9) |
| Surgery history [†] | Yes | 7865 (2.8) | 50.8 (50.1–51.5) | 0.0016 ** | 41.1 (40.4–41.8) | 41.3 (40.6–42.0) | 48.8 (48.1–49.5) | 53.1 (52.4–53.8) | 67.3 (66.7–67.9) |
| | No | 274,131 (97.2) | 49.6 (49.5–49.7) | | 36.9 (36.8–37.0) | 39.1 (39.0–39.2) | 47.7 (47.6–47.8) | 56.5 (56.4–56.6) | 65.6 (65.5–65.7) |
| Surgery [†] | Forearm | 2134 (27.1) | 48.5 (47.1–49.9) | 0.0019 * | 35.3 (33.8–36.8) | 37.9 (36.5–39.3) | 47.4 (45.9–48.9) | 53.0 (51.6–54.4) | 64.1 (62.9–65.3) |
| | Hip | 2172 (27.6) | 51.3 (50.0–52.6) | | 46.2 (44.8–47.6) | 44.5 (43.1–45.9) | 49.1 (47.8–50.4) | 46.8 (45.5–48.1) | 69.5 (68.4–70.6) |
| | Humerus | 525 (6.7) | 51.4 (48.6–54.2) | | 41.4 (38.8–44.0) | 39.3 (36.5–42.1) | 47.4 (44.5–50.3) | 53.9 (51.3–56.5) | 69.0 (66.7–71.3) |
| | Spine | 2913 (37) | 51.8 (50.6–53.0) | | 37.7 (36.5–38.9) | 41.3 (40.1–42.5) | 50.4 (49.2–51.6) | 56.6 (55.4–57.8) | 67.4 (66.4–68.4) |
| | Multi fractures | 121 (1.5) | 55.0 (49.0–61.0) | | 33.9 (28.7–39.1) | 45.7 (39.8–51.6) | 37.4 (32.1–42.7) | 61.9 (55.7–68.1) | 73.5 (68.3–78.7) |
| Total | | 281,996 (100) | 49.6 (49.5–49.7) | | 37.1 (37.0–37.2) | 39.2 (39.1–39.3) | 47.7 (47.6–47.8) | 56.4 (56.3–56.5) | 65.7 (65.6–65.8) |

* One-way ANOVA test. ** T-test. [†] Denominator used to calculate the percentage is fixed as the total number of patients. Percentages are over total in columns. [†] 'Surgery' and 'Fracture' occurred during wash-out and index period.