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INTRODUCTION

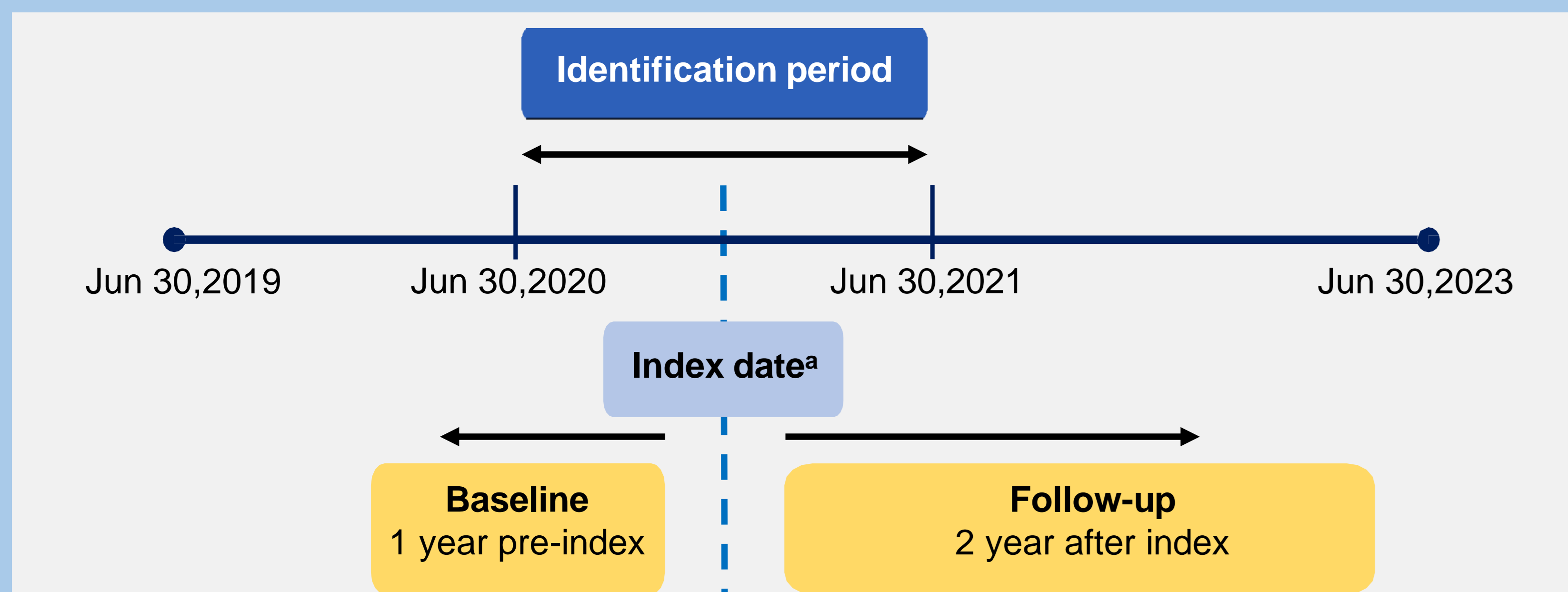
- Compared to patients with Osteoporosis (OP), those with OP at very high risk of fracture (VHRF) face worse treatment conditions and bear heavier economic burden. In the USA, only 16.8% of patients with OP at VHRF received anti-osteoporosis treatment.
- However, the fracture incidence and economic burden of OP at VHRF were still unknown in China. Better understanding of the real-world clinical characteristics and economic burden of OP at VHRF is important to improve the disease management in China.

OBJECTIVES

- To investigate the real-world fracture incidence and economic burden of female patients with Osteoporosis at very high risk of fracture in China.

METHODS

- Data were obtained from Tianjin Healthcare Big Data Super Platform (2019-2023), which had covered records of patient visits to 40 tertiary hospitals and 30 secondary hospitals in Tianjin, covering about 17 million patients as of 2023.
- Patients aged ≥ 50 years with diagnosis of OP (ICD-10 codes M80.x or M81.x) supplemented with Chinese descriptions were identified during the identification period (Jun 30, 2020 to Jun 30, 2021).
- The identification criteria for VHRF were based on the Guidelines for the Diagnosis and Treatment of Primary Osteoporosis in China (2022). The VHRF patients' index date was the earliest VHRF diagnosis date, with a 12-month baseline and ≥ 2 years of follow-up until study end, death, or loss to follow-up. OP patients who didn't have any diagnosis of VHRF during the selection period were classified as the high risk of fracture (HRF) group.



a) Index date: the date of the first VHRF diagnosis for VHRF group; the date of the first OP diagnosis for HRF group

Figure 1. Overview of the study period

- Fracture outcomes included the total number of fractures, fracture incidence, number of patients with fractures, mean number of fractures per patient with fractures, fracture frequency, distribution of fracture sites, and fracture-related complications during follow-up.
- OP-specific and all-cause healthcare resource utilization were estimated during the follow-up period.

RESULTS

1. Fracture incidence

- 44,493 OP patients were identified, among whom 11,433 (25.7%) were diagnosed with VHRF. The mean (SD) age was 66.6 (9.83) years in VHRF patients and 65.0 (9.18) years in the HRF group.
- In first year of follow-up, the fracture incidence among VHRF patients was 136.11 per 100 person years while the HRF group was 1.44 per 100 person years ($P < 0.01$). The proportion of ≥ 4 fracture counts of VHRF patients was significantly higher than HRF group (10.65% vs 5.00%, $P < 0.01$). Among surgical complications, subsequent fracture was the most common event in both follow-up years 1 and 2, and the proportion was higher in the VHRF group than in the HRF group (year 1: 43.40% vs 32.19%, $P < 0.001$; year 2: 44.78% vs 29.53%, $P < 0.001$).

Table 1. Fracture outcomes and fracture-related clinical complications during follow-up

| | Overall N=44,493 | VHRF N=11,433 | HRF N=33,060 | P value |
|---|---------------------|------------------|-----------------|---------|
| Follow-up year 1 | | | | |
| Total number of fractures | 16037 | 15562 | 475 | |
| Fracture incidence, per 100 person-years | 36.04 | 136.11 | 1.44 | <0.001 |
| Number of patients with fractures | 8318 (18.70%) | 7998 (69.96%) | 320 (0.97%) | <0.001 |
| Mean number of fractures per patient with fractures | 1.93 \pm 1.82 | 1.95 \pm 1.85 | 1.48 \pm 0.85 | <0.001 |
| Distribution of fracture frequency | | | | <0.001 |
| 1 | 4744 (57.03%) | 4527 (56.60%) | 217 (67.81%) | |
| 2 | 2062 (24.79%) | 1992 (24.91%) | 70 (21.88%) | |
| 3 | 644 (7.74%) | 627 (7.84%) | 17 (5.31%) | |
| ≥ 4 | 868 (10.44%) | 852 (10.65%) | 16 (5.00%) | |
| Medical complications | | | | |
| Constipation | 252 (3.03%) | 244 (3.05%) | 8 (2.50%) | 0.691 |
| Urinary tract infection | 330 (3.97%) | 320 (4.00%) | 10 (3.12%) | 0.521 |
| Stroke | 88 (1.06%) | 86 (1.08%) | 2 (0.62%) | 0.622 |
| Pneumonia | 452 (5.43%) | 438 (5.48%) | 14 (4.38%) | 0.468 |
| Electrolyte disturbances | 602 (7.24%) | 575 (7.19%) | 27 (8.44%) | 0.462 |
| Pressure ulcer | 43 (0.52%) | 40 (0.50%) | 3 (0.94%) | 0.501 |
| Surgical complications | | | | |
| Osteoarthritis | 678 (8.15%) | 656 (8.20%) | 22 (6.88%) | 0.455 |
| Subsequent fracture | 3574 (42.97%) | 3471 (43.40%) | 103 (32.19%) | <0.001 |
| Hematoma/Infection | 132 (1.59%) | 126 (1.58%) | 6 (1.88%) | 0.847 |
| Osteonecrosis of the femoral head | 61 (0.73%) | 57 (0.71%) | 4 (1.25%) | 0.441 |
| Follow-up year 2 | | | | |
| Total number of fractures | 2236 | 1643 | 593 | |
| Fracture incidence, per 100 person-years | 5.03 | 14.37 | 1.79 | <0.001 |
| Number of patients with fractures | 1073 (2.41%) | 670 (5.86%) | 403 (1.22%) | <0.001 |
| Mean number of fractures per patient with fractures | 2.08 \pm 2.09 | 2.45 \pm 2.47 | 1.47 \pm 0.97 | <0.001 |
| Distribution of fracture frequency | | | | <0.001 |
| 1 | 654 (60.95%) | 370 (55.22%) | 284 (70.47%) | |
| 2 | 200 (18.64%) | 115 (17.16%) | 85 (21.09%) | |
| 3 | 66 (6.15%) | 51 (7.61%) | 15 (3.72%) | |
| ≥ 4 | 153 (14.26%) | 134 (20.00%) | 19 (4.71%) | |
| Medical complications | | | | |
| Constipation | 31 (2.89%) | 20 (2.99%) | 11 (2.73%) | 0.957 |
| Urinary tract infection | 69 (6.43%) | 51 (7.61%) | 18 (4.47%) | 0.057 |
| Stroke | 17 (1.58%) | 13 (1.94%) | 4 (0.99%) | 0.341 |
| Pneumonia | 86 (8.01%) | 59 (8.81%) | 27 (6.70%) | 0.265 |
| Electrolyte disturbances | 118 (11.00%) | 77 (11.49%) | 41 (10.17%) | 0.570 |
| Pressure ulcer | 3 (0.28%) | 3 (0.45%) | 0 (0.00%) | 0.454 |
| Surgical complications | | | | |
| Osteoarthritis | 147 (13.70%) | 117 (17.46%) | 30 (7.44%) | <0.001 |
| Subsequent fracture | 419 (39.05%) | 300 (44.78%) | 119 (29.53%) | <0.001 |
| Hematoma/Infection | 27 (2.52%) | 20 (2.99%) | 7 (1.74%) | 0.288 |
| Osteonecrosis of the femoral head | 12 (1.12%) | 11 (1.64%) | 1 (0.25%) | 0.071 |

- vertebral fractures were the most common fracture site in both groups (year 1: 30.32% vs 29.47%, $P=0.693$; year 2: 35.91% vs 27.66%, $P<0.001$).

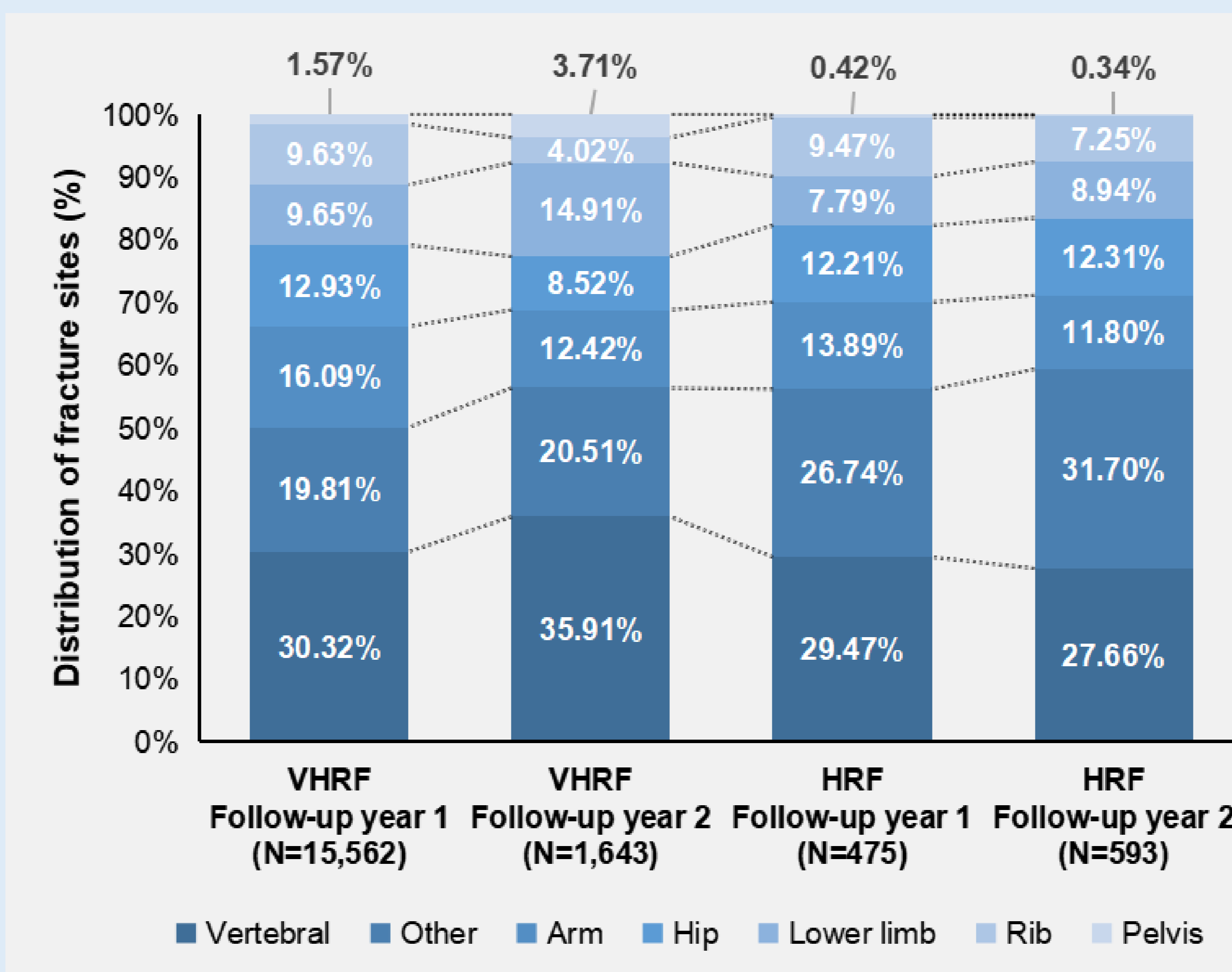


Figure 1. Distribution of fracture sites during follow-up

2. Economic burden

- In first year of follow-up, the annual OP-specific hospitalization visits, outpatient visits and total direct medical costs (mean \pm SD) between VHRF and HRF group were 0.42 \pm 0.77 vs 0.10 \pm 0.45 ($P < 0.01$), 2.79 \pm 4.63 vs 2.28 \pm 4.22 ($P < 0.01$) and ¥14,152 \pm 37,173 vs ¥3,362 \pm 15,592 ($P < 0.01$), respectively.

Table 2. OP-specific and all-cause healthcare resource utilization during follow-up

| | Overall N=44,493 | VHRF N=11,433 | HRF N=33,060 | P value |
|---|---------------------|-------------------|-------------------|---------|
| OP-specific | | | | |
| Follow-up year 1 | | | | |
| Total number of inpatient | 6370 (14.32%) | 3789 (33.14%) | 2581 (7.81%) | <0.001 |
| Annual average number of hospitalizations per person | 0.18 \pm 0.57 | 0.42 \pm 0.77 | 0.10 \pm 0.45 | <0.001 |
| Annual average number of hospital stays per person | 2.95 \pm 21.11 | 5.87 \pm 24.25 | 1.93 \pm 19.81 | <0.001 |
| Total number of outpatient | 32475 (72.99%) | 8892 (77.77%) | 23583 (71.33%) | <0.001 |
| Annual average number of outpatient visits per person | 2.41 \pm 4.33 | 2.79 \pm 4.63 | 2.28 \pm 4.22 | <0.001 |
| Annual per capita total direct medical costs | 6135 \pm 23620 | 14152 \pm 37173 | 3362 \pm 15592 | <0.001 |
| Annual average hospitalization cost per person | 4783 \pm 23431 | 12469 \pm 37123 | 2125 \pm 15323 | <0.001 |
| Annual average outpatient cost per person | 1352 \pm 3474 | 1683 \pm 4200 | 1237 \pm 3176 | <0.001 |
| Follow-up year 2 | | | | |
| Total number of inpatient | 1068 (2.40%) | 439 (3.84%) | 629 (1.90%) | <0.001 |
| Annual average number of hospitalizations per person | 0.03 \pm 0.24 | 0.05 \pm 0.33 | 0.02 \pm 0.20 | <0.001 |
| Annual average number of hospital stays per person | 0.52 \pm 7.49 | 0.78 \pm 10.82 | 0.43 \pm 5.92 | <0.001 |
| Total number of outpatient | 8741 (19.65%) | 2104 (18.40%) | 6637 (20.08%) | <0.001 |
| Annual average number of outpatient visits per person | 0.68 \pm 2.54 | 0.83 \pm 3.47 | 0.63 \pm 2.12 | 0.002 |
| Annual per capita total direct medical costs | 1079 \pm 9489 | 1661 \pm 14055 | 877 \pm 6947 | 0.269 |
| Annual average hospitalization cost per person | 643 \pm 9170 | 1085 \pm 14120 | 490 \pm 6644 | <0.001 |
| Annual average outpatient cost per person | 435 \pm 2179 | 577 \pm 2992 | 387 \pm 1813 | <0.001 |
| All-cause | | | | |
| Follow-up year 1 | | | | |
| Total number of inpatient | 10094 (22.69%) | 4398 (38.47%) | 5696 (17.23%) | <0.001 |
| Annual average number of hospitalizations per person | 0.33 \pm 0.83 | 0.54 \pm 0.97 | 0.25 \pm 0.77 | <0.001 |
| Annual average number of hospital stays per person | 4.95 \pm 24.92 | 7.99 \pm 29.92 | 3.90 \pm 22.84 | <0.001 |
| Total number of outpatient | 41124 (92.43%) | 10401 (90.97%) | 30723 (92.93%) | <0.001 |
| Annual average number of outpatient visits per person | 8.90 \pm 20.67 | 10.10 \pm 23.26 | 8.49 \pm 19.68 | 0.006 |
| Annual per capita total direct medical costs | 13581 \pm 36741 | 22206 \pm 51782 | 10598 \pm 29237 | <0.001 |
| Annual average hospitalization cost per person | 7907 \pm 31713 | 15854 \pm 47980 | 5159 \pm 22980 | <0.001 |
| Annual average outpatient cost per person | 5673 \pm 17540 | 6352 \pm 18652 | 5439 \pm 17133 | 0.318 |
| Follow-up year 2 | | | | |
| Total number of inpatient | 2467 (5.54%) | 898 (7.85%) | 1569 (4.75%) | <0.001 |
| Annual average number of hospitalizations per person | 0.08 \pm 0.46 | 0.12 \pm 0.52 | 0.07 \pm 0.43 | <0.001 |
| Annual average number of hospital stays per person | 1.31 \pm 12.07 | 1.79 \pm 15.82 | 1.14 \pm 10.46 | <0.001 |
| Total number of outpatient | 21979 (49.40%) | 5211 (45.58%) | 16768 (50.72%) | <0.001 |
| Annual average number of outpatient visits per person | 5.17 \pm 18.27 | 5.57 \pm 19.66 | 5.03 \pm 17.76 | <0.001 |
| Annual per capita total direct medical costs | 5109 \pm 22884 | 6260 \pm 29741 | 4710 \pm 19957 | <0.001 |
| Annual average hospitalization cost per person | 1640 \pm 15392 | 2572 \pm 23598 | 1318 \pm 11219 | <0.001 |
| Annual average outpatient cost per person | 3468 \pm 15584 | 3688 \pm 16395 | 3393 \pm 15294 | <0.001 |

CONCLUSION

- More than one-quarter of OP patients were identified as VHRF associated with much higher fracture incidence, multiple fracture rate and economic burden in China, leading to substantial clinical and economic burden to the Chinese health care system. Enhanced attention and targeted management are needed for these patients.

References

- DIFFENDERFER B W, WANG Y, PEARMAN L, et al. Real-World Management of Patients With Osteoporosis at Very High Risk of Fracture[J]. The Journal of the American Academy of Orthopaedic Surgeons, 2023, 31(6): e327-e335.
- SARAFRAZI N, WAMBOGO E A, SHEPHERD J A. Osteoporosis or Low Bone Mass in Older Adults: United States, 2017-2018[J]. NCHS data brief, 2021(405): 1-8.
- WANG L, YU W, YIN X, et al. Prevalence of Osteoporosis and Fracture in China: The China Osteoporosis Prevalence Study[J]. JAMA network open, 2021, 4(8): e2121106.
- CAMACHO P M, PETAK S M, BINKLEY N, et al. AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS/AMERICAN COLLEGE OF ENDOCRINOLOGY CLINICAL PRACTICE GUIDELINES FOR THE DIAGNOSIS AND TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS-2020 UPDATE[J/OL]. Endocrine Practice: Official Journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists, 2020, 26(Suppl 1): 1-46.