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Original article

Cost-effectiveness of opportunistic osteoporosis screening using artificial-intelligence assisted chest radiographs in Japan

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ABSTRACT

Objectives: Osteoporosis is often undiagnosed due to the shortcomings of conventional screening, resulting in missed chances for early treatment. Advances in artificial intelligence (AI), particularly deep learning applied to chest X-rays, offer a new opportunity for opportunistic screening. This study assesses the cost-effectiveness of this approach in Japanese women aged ≥ 50 years.

Methods: An economic model estimated the cost per quality-adjusted life year (QALY) gained (in 2024 Japanese Yen, ¥) for a strategy involving AI-assisted chest X-ray screening followed by treatment, compared to no screening. Patient trajectories were modeled using the AI system's diagnostic performance and aligned with the Japanese osteoporosis guidelines. Analyses were conducted for Japan overall, in Kure City (a high-fracture-incidence area), and in a lower-incidence scenario. Real-world medication persistence, the probabilities of dual-energy X-ray absorptiometry examination after screening detection, and treatment initiation rates were incorporated.

Results: Nationwide in Japan, the cost per QALY gained from opportunistic osteoporosis screening was estimated at ¥189,713 for women aged ≥ 50, substantially lower than the accepted cost-effectiveness threshold of ¥5 million. In Kure City, opportunistic screening was dominant (lower total costs for more QALYs). In the lower-incidence scenario, 25% below the national average, the cost per QALY was ¥1,055,095, remaining below the threshold. Results were robust across all age-specific populations and in sensitivity analyses.

Conclusions: Leveraging AI-assisted chest X-rays for incidental osteoporosis detection demonstrates strong economic viability for older Japanese women. This approach also proves to be a dominant strategy in areas with elevated fracture rates.

1. Introduction

Japan is one of the few countries that recommend universal screening for lung cancer [1]. Given the routine use of chest radiographs in such programs, there is growing interest in exploring their potential for additional applications, such as osteoporosis screening. While chest radiographs are currently not used for osteoporosis screening, they present a valuable opportunity to help address the growing burden of osteoporosis and fragility fractures. Recent advancements in artificial intelligence (AI), and deep learning models in particular, offer a promising avenue for opportunistic screening, by utilizing existing imaging resources and expanding access without requiring separate screening initiatives. Deep learning models have demonstrated the potential to assess bone health through radiographs, providing a scalable and potentially cost-effective alternative for opportunistic osteoporosis screening [2,3].

In Japan, population-based osteoporosis screening is currently offered only every five years to select age groups, with low participation rates, although comprehensive national data are limited. In contrast, nearly 50% of adults aged 40–69 reported participating in lung cancer screening in 2022, which included methods such as chest X-ray and sputum tests [4]. At the same time, chest X-rays are almost universally

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performed across the population through workplace health checkups, national cancer screening programs, and comprehensive medical examinations, as well as routinely prior to hospital admissions or surgery. The widespread use of chest radiographs in Japan creates a unique opportunity to expand screening efforts to include osteoporosis, a condition that remains significantly underdiagnosed despite its substantial public health impact. An estimated 13–15 million people in Japan, approximately 10% of the total population, are affected by osteoporosis [5], yet only 20% receive treatment [6]. Each year, about 200,000 hip fractures are reported [7], leading to an estimated annual healthcare expenditure of USD $2.99 billion [8]. Improving osteoporosis diagnosis is therefore critical to reducing this burden. Although dual-energy X-ray absorptiometry (DXA) is recommended by the Japanese guideline for assessing bone mineral density (BMD) [5], limited accessibility and associated cost remain barriers to widespread screening.

Evaluating the cost-effectiveness of alternative screening approaches is increasingly important in public health decision-making, as it helps determine suitability for large-scale adoption and supports the optimal use of healthcare resources. While similar cost-effectiveness studies of opportunistic AI-assisted osteoporosis screening using chest radiographs have recently been conducted in the United States and Germany [9,10], the Japanese context presents distinctive features that justify a separate analysis. Japan is experiencing the fastest demographic transition worldwide, with more than 29% of its population aged 65 years or older. This unprecedented pace of aging, combined with one of the highest incidences of hip fractures globally, not only results in a growing clinical burden but also has significant implications for cost-effectiveness, highlighting the economic importance of evaluating AI-assisted screening strategies in Japan. In addition, the Japanese healthcare system, characterized by universal National Health Insurance with nationally regulated drug prices and monitoring costs, differs substantially from Western systems. These structural differences influence adherence, and the economic value of osteoporosis treatment, potentially improving the cost-effectiveness of preventive interventions. Furthermore, economic evaluations in Japan follow distinct methodological guidelines, including a lower discount rate of 2% for both costs and health outcomes, which increases the relative weight of long-term benefits and favors early detection and treatment. Taken together, Japan's demographic profile, high fracture burden, unique healthcare and cost structure, and methodological framework uniquely shape both the clinical and economic consequences of opportunistic AI-assisted screening. Accordingly, this study evaluates the cost-effectiveness of using deep learning models applied to chest radiographs for osteoporosis screening and treatment in Japan, compared to no intervention. To provide granular and policy-relevant insights, we additionally conduct age-stratified analyses in 10-year groups, as well as regional analyses across both high-incidence areas such as Kure City in Hiroshima Prefecture and districts with lower fracture incidence, thereby capturing variation across demographic and epidemiologic contexts.

2. Methods

2.1. Economic model and interventions

In this study, we compared opportunistic AI-assisted detection of osteoporosis through deep learning analysis of chest radiographs, followed by treatment, to a scenario without screening and treatment. Our analysis does not propose chest radiographs as a primary screening tool or a replacement for DXA, but as an opportunistic adjunct using images obtained for other clinical reasons. Since these are not ordered for osteoporosis screening, comparison to "no screening" reflects real-world settings as formal programs are often absent, leaving many people undiagnosed. This allows evaluation of the added value of this pragmatic approach.

In the opportunistic AI-assisted screening strategy, all patients received AI-enhanced chest radiographs (Fig. 1). Patients were classified according to the tool's sensitivity and specificity. A portion of those suspected of osteoporosis proceeded to DXA scanning for confirmation. Those with a positive DXA result were eligible to begin medication, following real-world treatment initiation and persistence levels.

A dual-component model was developed with TreeAge Pro 2024 R1.0 software (TreeAge Pro Inc., Williamstown, MA): a decision tree to outline the screening pathways followed by a microsimulation Markov model to project fracture events at the hip, vertebrae, or non-hip non-vertebral (NHNV) sites and simulate costs and QALYs over a lifetime horizon, terminating at age of 105 years [11–13].

The study adhered to established standards for conducting and reporting economic evaluations, including guidelines from the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) and the International Osteoporosis Foundation (IOF) (ESCEO-IOF) [12], the 2022 Consolidated Health Economic Evaluation Reporting Standards (CHEERS)

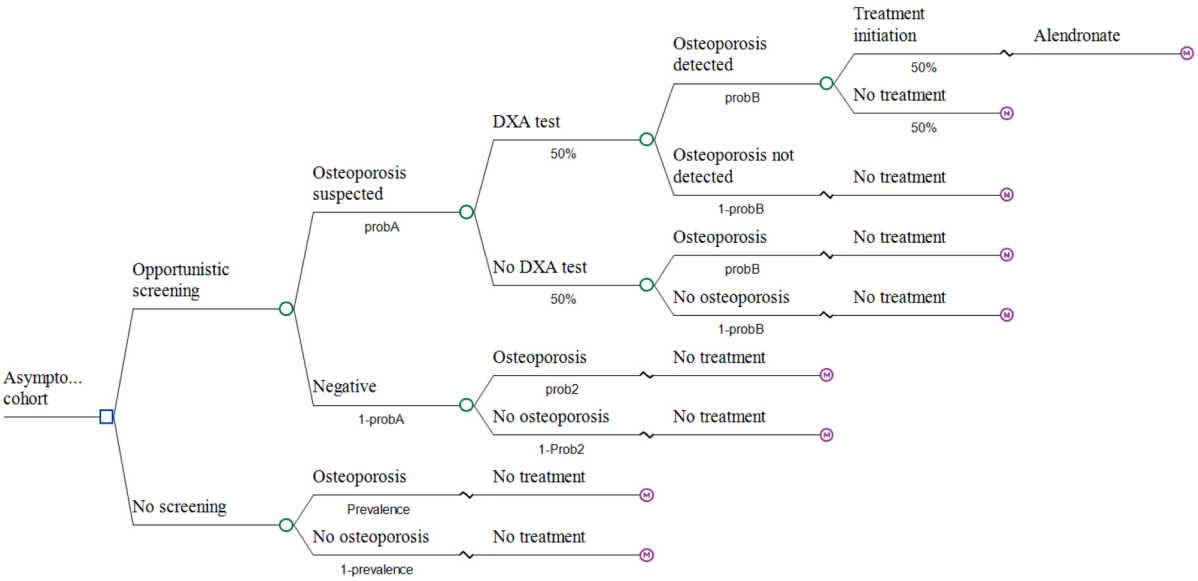

Fig. 1. Decision tree for opportunistic AI-assisted osteoporosis screening and treatment pathways in Japanese women aged 50 years and over. DXA, dual-energy X-ray absorptiometry.

statement [14] and the Japanese economic evaluation guideline [15]. The completed CHEERS 2022 checklist, together with the ESCEO-IOF osteoporosis checklists, are available in Appendix A.

To confirm the model's reliability, multiple validation steps were performed, including review and approval of the protocol by a Japanese clinical expert prior to analysis. Additionally, sensitivity analyses using alternative parameters and assumptions were conducted to verify that observed changes followed expected trends. Model parameters are summarized in Table 1.

2.2. Population and transitions probabilities

Analyses were conducted in Japanese women aged 50 years and over. The Japanese population estimates by age are sourced from Statistics of Japan via e-Stat, the official portal for Japanese Government Statistics (2023 data). This study focused on women due to the higher prevalence of osteoporosis and fracture incidence among older women, as well as the availability of robust, sex-specific epidemiological and cost data in Japan. The osteoporosis prevalence aligns with that of the general Japanese population. Specifically, osteoporosis prevalence (occurring in femoral neck or L2–L4) in Japanese women is derived from the fourth survey of the Research on Osteoarthritis/Osteoporosis Against Disability (ROAD) study (data from 2015 to 2016) and estimated at 13.2% (50 years), 22.8% (60 years), 31.1% (70 years) and 56.2% in those aged over 80 years [16]. Consistent with the 2015 Japanese guideline [5], osteoporosis was defined as a T-score ≤ -2.5 or a BMD $\leq$ 70% of the young adult mean (YAM), as measured by DXA.

In the base case, for overall Japan, the incidence of hip fractures is derived from Tamaki et al. [17], using data from the National Health Insurance Claim Database for the years 2012–2015, the average incidence over this period was calculated and utilized for analysis. Vertebral, and NHNV fracture rates for each age were determined using risk equations derived from a previous economic evaluation based on Japanese epidemiological survey data and curving fitting techniques [18]. In line with the same study, 30% of vertebral fractures were considered clinical and therefore included in the analysis. We also conducted analysis using data from the city of Kure, located in Hiroshima Prefecture, which has the advantage of having estimates of the incidence of hip and clinical vertebral fractures in a large population [19]. This Hiroshima Prefecture has been considered as one associated with high fracture incidence in Japan [7]. Finally, to explore generalizability, we conducted a scenario analysis assuming a lower-incidence setting, with fracture rates 25% below the national average.

The increased fracture risk in women with BMD T-score ≤ -2.5 was calculated using a previously validated method [20]. Additionally, the elevated risk of fractures due to a fracture was modeled using data from a large Swedish study. This study provided estimates of subsequent fracture risk based on the time elapsed since a fracture and the number of prior fractures [21]. An increased risk was assumed after a fracture occurred during the simulation, with the magnitude of risk elevation depending on the time since the initial fracture, as described by Soreskog et al. [22].

The most recent age specific mortality rate from the Japanese National Institute of Population and Social Security research were used as baseline mortality (year 2022). Consistent with previous economic analyses, the model included elevated mortality rates following hip and vertebral fractures [13,22,23], attributing 25% of the excess mortality to fracture events [24,25].

Table 1
Model parameters.

Parameter	Data	
Fracture incidence rate (per 100) – Japanese Population		
Hip	0.012 (50–54), 0.024 (55–59), 0.048 (60–64), 0.077 (65–69), 0.164 (70–74), 0.384 (75–79), 0.867 (80–84), 1.602 (85–89), 2.352 (90–94), 2.484 (95+)	
Vertebral	0.130 (50–54), 0.194 (55–59), 0.292 (60–64), 0.437 (65–69), 0.656 (70–74), 0.984 (75–79), 1.476 (80–84), 2.215 (85–89), 3.322 (90–94), 4.983 (95+)	
NHNV	0.198 (50–54), 0.250 (55–59), 0.304 (60–64), 0.359 (65–69), 0.415 (70–74), 0.470 (75–79), 0.524 (80–84), 0.578 (85–89), 0.630 (90–94), 0.681 (95+)	
Fracture incidence rate (per 100) – Kure City		
Hip	0.022 (50–54), 0.043 (55–59), 0.085 (60–64), 0.140 (65–69), 0.290 (70–74), 0.620 (75–79), 1.640 (80–84), 3.230 (85–89), 4.120 (90–94), 4.120 (95+)	
Vertebral	0.184 (50–54), 0.276 (55–59), 0.413 (60–64), 0.390 (65–69), 0.690 (70–74), 1.620 (75–79), 3.680 (80–84), 4.480 (85–89), 3.630 (90–94), 3.630 (95+)	
NHNV	0.354 (50–54), 0.448 (55–59), 0.544 (60–64), 0.657 (65–69), 0.735 (70–74), 0.758 (75–79), 0.991 (80–84), 1.165 (85–89), 1.103 (90–94), 1.129 (95+)	
Elevated relative risk associated with osteoporosis		
Hip	5.659 (50–59), 3.390 (60–69), 2.250 (70–79), 1.570 (80+)	
Vertebral	2.680 (50–59), 2.176 (60–69), 1.772 (70–79), 1.514 (80+)	
NHNV	2.250 (50–59), 1.902 (60–69), 1.610 (70–79), 1.416 (80+)	
Elevated risk of subsequent fractures following a fracture		
First fracture	2.1 (0–6M), 2.0 (7–12M), 1.9 (13–18M), 1.7 (19–24M), 1.6 (25–36M), 1.5 (37–48M), 1.5 (49M+)	
Second and more fracture	2.4 (0–6M), 2.1 (7–12M), 1.8 (13–18M), 1.7 (19–24M), 1.7 (25–36M), 1.5 (37–48M), 1.5 (49M+)	
Mortality excess [12,44]		
Hip (0–6M/7–12M/subs. yrs)	4.54 (3.56–5.88)/1.76 (1.43–2.16)/1.78 (1.33–2.39)	
Vertebral (0–6M/7–12M/subs. yrs)	4.54 (3.56–5.88)/1.76 (1.43–2.16)/1.78 (1.33–2.39)	
% attributable to Fx	25%	
Fracture costs (estimated in ¥2024)		
Hip	2,747,971	
Vertebral	460,991	
NHNV	514,104	
Utility values		
Baseline utility	0.928 (50–59Y), 0.899 (60–69Y), 0.853 (70–74Y), 0.771 (75–79Y), 0.769 (80–84Y), 0.684 (85+)	
After hip fracture	1st year RR 0.775 (0.719–0.831); subsequent years RR 0.855 (0.819–0.891)	
After vertebral fracture	1st year RR 0.848 (0.810–0.886); subsequent years RR 0.950 (0.938–0.963)	
After NHNV fracture	1st year RR 0.902 (0.878–0.927); subsequent years RR 1.00	
	ALN	ZOL
Persistence rate	56.6% (year 1), 46.3% (year 2), 30% (year 5)	70.3% (year 1), 51.7% (year 2), 30% (year 5)
Drug cost (¥ per week)	229	1307
Relative risk reduction of fractures by medications compared to placebo		
Hip	0.67 (0.48–0.96)	
Vertebral	0.45 (0.31–0.65)	
NHNV	0.81 (0.68–0.97)	
Sensitivity and specificity	86.16%; 74.19%	
Cost of AI-tool (¥)	1350	
% DXA after OP suspected	50%	
Treatment initiation after OP diagnosed	50%	

ALN, alendronate; M, months; NHNV, nonhip nonvertebral; OP, osteoporosis; SUBS, subsequent; RR, relative reduction; Y, year; ZOL, zoledronic acid.

2.3. Costs and quality of life impact of fractures

We followed the public healthcare payer's perspective, in accordance with Japan's economic evaluation guidelines. All costs were adjusted to year 2024 values in Japanese Yen (¥) using the official Japanese Consumer Price Index. Fracture-related costs included direct medical expenses. Cost estimates for hip fractures were based on the study by Mori et al. [8], which analyzed data from 113,493 Japanese women aged 60 and older within the nationwide health insurance claims database. For vertebral and NHNV fractures, estimates were derived from Taguchi et al. [26], using insurance claims data. These cost estimates are comparable to those used in a recent economic evaluation of osteoporosis in Japan [27]. Long-term care costs were considered for hip fractures, reflecting the proportion of patients requiring nursing home

admission. Among patients aged 75 years and older, 26.6% were assumed to enter institutional care, with an estimated cost of ¥4950 per day (based on 2020 values from Mori et al. [8]) until death. For individuals younger than 75 years, expert opinion and international literature suggest that 10% require nursing home care.

Health outcomes are quantified in QALYs, which capture the effects of fractures on both lifespan and quality of life. Calculating QALYs requires health utility values that range from 0 (equivalent to death) to 1 (representing perfect health). Health utilities for patients in the 'baseline' states were based on Japanese population norms for EQ-5D-5L scores [28]. Since this study did not provide specific estimates for the very elderly, we utilized the estimates from Nawata et al. for individuals aged 75 years and older [29]. The effects of fractures on utility is similar to a recent cost-effectiveness analysis in Japan [27], using health related quality of life data after fractures in Japan with the same lead author [30].

In cases of multiple fractures, only the highest incremental cost and the greatest impact on utility from a single fracture were considered, without incorporating additional costs or utility decrements from multiple fractures in the analysis.

2.4. Interventions

The sensitivity and specificity of AI-enhanced chest radiographs are estimated at 86.16% and 74.19%, respectively. These estimates are derived from the external test of Jang et al. [2] using a predefined threshold of 0.5, based on the Asan osteoporosis cohort dataset from South Korea with 1089 chest radiographs between 2010 and 2017. While absolute BMD levels vary among populations, multi-ethnic studies consistently demonstrate that the association between low BMD and fracture risk is stable across ethnic groups [31,32]. Because our AI model relies on radiograph-derived structural features rather than absolute BMD values, its applicability is expected to extend across diverse populations.

Based on Japanese expert opinion, it was assumed that 50% of patients suspected of having osteoporosis would undergo a DXA examination, and that 50% of those with a positive DXA result would initiate osteoporosis treatment. In line with the Japanese guideline for osteoporosis, alendronate therapy was assumed as base case treatment for a duration of maximum 5 years. Alendronate is among the most widely prescribed first-line therapies due to its established efficacy, safety profile, and cost-effectiveness, making it an appropriate reference treatment for modeling. To test the robustness of our results, we additionally conducted a sensitivity analysis using zoledronic acid as an alternative treatment.

The treatment effects are based on the latest meta-analysis of the National Institute for Health and Care Excellence (NICE) [33], which indicates comparable efficacy for alendronate and zoledronic acid. A linear reduction in treatment effects is assumed over a time period equivalent to the therapy duration, consistent with previous economic analyses of bisphosphonates [34,35]. The drug costs are derived from the Japanese Medical fee Schedule (2024) of the Japan Ministry of Health, Labor, and Welfare. The base case analysis uses the cost of generic alendronate, priced at ¥229 per week. Sensitivity analyses included the cost of the branded version, priced at ¥237.5 per week, as well as the lowest generic price (¥204.9). Medications for osteoporosis are typically associated with minimal or mild, transient side effects, which have a limited impact on both costs and quality of life. In our analysis, we conservatively included an additional cost of ¥500 during the first six months of alendronate therapy and ¥250 for each subsequent six-month period. These estimates are based on previous economic analyses and NICE appraisals, which accounted for occasional additional general practitioner consultations and the use of proton-pump inhibitors. No adverse events or associated costs were assumed for zoledronic acid therapy in line with previous economic evaluation.

Monitoring costs were based on clinical expert recommendations and included a physician visit every two months, along with a follow-up DXA measurement and blood test every six months. For patients receiving zoledronic acid, two physician visits per year were assumed, as well as DXA measurement and blood test every six months. The costs for physician visits (¥2910 for the initial visit and ¥750 for follow-up visits) along with blood tests (¥2770) and DXA measurements (¥4500), were derived from the Japanese Medical Fee Schedule (2024). The DXA costs include both the bone density scan and femoral bone imaging.

Real-world medication persistence was incorporated into the base case analysis. Persistence rates for alendronate were derived from a study by Nakatoh et al. [36], which analyzed continuation rates for osteoporosis treatments using medical insurance data from the National Database of Health Insurance Claims and Specific Health Checkups of Japan, covering the period from April 2012 to March 2019. The study reported persistence rates of 56.6% in the first year and 46.3% in the second year. For zoledronic acid, persistence was estimated at 70.3% over two years and 51.7% over three years, based on another study [37]. Additionally, clinical expert opinion was used to estimate persistence at 30% after five years, assuming a linear decline from the last available data point. Costs, treatment effectiveness, and offset periods of medications were adjusted proportionally to patient persistence.

In the base case, the cost of the AI-screening is assumed to be 30% of the cost of a DXA (ie, ¥1350).

2.5. Analyses

Based on 5,000,000 individual simulations, the model estimated healthcare costs, fracture events, life years, and QALYs for both opportunistic AI-assisted osteoporosis screening and no intervention. The main outcome was the incremental cost-effectiveness ratio (ICER), calculated as the difference in total costs between the screening strategy and no intervention (in 2024; ¥1 equals approximately €0.0061 and US $0.0068 as of May 2025), divided by the difference in their cumulative QALYs. The ICER is reported as cost per QALY gained. In Japan, an intervention with an ICER below ¥5 million is considered cost-effective [38]. In situations where the screening strategy is associated with lower total healthcare costs and higher QALY gained, it is considered as a dominant intervention.

Analyses were conducted for Japan nationwide, Kure City and a lower-incidence setting assuming fracture rates 25% below the national average. Furthermore, age–specific analyses in 10-year intervals were performed to provide more detailed, policy-relevant insights across different age cohorts. To further verify the reliability of the findings, various sensitivity analyses were performed. One-way sensitivity analyses involved varying individual parameters in both screening and no-screening scenarios. Screening-related inputs were adjusted to reflect uncertainty, including altering by ±50% the proportion of patients receiving DXA after osteoporosis detection, the prevalence of osteoporosis, and rates of treatment initiation. Alternative sensitivity and specificity figures derived from the internal test from Jang et al. [2] were also tested. Additional scenarios considered full medication adherence and a 50% decrease in non-persistence. Screening costs were varied from 10% to 50% of the cost of DXA. Non-screening parameters were also modified, including fracture-related costs (±25%), and fracture impact on health utilities (±25%). Other factors tested included discount rates (ranging from 0% to 5%), mortality rates after fractures (±25%), anti-fracture treatment efficacy (±25%), and drug pricing (±25%).

To assess the uncertainty across model variables, a probabilistic sensitivity analysis (PSA) was performed. In each of the 200 iterations, which included 250,000 microsimulations per iteration, random values were drawn for nearly all model variables based on their probability distributions: beta distributions for fracture risk and the impact of fractures on utilities; log-normal distributions for all increased risks, including excess mortality; and normal distributions for costs. The PSA results were reported on a cost-effectiveness plane and through a cost-effectiveness acceptability curve, showing the percentage of

simulations where opportunistic AI-assisted osteoporosis screening was cost-effective at various thresholds per QALY gained.

3. Results

3.1. Base-case analysis

Table 2 presents healthcare costs, fracture events, life years, QALYs, and the ICER (expressed in ¥ per QALY gained) for opportunistic AI-assisted osteoporosis screening followed by treatment, compared to no intervention, among Japanese women aged 50 and above. Results are shown for the national population, Kure City in Hiroshima Prefecture (high-incidence), and a lower-incidence scenario (25% below the national average).

Nationwide, per 1000 women screened, the incremental lifetime cost was ¥496,000. This reflected healthcare savings of ¥3,815,000, offset by treatment expenses of ¥4,311,000. Opportunistic AI-assisted screening prevented 3.9 fractures and resulted in a gain of 2.6 QALYs, resulting in an ICER of ¥189,713 per QALY gained, largely below the ¥5 million cost-effectiveness threshold, highlighting the strong economic value of opportunistic AI-assisted screening.

In Kure City, treatment costs of ¥4,324,000 were entirely offset by healthcare savings (¥9,407,000), leading to total net savings of ¥5,083,000. The screening strategy prevented 8.1 fractures and resulted in a gain of 3.2 QALYs, and was therefore dominant. In the lower-incidence scenario, the cost per QALY gained of opportunistic AI-assisted screening was estimated at ¥1,055,095 per QALY gained, also below the ¥5 million cost-effectiveness threshold.

Across all age-group sensitivity analyses, the cost per QALY gained remained below the ¥5 million Japanese cost-effectiveness threshold (see Fig. 2). Cost-effectiveness improved with increasing age and was generally dominant in individuals aged 70 years and older.

Table 2
(Incremental) lifetime costs, QALYs, fracture events, and ICER of opportunistic AI-assisted osteoporosis screening vs. -> vs no screening and treatment in Japanese women aged ≥ 50, including nationwide, Kure City (high-incidence), and a lower-incidence scenario (~25% below national average).

	Opportunistic AI-assisted osteoporosis screening	No screening and treatment	Incremental per women	Incremental per 1000 women
Nationwide				
Total costs	866,606	866,110	496	496,000
Healthcare costs	862,295	866,110	−3815	−3,815,000
Treatment costs	4311	0	+4311	+4,311,000
Fracture events	0.5817	0.5856	−0.0039	3.9
Life years	15.4982	15.4956	0.0026	2.6
QALY	9.5216	9.5189	0.0026	2.6
ICER of opportunistic AI-assisted screening (¥ per QALY)			**¥ 189,713**	
Kure city (High-incidence)				
Total costs	1,657,864	1,662,947	−5083	−5,083,000
Healthcare costs	1,653,541	1,662,947	−9406	−9,406,000
Treatment costs	4323	0	+4323	+4,323,000
Fracture events	1.1842	1.1922	−0.0080	8.0
Life years	15.2863	15.2837	0.0026	2.6
QALY	9.3279	9.3247	0.0032	3.2
ICER of opportunistic AI-assisted screening (¥ per QALY)			**Dominant (¥ -1,571,632)**	
Lower-incidence scenario (~25 % below national average)				
Total costs	648,411	646,140	2271	2,271,000
Healthcare costs	644,090	646,140	−2050	−2,050,000
Treatment costs	4321	0	+4321	+4,321,000
Fracture events	0.4314	0.4285	−0.0029	2.9
Life years	15.5563	15.5540	0.0023	2.3
QALY	9.5793	9.5772	0.0021	2.1
ICER of opportunistic AI-assisted screening (¥ per QALY)			**¥ 1,055,095**	

¥1 equals approximately €0.0061 and US$0.0068 (as of May 2025).
ICER, Incremental cost-effectiveness ratio; QALY, quality-adjusted life years.

3.2. Sensitivity analyses

Results from sensitivity analyses reinforced the economic value of opportunistic AI-assisted osteoporosis screening (Table 3). In all scenarios tested, the cost per QALY gained remained below ¥2,000,000—thus largely below the cost-effectiveness threshold—even under conservative assumptions, such as a 25% reduction in treatment efficacy, fracture costs, or fracture incidence. When zoledronic acid was used, cost-effectiveness also remained favorable, with an ICER of ¥1,260,699 per QALY gained.

Follow-up after screening also influenced cost-effectiveness. For example, increasing treatment initiation by 50%, improving DXA utilization after osteoporosis detection, or reducing medication non-persistence by 50% resulted in screening being a dominant strategy. Notably, variations in specificity and sensitivity based on internal test data had minimal impact on cost-effectiveness.

Figure 3 presents the cost-effectiveness acceptability curves, which confirm the cost-effectiveness of opportunistic AI-assisted osteoporosis screening. At a threshold of ¥5,000,000 per QALY gained, the probability of cost-effectiveness was 95% for Japan overall, 100% for Kure City and 87% for the lower-incidence scenario. The probabilities of dominance, represented by the proportion of simulations in which the screening strategy was cost-saving (ie, cost-effective at a threshold of ¥0 per QALY gained), were 35% for Japan, 92% for Kure City and 7% for the lower-incidence scenario.

4. Discussion

Deep learning models have recently demonstrated significant potential in assessing bone health through chest radiographs [2,3]. Given the costs associated with screening and potential treatment, it is crucial to evaluate the cost-effectiveness of this approach, as decision-makers increasingly rely on economic data to guide funding and coverage decisions. Our study suggests that opportunistic AI-assisted osteoporosis screening using chest radiographs enhanced with deep learning is highly

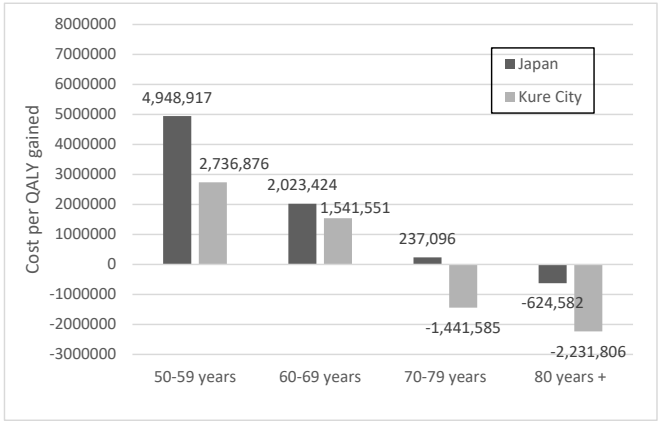

Fig. 2. Cost-effectiveness of opportunistic AI-assisted osteoporosis screening vs no screening in women from Japan and Kure City: age-group sensitivity analyses (¥ per QALY gained).
¥1 equals approximately €0.0061 and US$0.0068 (as of May 2025).
QALY, quality-adjusted life-years.

Table 3
Sensitivity analyses of cost-effectiveness (¥ per QALY gained) comparing opportunistic AI-assisted osteoporosis screening followed by treatment versus no screening and treatment in Japanese women aged ≥ 50.

	Cost per QALY gained	
Base case	¥ 189,713	
Treatment non-initiation +50%, −50%	¥ 948,751	Dominant
Prevalence osteoporosis +50%, −50%	Dominant	¥ 794,758
% DXA after osteoporosis detected +50%, −50%	¥ 16,719	¥ 680,119
Screening cost: 10%DXA, 50%DXA	Dominant	¥ 533,974
Specificity/Sensitivity Internal Test	¥ 141,148	
Full medication adherence	Dominant	
Medication non-persistence 50% lower	¥ 68,767	
Lowest generic price ALN	¥ 14,881	
Branded price ALN	¥ 249,430	
Zoledronic acid	¥ 1,260,699	
Treatment efficacy +25%, −25%	Dominant	¥ 1,664,392
Fracture incidence +25%, −25%	Dominant	¥ 1,055,095
Fracture costs +25%, −25%	Dominant	¥ 890,635
Discount rates 0%, 4%	Dominant	¥ 577,619
Fracture effects on mortality +25%, −25%	¥ 119,126	¥ 236,234
Treatment costs +25%, −25%	Dominant	¥ 383,432
Fracture effects on utilities +25%, −25%	¥ 142,196	¥ 367,539
ICUROS quality of life	¥ 182,142	

Dominant indicates higher QALY for lower costs. ¥1 equals approximately €0.0061 and US$0.0068 (as of May 2025).
DXA, dual-energy X-ray absorptiometry; NHNV, non-hip non-vertebral; QALY, quality-adjusted life-years; VHR, very-high risk.

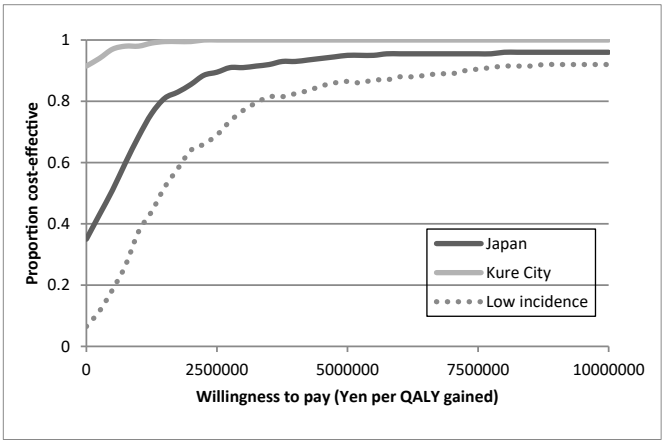

Fig. 3. Probabilistic sensitivity analysis of opportunistic AI-assisted osteoporosis screening: cost-effectiveness results in Japan, Kure City and the lower-incidence scenario. The cost-effectiveness acceptability curve depicts the likelihood that opportunistic osteoporosis screening is cost-effective across various cost-per-QALY thresholds, representing the percentage of simulations where screening outperforms no screening and treatment.
¥1 equals approximately €0.0061 and US$0.0068 (as of May 2025).
QALY, quality-adjusted life-years.

cost-effective for Japanese women aged 50 and older. The ICER was estimated at ¥189,713 per QALY gained, largely below Japan's cost-effectiveness threshold of ¥5 million. In the city of Kure from Hiroshima Prefecture, which is associated with a high fracture incidence, opportunistic AI-assisted osteoporosis screening was even dominant, meaning that the costs of screening and treatment were outweighed by the savings from prevented fractures. In a lower-incidence scenario, assuming fracture rates 25% below the national average, the cost per QALY increased to ¥1,055,095 but remained below the threshold, demonstrating that opportunistic AI-assisted screening remains economically attractive across regions with varying fracture risk. Taken together with age-stratified analyses, these findings highlight both the robustness and the generalizability of this strategy, providing nuanced evidence to inform national and regional policy decisions.

Notably, the base case analysis incorporated real-world estimates based on clinical expert opinion regarding screening follow-up. It is unexpected that all patients suspected of having osteoporosis would receive a DXA scan, and that all patients undergoing DXA would begin treatment. Despite uncertainties regarding these variables, the base case analysis was conservative, and sensitivity analyses with even more conservative assumptions did not alter the conclusions. To further enhance cost-effectiveness and ensure substantial economic benefits, efforts should focus on optimizing screening follow-up, treatment initiation, and medication adherence.

Our findings are particularly relevant within the Japanese healthcare system, which is characterized by universal coverage and relatively high fracture incidence among older women. Nevertheless, the potential applicability of opportunistic AI-assisted osteoporosis screening extends beyond Japan. Similar modeling studies conducted in the United States and Germany have demonstrated favorable cost-effectiveness of opportunistic screening strategies in their respective healthcare contexts [9,10]. These reports, together with our results, suggest that AI-based opportunistic screening may be a broadly promising approach across diverse systems, with even improved economic results in Japan. This may be partially attributed to Japan's aging population, reduced discount rates, and comparatively low drug costs. Our study highlights that an even older population, lower drug costs, and low discount rates magnify the potential benefit of opportunistic AI screening, even leading to dominance in some districts with high fracture risk. These findings underscore the importance of country-specific modeling rather than assuming generalizability across settings. The degree of benefit is likely to vary according to fracture incidence, baseline screening practices, healthcare costs, and reimbursement structures. In countries with lower fracture incidence or different screening infrastructures, the cost-effectiveness observed in our study may not be directly generalizable. Therefore, while our findings contribute to a growing international body of evidence, future research should assess implementation in other healthcare environments.

Another cost-effectiveness study found that opportunistic AI-assisted screening for osteoporotic vertebral compression fractures using existing radiographs was cost-effective from a societal perspective [39], reinforcing the growing evidence for the value of AI in osteoporosis screening. Given the growing global burden of osteoporosis in aging societies, particularly in super-aged countries such as Japan, South Korea, and several EU member states, the cost-effectiveness of AI-enhanced chest radiograph screening may have far-reaching implications beyond the Japanese context.The findings of this study are particularly relevant in the context of Japan, one of the few countries with a nationwide lung cancer screening program. This existing imaging infrastructure offers a unique opportunity to reach a broad segment of the population without requiring additional resources for dedicated osteoporosis screening. As such, it is essential for policymakers, hospital administrators, and clinicians to consider integrating opportunistic AI-assisted osteoporosis screening into routine chest radiograph assessments, especially in regions where osteoporosis remains underdiagnosed. The affordability and scalability of this approach make it a compelling strategy to improve public health outcomes and reduce the clinical and economic burden of osteoporotic fractures in aging populations. The evidence presented here can support policy efforts to secure reimbursement and funding for AI-based screening, ultimately improving accessibility and reducing long-term healthcare costs. Furthermore, AI-enhanced screening may contribute to reducing healthcare disparities, particularly in underserved populations with limited access to DXA scanning and specialized osteoporosis care.

To translate opportunistic AI-assisted screening into clinical practice, we outline a regionally adaptable referral protocol. Patients identified as high-risk by the AI model on routine chest radiographs could be referred for DXA scanning at the nearest accessible facility, with treatment initiation following current Japanese osteoporosis guidelines. The protocol is designed to accommodate regional differences in DXA

availability and healthcare infrastructure, ensuring feasibility across both high-incidence areas, such as Kure City, and districts with lower fracture incidence. While not yet implemented, this framework illustrates a practical approach for integrating AI screening into real-world care and informs future implementation studies.

Real-world implementation of opportunistic AI-assisted screening will face several potential challenges. Variations in DXA availability, differences in healthcare infrastructure, and the need for provider training must be addressed to ensure effective integration into clinical practice. In addition, notable regional disparities in osteoporosis awareness and screening rates may affect uptake and equity of screening programs. Furthermore, reimbursement policies and legal frameworks governing national screening programs may require reform to support systematic adoption. Recognizing and planning for these logistical, educational, and policy-related barriers will be essential to realize the full clinical and economic potential of AI-based osteoporosis screening in Japan.

This economic evaluation is grounded in the diagnostic performance of the AI-assisted screening model developed by Jang et al. [2] which was trained on paired data with 13,026 chest radiographs and corresponding DXA results from the Health Screening and Promotion Center of Asan Medical Center (2012–2019) and an external test with 1089 radiographs (2010–2017) was also conducted. Validation in the Japanese population would be important to confirm the technical reproducibility of the AI model, originally developed and tested in a South Korean cohort, as well as its real-world clinical utility and cost-effectiveness within the Japanese healthcare system. Although several other AI-based tools have been created for osteoporosis detection using standard radiographs [3,40,41], the cost-effectiveness results presented here are specific to the model evaluated and may not be applicable to other tools due to differences in diagnostic accuracy and implementation costs—both of which influence economic outcomes. Direct comparison is further complicated by the fact that the tools have been developed in different populations and settings. Similarly, comparison with other diagnosis tests such as DXA, REMS, QCT, and QUS, that have also been shown to be cost-effective in some populations [13,42], is challenging given the variability in study populations, the severity of osteoporosis assessed, and methodological approaches. Importantly, AI-based screening using chest radiographs is inherently opportunistic: it leverages images acquired for other clinical reasons and does not require dedicated appointments or additional imaging. This makes direct comparisons with primary screening tools like DXA, REMS and QUS, which involve specific visits, less appropriate. Given the significant treatment gap, such tools should be seen as complementary, contributing to a broader, integrated screening strategy.

The results of this economic evaluation should be viewed in light of certain limitations. One key area of uncertainty involves the follow-up process after initial screening—specifically, the percentage of individuals identified as likely osteoporotic who proceed to DXA confirmation and begin treatment thereafter. These estimates were based on expert input, and the use of real-world data in future analyses would improve precision. Nevertheless, extensive sensitivity analyses were carried out to explore these uncertainties, and the findings consistently supported the cost-effectiveness of the screening strategy. Additionally, our screening pathway may be seen as simplified and therefore conservative. The model assumed no treatment for patients with osteopenia, although guidelines might recommend treatment for those with additional risk factors or a FRAX® score $\geq$ 15% [43]. This conservative choice reflects a lack of published data on the sensitivity and specificity of the intervention for osteopenia and the uncertainty around how many osteopenia patients would effectively receive treatment.

5. Conclusions

Opportunistic AI-assisted osteoporosis screening through chest radiographs offers substantial economic value for Japanese women aged 50 and above in practical healthcare settings. In regions with elevated fracture rates, this strategy proves to be dominant. These results highlight the public health benefit of utilizing existing imaging resources to enhance early diagnosis and help close the diagnostic gap in osteoporosis management.

CRediT author statement

Jean-Yves Reginster: Conceptualization, Formal analyses, Data curation, Validation, Investigation, Writing – Original Draft, Writing – Review & editing. **Takahiko Hamasaki**: Data curation, Investigation, Writing – Review & editing. **Saeko Fujiwara**: Data curation, Investigation, Writing – Review & editing. **Majed Alokail:** Validation, Writing – Review & editing. **Mickael Hiligsmann:** Conceptualization, Formal analyses, Data curation, Validation, Investigation, Writing – Original Draft, Writing – Review & editing.

Declaration of generative AI in scientific writing

The authors did not use generative AI or AI-assisted technologies in the preparation of this manuscript.

Conflicts of interest

Jean-Yves Reginster has received consultancy fees from and joined the Speakers Bureau for Echolight, Viatris, Theramex, Promedius and Besins.

Mickael Hiligsmann has received research grants (paid to institution) from Radius Health, and Angelini Pharma, lecture fees from IBSA (paid to institution) and Echolight, and was grant advisor for Pfizer (paid to institution) and consultant (paid to institution) for Grünenthal and Teva.

All other authors declare no competing interests.

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Appendix A

Table 1
CHEERS 2022 Checklist.

Topic	No.	Item	Location where item is reported
Title			
Abstract	1	Identify the study as an economic evaluation and specify the interventions being compared.	Title
	2	Provide a structured summary that highlights context, key methods, results, and alternative analyses.	Abstract
Introduction			
Background and objectives	3	Give the context for the study, the study question, and its practical relevance for decision making in policy or practice.	Introduction
Methods			
Health economic analysis plan	4	Indicate whether a health economic analysis plan was developed and where available.	Methods
Study population	5	Describe characteristics of the study population (such as age range, demographics, socioeconomic, or clinical characteristics).	Methods
Setting and location	6	Provide relevant contextual information that may influence findings.	Methods
Comparators	7	Describe the interventions or strategies being compared and why chosen.	Methods
Perspective	8	State the perspective(s) adopted by the study and why chosen.	Methods
Time horizon	9	State the time horizon for the study and why appropriate.	Methods
Discount rate	10	Report the discount rate(s) and reason chosen.	Methods
Selection of outcomes	11	Describe what outcomes were used as the measure(s) of benefit(s) and harm(s).	Methods
Measurement of outcomes	12	Describe how outcomes used to capture benefit(s) and harm(s) were measured.	Methods
Valuation of outcomes	13	Describe the population and methods used to measure and value outcomes.	Methods
Measurement and valuation of resources and costs	14	Describe how costs were valued.	Methods
Currency, price date, and conversion	15	Report the dates of the estimated resource quantities and unit costs, plus the currency and year of conversion.	Methods
Rationale and description of model	16	If modelling is used, describe in detail, and why used. Report if the model is publicly available and where it can be accessed.	Methods
Analytics and assumptions	17	Describe any methods for analysing or statistically transforming data, any extrapolation methods, and approaches for validating any model used.	Methods
Characterising heterogeneity	18	Describe any methods used for estimating how the results of the study vary for subgroups.	Methods
Characterising distributional effects	19	Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations.	Methods
Characterising uncertainty	20	Describe methods to characterise any sources of uncertainty in the analysis.	Methods
Approach to engagement with patients and others affected by the study	21	Describe any approaches to engage patients or service recipients, the public, communities, or stakeholders (such as clinicians or payers) in the design of the study.	Methods
Results			
Study parameters	22	Report all analytic inputs (such as values, ranges, references) including uncertainty or distributional assumptions.	Results
Summary of main results	23	Report the mean values for the main categories of costs and outcomes of interest and summarise them in the most appropriate overall measure.	Results
Effect of uncertainty	24	Describe how uncertainty about analytic judgments, inputs, or projections affect findings. Report the effect of choice of discount rate and time horizon, if applicable.	Results
Effect of engagement with patients and others affected by the study	25	Report on any difference patient/service recipient, public, community, or stakeholder involvement made to the approach or findings of the study	Not reported
Discussion			
Study findings, limitations, generalizability, and current knowledge	26	Report key findings, limitations, ethical or equity considerations not captured, and how these could affect patients, policy, or practice.	Discussion
Other relevant information			
Source of funding	27	Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis	Funding
Conflicts of interest	28	Report authors conflicts of interest according to journal or International Committee of Medical Journal Editors requirements.	Conflicts of interest

From: Husereau D, Drummond M, Augustovski F et al. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) Explanation and Elaboration: A Report of the ISPOR CHEERS II Good Practices Task Force. Value Health 2022; 25:10–31.

Table 2
IOF-ESCEO Osteoporosis-specific checklist.

Item	No.	Recommendation	Reported
Transition probabilities	1	Report the transition probabilities and how they were estimated (including increased fracture risk)	Methods
Excess mortality after fractures	2	Describe approaches and data sources used for the excess mortality after fractures	Methods
Fractures costs	3	Describe approaches and data sources used for fractures costs	Methods
Fractures effects on utility	4	Describe approaches and data sources used for the effects of fractures on utility	Methods
Treatment effect during treatment	5	Describe fully the methods used for the identification, selection and synthesis of clinical effectiveness data (per fracture site)	Methods
Treatment effect after discontinuation	6	Describe fully the methods used for the treatment effect after discontinuation	Methods
Medication adherence	7	Describe approaches and data sources used for modelling medication adherence	Methods
Treatment costs	8	Describe approaches and data sources used for therapy costs	Methods
Treatment side effects	9	Describe approaches and data sources used for costs and utilities effects of adverse events	Methods

IOF, the International Osteoporosis Foundation; ESCEO, the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases.

Table 3
IOF-ESCEO checklist for the design and conduct of an economic evaluation in osteoporosis.

Type of economic evaluation	Status
• Cost-utility analysis using QALY as outcome	YES
Method for the conduct of economic evaluation	
• A model based economic evaluation	YES
Modelling technique	
• Lifetime horizon	YES
• Markov model is appropriate (6 months/1 year cycle length)	YES (6 months)
• Avoid hierarchy of fractures and restrictions after fracture events	YES
• Hip, clinical vertebral and non-vertebral non-hip fracture	YES
Base-case analysis and population	
• Multiple scenarios: age range, BMD and fracture risk scenarios	YES
• At least a scenario including a 10-year risk of a major osteoporotic fracture equal to 20% or with a BMD T-score ≤ -2.5 with or without fractures	YES
• The FRAX® or GARVAN® tools can be used to model fracture risk	NA
• Increased risk after fracture events within the model	YES
Mortality	
•An additional effect (on ciosts and/or utility) after multiple fractures	YES
• Excess mortality after hip fractures	YES
• Proportion attribute to the fracture (eg., 25–30%)	YES
Fracture costs and utility	
• Societal and/or healthcare payor perspective	YES
Acute fracture costs	
• Long-term costs after hip fracture (attributable to the fracture)	YES
• First year and subsequent years effects of fractures on disutility	YES
• National ICUROS data if available	YES (whole ICUROS study)
Treatment characteristics	
• Treatment duration similar to guidelines or RCTs	YES
• Comparators: no treatment and relevant active osteoporotic agent(s)	YES
• Sequential therapy may be considered as intervention/comparators	YES
• Efficacy data from RCTs, (network) meta-analysis	YES
• In the absence of hip/wrist specific efficacy data, use of non-vertebral or clinical fracture efficacy data	YES
• Treatment effects after discontinuation depending on treatment	YES
• Medication adherence as sensitivity analysis	YES (base case)
• Drug costs and administration/monitoring costs	YES
• Adverse events	YES

IOF, the International Osteoporosis Foundation; ESCEO, the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases.

References

[1] Lam DC, Liam CK, Andarini S, Park S, Tan DSW, Singh N, et al. Lung cancer screening in Asia: an expert consensus report. J Thorac Oncol 2023;18:1303–22.
[2] Jang M, Kim M, Bae SJ, Lee SH, Koh JM, Kim N. Opportunistic osteoporosis screening using chest radiographs with deep learning: development and external validation with a cohort dataset. J Bone Miner Res 2022;37:369–77.
[3] He Y, Lin J, Zhu S, Zhu J, Xu Z. Deep learning in the radiologic diagnosis of osteoporosis: a literature review. J Int Med Res 2024;52:3000605241244754.
[4] National Cancer Center Japan. Cancer screening participation rates (estimates based on the national survey of basic living conditions). Ganjoho.jp. Available from: URL: .https://ganjoho.jp/reg_stat/statistics/stat/screening/screening.html (accessed 25 August, 2025). (in Japanese).
[5] Yamauchi M, Sugimoto T. On "2015 Guidelines for Prevention and Treatment of Osteoporosis". Medical treatment for osteoporosis. Clin Calcium 2015 Sep;25: 1285–92.
[6] Iki M. Epidemiology of osteoporosis in Japan. Clin Calcium 2012;22:797–803.
[7] Takusari E, Sakata K, Hashimoto T, Fukushima Y, Nakamura T, Orimo H. Trends in hip fracture incidence in Japan: estimates based on nationwide hip fracture surveys from 1992 to 2017. JBMR Plus 2020;30:e10428.
[8] Mori T, Komiyama J, Fujii T, Sanuki M, Kume K, Kato G, et al. Medical expenditures for fragility hip fracture in Japan: a study using the nationwide health insurance claims database. Arch Osteoporosis 2022;17:61.
[9] Reginster JY, Schmidmaier R, Alokail M, Hiligsmann M. Cost-effectiveness of opportunistic osteoporosis screening using chest radiographs with deep learning in Germany. Aging Clin Exp Res 2025;37:149.
[10] Hiligsmann M, Silverman SL, Reginster JY. Cost-effectiveness of opportunistic osteoporosis screening using chest radiographs with deep learning in the United States. J Am Coll Radiol Aug 8 2025. Published Online First.
[11] Hiligsmann M, Reginster JY, Silverman S. The value of a patient-level modeling approach and need for better reporting in economic evaluations of osteoporosis. J Manag Care Spec Pharm 2020;26:334–5.
[12] Hiligsmann M, Reginster JY, Tosteson ANA, Bukata SV, Saag KG, Gold DT, et al. Recommendations for the conduct of economic evaluations in osteoporosis: outcomes of an experts' consensus meeting organized by the european society for clinical and economic aspects of osteoporosis, osteoarthritis and musculoskeletal diseases (ESCEO) and the US branch of the international osteoporosis foundation. Osteoporos Int 2019;30:45–57.
[13] Reginster JY, Silverman SL, Alokail M, Al-Daghri N, Hiligsmann M. Cost-effectiveness of radiofrequency echographic multi-spectrometry for the diagnosis of osteoporosis in the United States. JBMR Plus 2024;9:ziae138.
[14] Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs AH, Carswell C, et al. Consolidated health economic evaluation reporting standards 2022 (CHEERS 2022) statement: updated reporting guidance for health economic evaluations. Value Health 2022;25:3–9.
[15] Center for Outcomes Research and Economic Evaluation for Health (C2H), National Institute of Public Health. Guideline for preparing cost-effectiveness evaluation to the central social insurance medical council. Version 3.0, approved on 19th January, 2022. Tokyo: National Institute of Public Health (Japan). Available from: https://c2h.niph.go.jp/tools/guideline/guideline_en.pdf.
[16] Yoshimura N, Iidaka T, Horii C, Muraki S, Oka H, Kawaguchi H, et al. Trends in osteoporosis prevalence over a 10-year period in Japan: the ROAD study 2005-2015. J Bone Miner Metabol 2022;40:829–38.
[17] Tamaki J, Fujimori K, Ikehara S, Kamiya K, Nakatoh S, Okimoto N, et al. Estimates of hip fracture incidence in Japan using the national health insurance claim database in 2012-2015. Osteoporos Int 2019;30:975–83.
[18] Moriwaki K, Fukuda H. Cost-effectiveness of implementing guidelines for the treatment of glucocorticoid-induced osteoporosis in Japan. Osteoporos Int 2019; 30:299–310.
[19] Hamasaki T, Okimoto N, Teramoto H, Shirakawa T, Nakagawa T, Mizuno N, et al. Incidence of clinical vertebral fractures and hip fractures of the elderly (65 years or over) population-large-scale data analysis using claim database in kure city, Hiroshima, Japan. Arch Osteoporosis 2020;15:124.
[20] Kanis JA, Johnell O, Oden A, Jonsson B, De Laet C, Dawson A. Risk of hip fracture according to the world health organization criteria for osteopenia and osteoporosis. Bone 2000;27:585–90.

[21] Söreskog E, Ström O, Spångéus A, Åkesson KE, Borgström F, Banefelt J, et al. Risk of major osteoporotic fracture after first, second and third fracture in Swedish women aged 50 years and older. Bone 2020;134:115286.
[22] Hiligsmann M, Silverman SL, Singer AJ, Pearman L, Wang Y, Caminis J, et al. Comparison of the cost-effectiveness of sequential treatment with abaloparatide in US men and women at very high risk of fractures. Aging Clin Exp Res 2024;36:14.
[23] Hiligsmann M, Williams SA, Fitzpatrick LA, Silverman SS, Weiss R, Reginster JY. Cost-effectiveness of sequential treatment with abaloparatide followed by alendronate vs. alendronate monotherapy in women at increased risk of fracture: a US payer perspective. Semin Arthritis Rheum 2020;50:394–400.
[24] Kanis JA, Oden A, Johnell O, De Laet C, Jonsson B. Excess mortality after hospitalisation for vertebral fracture. Osteoporos Int 2004;15:108–12.
[25] Kanis JA, Oden A, Johnell O, De Laet C, Jonsson B, Oglesby AK. The components of excess mortality after hip fracture. Bone 2003;32:468–73.
[26] Taguchi Y, Inoue Y, Kido T, Arai N. Treatment costs and cost drivers among osteoporotic fracture patients in Japan: a retrospective database analysis. Arch Osteoporosis 2018;13:45.
[27] Hagino H, Tanaka K, Silverman S, McClung M, Gandra SR, Charokopou M, et al. Cost effectiveness of romosozumab versus teriparatide for severe postmenopausal osteoporosis in Japan. Osteoporos Int 2021;32:2011–21.
[28] Shiroiwa T, Fukuda T, Ikeda S, Igarashi A, Noto S, Saito S, et al. Japanese population norms for preference-based measures: EQ-5D-3L, EQ-5D-5L, and SF-6D. Qual Life Res 2016;25:707–19.
[29] Nawata S. Society, EuroQol study of the elderly general population: relationship with IADL and other attributes. J Health Care 2000;10:75–86.
[30] Hagino H, Nakamura T, Fujiwara S, Oeki M, Okano T, Teshima R. Sequential change in quality of life for patients with incident clinical fractures: a prospective study. Osteoporos Int 2009;20:695–702.
[31] Shin MH, Zmuda JM, Barrett-Connor E, Sheu Y, Patrick AL, Leung PC, et al. Race/ethnic differences in associations between bone mineral density and fracture history in older men. Osteoporos Int 2014;25:837–45.
[32] Zengin A, Prentice A, Ward KA. Ethnic differences in bone health. Front Endocrinol 2015;6:24.
[33] National Institute for Health and Care Excellence (GB). *Bisphosphonates for treating osteoporosis* [Internet]. London: NICE; 2017 Aug 9 [updated 2019 Jul 8; cited 2025 May 15]. (Technology appraisal guidance; no. 464). Available from: https://www.nice.org.uk/guidance/ta464.
[34] Hiligsmann M, Evers SM, Ben Sedrine W, Kanis JA, Ramaekers B, Reginster JY, et al. A systematic review of cost-effectiveness analyses of drugs for postmenopausal osteoporosis. Pharmacoeconomics 2015;33:205–24.
[35] Hiligsmann M, Reginster JY. Cost effectiveness of denosumab compared with oral bisphosphonates in the treatment of post-menopausal osteoporotic women in Belgium. Pharmacoeconomics 2011;29:895–911.
[36] Nakatoh S, Fujimori K, Ishii S, Tamaki J, Okimoto N, Ogawa S, et al. Insufficient persistence to pharmacotherapy in Japanese patients with osteoporosis: an analysis of the national database of health insurance claims and specific health checkups in Japan. Arch Osteoporosis 2021;16:131.
[37] Takada J, Sato S, Arai K, Kito Y, Oshita Y, Saito K. Safety and effectiveness of once-yearly zoledronic acid in Japanese osteoporosis patients: three-year post-marketing surveillance. J Bone Miner Metabol 2023;41:268–77.
[38] Hasegawa M, Komoto S, Shiroiwa T, Fukuda T. Formal implementation of cost-effectiveness evaluations in Japan: a unique health technology assessment system. Value Health 2020;23:43–51.
[39] Curl PK, Jacob AM, Bresnahan B, Cross NM, Jarvik JG. Cost-effectiveness of artificial intelligence-based opportunistic compression fracture screening of existing radiographs. J Am Coll Radiol 2024;21:1489–96.
[40] Asamoto T, Takegami Y, Sato Y, Takahara S, Yamamoto N, Inagaki N, et al. External validation of a deep learning model for predicting bone mineral density on chest radiographs. Arch Osteoporosis 2024;19:15.
[41] Sato Y, Yamamoto N, Inagaki N, Iesaki Y, Asamoto T, Suzuki T, et al. Deep learning for bone mineral density and T-Score prediction from chest X-rays: a multicenter study. Biomedicines 2022;10:2323.
[42] Ruhling S, Schwarting J, Froelich MF, Loffler MT, Bodden J, Hernandez Petzsche MR, et al. Cost-effectiveness of opportunistic QCT-based osteoporosis screening for the prediction of incident vertebral fractures. Front Endocrinol 2023;14:1222041.
[43] Orimo H, Nakamura T, Hosoi T, Iki M, Uenishi K, Endo N, et al. Japanese 2011 guidelines for prevention and treatment of osteoporosis–executive summary. Arch Osteoporosis 2012;7:3–20.
[44] Haentjens P, Magaziner J, Colon-Emeric CS, Vanderschueren D, Milisen K, Velkeniers B, et al. Meta-analysis: excess mortality after hip fracture among older women and men. Ann Intern Med 2010;152:380–90.