ORIGINAL ARTICLE

Cost-Effectiveness of Opportunistic Osteoporosis Screening Using Chest Radiographs With Deep Learning in the United States

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Abstract

Objectives: Deep learning models applied to chest radiographs obtained for other clinical reasons have shown promise in opportunistic osteoporosis screening, particularly among middle-aged to older individuals. This study evaluates the cost-effectiveness of this approach in US women aged 50 years and over.

Methods: An economic model, incorporating both a decision tree and a microsimulation Markov model, estimated the cost per quality-adjusted life-year (QALY) gained (in 2024 US dollars) for screening via chest radiographs with deep learning, followed by treatment, versus no screening and treatment. The patient pathways were based on the sensitivity and specificity of artificial intelligence-enhanced radiographs. Real-world medication persistence, realistic assumptions for probabilities of dual-energy x-ray absorptiometry examination postscreening detection and for treatment initiation rates were incorporated. Women with osteoporosis were stratified into high risk (receiving alendronate monotherapy for 5 years) and very high risk (receiving an 18-month anabolic treatment with abaloparatide followed by 5 years of alendronate). Parameter uncertainty was analyzed through sensitivity analyses.

Results: The opportunistic screening strategy improved health outcomes, yielding more QALYs and fewer fractures while increasing treatment costs. The cost per QALY gained of opportunistic screening was estimated at $72,085 per QALY gained among women 50+, remaining below the US cost-effectiveness threshold of $100,000 per QALY. Further improvements in cost-effectiveness could be achieved by optimizing follow-up, treatment initiation, and medication adherence.

Discussion: This study underscores the cost-effectiveness and public health value of opportunistic, artificial intelligence-driven screening osteoporosis screening using existing chest radiographs, demonstrating its potential to improve early detection and address unmet diagnostic needs in osteoporosis care.

Key Words: Artificial intelligence, chest radiographs, cost-effectiveness, osteoporosis, screening

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INTRODUCTION

Advancements in artificial intelligence (AI) are transforming health care by offering innovative solutions to long-standing challenges, particularly in areas such as early disease detection [1]. Often referred to as a "silent disease," osteoporosis is common and linked to reduced bone strength and higher fracture risk. It often goes undiagnosed until a fracture occurs, leading to substantial health care costs, lower quality of life, and excess mortality. Traditional diagnostic methods, such as dual-energy x-ray absorptiometry (DXA), the gold standard for assessing bone mineral density (BMD), face barriers such as technical complexity, limited accessibility, costs, and the need for specialized equipment. These limitations restrict the applicability of DXA for widespread screening and diagnosis at the population level [2].

Recent advancements in deep learning have shown promise in addressing these challenges. Deep learning-based models using chest radiographs have demonstrated favorable performance in the opportunistic screening of osteoporosis, particularly in middle-aged and older adults [2]. In this context, opportunistic screening refers to the use of chest radiographs that were originally acquired for other clinical indications (eg, evaluation of respiratory symptoms), rather than for the purpose of osteoporosis detection. This approach offers a scalable and accessible way to detect osteoporosis, especially in the large proportion of women over 50 who are eligible for BMD but remain unscreened. By leveraging existing imaging studies, this strategy does not rely on additional imaging and may enhance the value of already-collected data. By enabling earlier diagnosis and treatment through opportunistic screening, AI-driven analysis of chest radiographs could help reduce the burden of osteoporotic fractures.

Although the clinical validation of deep learning models has shown encouraging outcomes [2], assessing their cost-effectiveness is equally important. Economic evaluations help to optimize health care resource allocation and guide reimbursement decisions. Such studies are crucial to determine the value of these AI-driven approaches and support informed decision making.

The aim of this study is therefore to estimate the cost-effectiveness of opportunistic osteoporosis screening using deep learning applied to chest radiographs originally obtained for other clinical purposes compared with no screening and treatment in US women aged 50 years and above.

MATERIALS AND METHODS

This economic study evaluated the cost-effectiveness of opportunistic osteoporosis screening using chest radiographs analyzed with deep learning, followed by treatment, compared with a scenario with no screening and treatment that reflects real-world conditions in which screening programs are often absent, leaving most patients untreated. Importantly, our analysis does not propose chest radiographs as a primary screening test or a replacement for DXA, but rather as an adjunct opportunistic approach that leverages imaging already obtained for other clinical indications. Since the chest radiographs are not ordered specifically for osteoporosis screening, the comparison to "no screening" remains appropriate to evaluate the incremental value of this pragmatic strategy in identifying individuals who would otherwise remain undetected. The analysis employed a two-part economic model developed in TreeAge Pro 2024 R1.0 software (TreeAge Pro Inc, Williamston, Massachusetts): a decision tree to outline the screening pathways and a Markov microsimulation model to project long-term costs and outcomes. Table 1 presents the key parameters used in the model.

Decision Tree

As shown in Figure 1, the opportunistic screening strategy used AI-enhanced chest radiographs, which operated according to the tool's sensitivity and specificity. A subset of patients suspected of having osteoporosis subsequently underwent a confirmatory DXA test. Diagnosed patients were stratified into high risk (HR) or very high risk (VHR) groups. Based on treatment initiation rates, HR patients received alendronate (ALN) monotherapy, and VHR patients were prescribed sequential therapy with an anabolic first.

Markov Microsimulation Model

Following recommendations [3-5], we employed a previously validated Markov microsimulation model to track fracture and simulate health outcomes and costs up to 100 years [3,6,7]. The model accounted for hip fractures, vertebral fractures, and nonhip nonvertebral (NHNV) fractures, allowing for multiple fractures at the same site or different sites.

Population and Transitions Probabilities

The analyses focused on US women aged 50 years and older, segmented into 5-year age groups using US Census data. Five groups were simulated: women without osteoporosis, women at HR or VHR, each with or without treatment. Osteoporosis prevalence, defined as affecting the femoral neck, lumbar spine, or both, was estimated at 13.1% for women aged 50 to 64 years and 27.1% for those aged 65 years and older, based on data from the 2017 to 2018 National Health and Nutrition Examination Survey [8]. Expert opinion estimated 20% of detected patients as VHR. In the model, women at VHR were assumed to have had a recent fracture (in addition to having a BMD

Table 1. Key model parameters

Parameter	Data
Incidence (annual rate per 100) of fracture [10,11]	
Hip	0.029 (50-54 y), 0.057 (55-59 y), 0.105 (60-64 y), 0.203 (65-69 y), 0.394 (70-74 y), 0.793 (75-79 y), 1.447 (80-84 y), 2.606 (85+ y)
Vertebral	0.064 (50-54 y), 0.132 (55-59 y), 0.124 (60-64 y), 0.233 (65-69 y), 0.473 (70-74 y), 0.523 (75-79 y), 0.622 (80-84 y), 1.095 (85+ y)
NHNV	0.820 (50-54 y), 1.340 (55-59 y), 1.597 (60-64 y), 1.722 (65-69 y), 2.106 (70-74 y), 2.722 (75-79 y), 3.256 (80-84 y), 3.923 (85+ y)
Increased relative risk due to osteoporosis [12]	
Hip	5.659 (50-59 y), 3.390 (60-69 y), 2.250 (70-79 y), 1.570 (80+)
Vertebral	2.680 (50-59 y), 2.176 (60-69 y), 1.772 (70-79 y), 1.514 (80+)
NHNV	2.250 (50-59 y), 1.902 (60-69 y), 1.610 (70-79 y), 1.416 (80+)
Increased relative risk of subsequent fracture after a fracture [13]	
1st fracture	2.1 (0-6 months), 2.0 (7-12 months), 1.9 (13-18 months), 1.7 (19-24 months), 1.6 (25-36 months), 1.5 (37-48 months), 1.5 (49 months+)
2nd and more fracture	2.4 (0-6 months), 2.1 (7-12 months), 1.8 (13-18 months), 1.7 (19-24 months), 1.7 (25-36 months), 1.5 (37-48 months), 1.5 (49 months+)
Mortality excess [3,45]	
Hip (0-6 m / 7-12 m / subs. year)	4.54 (3.56-5.88) / 1.76 (1.43-2.16) / 1.78 (1.33-2.39)
Vertebral (0-6 m / 7-12 m / subs. year)	4.54 (3.56-5.88) / 1.76 (1.43-2.16) / 1.78 (1.33-2.39)
NHNV (0-12 m)	1.38 (1.18-1.62)
% Attributable to fracture	25
First-year cost of a first and subsequent fracture (estimated in 2024 US dollars) (adjusted from [18])	
Hip	
1st fracture	123,804 (50-64 y), 78,309 (65+ y)
Subs. fractures	59,960 (50-64 y), 46,653 (65+ y)
Vertebral	
1st fracture	30,307 (50-64 y), 21,586 (65+ y)
Subs. fractures	62,577 (50-64 y), 36,233 (65+ y)
NHNV	
1st fracture	14,544 (50-64 y), 19,586 (65+ y)
Subs. fractures	30,029 (50-64 y), 32,877 (65+ y)
Fracture costs (estimated in 2024 US dollars) for year 2 up to year 5 (adjusted from [18])	
Hip	
Commercial	11,182 (year 2), 7,815 (year 3), 6,155 (year 4), 3,680 (year 5+)
Medicare	7,922 (year 2), 5,887 (year 3), 4,194 (year 4), 3,000 (year 5+)
Vertebral	
Commercial	8,483 (year 2), 4,686 (year 3), 2,656 (year 4), 1,807 (year 5)
Medicare	5,962 (year 2), 4,237 (year 3), 3,035 (year 4), 2,246 (year 5)
NHNV	
Commercial	1,818 (year 2), 1,135 (year 3), 664 (year 4), 390 (year 5)
Medicare	2,422 (year 2), 2,096 (year 3), 1,381 (year 4), 1,308 (year 5)
Health state utility values [19,20]	
Baseline utility	0.837 (50-59 y), 0.706 (60-69 y), 0.671 (70-79 y), 0.630 (80+ y)
RR after hip (1st y / subs. y)	0.55 (0.53-0.57) / 0.86 (0.84-0.89)
RR after vertebral (1st y / subs. y)	0.68 (0.65-0.70) / 0.85 (0.82-0.87)
RR after NHNV (1st y / subs. y)	0.79 (0.65-0.93) / 0.95 (0.81-1.09)

(continued)

Table 1. Continued

Parameter	Data
Effects on fracture (expressed as relative risk compared to placebo) of medications [25,26]	
Hip	
ABL	0.63 (0.41-0.98)
ALN	0.67 (0.48-0.96)
Vertebral	
ABL	0.16 (0.06-0.42)
ALN	0.45 (0.31-0.65)
NHNV	
ABL	0.42 (0.25-0.70)
ALN	0.81 (0.68-0.97)
Persistence rate, % [27]	
ABL	59.1
ALN	35.1 (17.5 from year 3)
Drug cost (US$ per year) [46]	
ABL	32,004
ALN	35
Nondrug costs	
General physician visit	140.6
DXA	66.3
Screening pathway	
Sensitivity, %; specificity, % [21]	86.16; 74.19
Cost	19.9
% DXA after OP suspected	50
Treatment initiation after OP diagnosed	57

ABL = abaloparatide; ALN = alendronate; DXA = dual-energy x-ray absorptiometry; m = month; NHNV = nonhip nonvertebral; OP = osteoporosis; Subs = subsequent; RR = relative reduction.

T-score ≤ -2.5) to meet the American Association of Clinical Endocrinology/American College of Endocrinology criteria [9], and those at HR were assumed to have no previous fracture (but having a BMD T-score ≤ -2.5).

Baseline incidences of hip and vertebral fractures in the US general female population, used for women without osteoporosis in the model, were based on Ettinger et al [10], which also informed the development of the US Fracture Risk Assessment Tool scores. The incidence of NHNV fractures including wrist, pelvis, and other fractures was derived from Burge et al [11]. The increased fracture risk in women with BMD T-score ≤ -2.5 was calculated using a previously validated method [12]. Additionally, the elevated risk of fractures due to a prior fracture, at baseline for VHR patients and during simulation for other groups, was modeled based on a large Swedish study [13].

Baseline mortality rates for US women, stratified by age for 2020, were obtained from official data published by the National Vital Statistics System. Consistent with previous studies, increased mortality after hip, vertebral, and NHNV fractures were included in the model [4,7,14]. Since excess mortality may also be attributable to comorbidities, only 25% of the excess mortality after fractures was attributed directly to the fractures themselves [15,16].

Fracture Costs and Quality of Life

Our analysis takes a health care sector perspective, with health care costs presented in 2024 US dollars, adjusted using the Consumer Price Index for Medical Care when relevant. A 3% discount rate was applied to both costs and quality-adjusted life-years (QALYs), following US guidelines [17]. Incremental costs for the first 5 years after hip, vertebral, and NHNV fractures were based on estimates from Tran et al, which estimated Medicare and commercial incremental costs for fractures [18]. For hip fractures, the incremental cost from year 5 in Tran et al's study was projected across the patient's lifetime, accounting for long-term nursing home admissions and related expenses.

Utility data were sourced from a report on nationally representative values for the noninstitutionalized US adult population, based on EuroQol 5-dimension scores [19]. The impact of fractures on utility was obtained from the International Costs and Utilities Related to Osteoporotic Fractures Study [20].

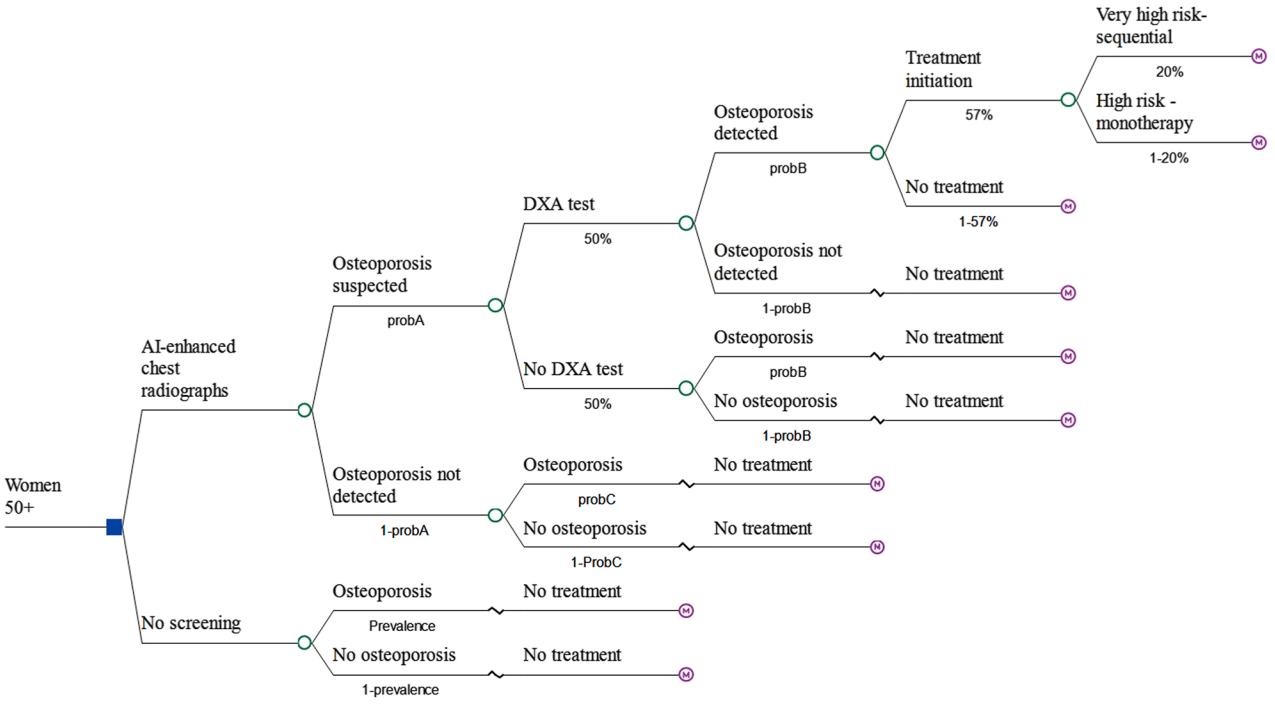

Fig. 1. Decision tree for osteoporosis screening and treatment pathways in US women aged 50 years and over. AI = artificial intelligence; DXA = dual-energy x-ray absorptiometry; probA = probability of osteoporosis suspected with AI-enhanced chest radiographs; probB = probability of osteoporosis confirmed after DXA test.

Opportunistic Screening and Treatment Strategies

The sensitivity and specificity of AI-enhanced chest radiographs, from Jang et al [21], are estimated at 86.16% and 74.19%, using a predefined threshold of 0.5. Chest radiographs were collected from a mix of clinical settings to ensure diversity and generalizability. For internal validation, images primarily originated from routine medical care, such as general health screenings, periodic checkups, and evaluations of clinical symptoms like cough or fever, at the Health Screening and Promotion Center of Asan Medical Center, representing an asymptomatic population. All chest radiographs were acquired following standardized protocols of the Asan Medical Center Radiology Department, typically using a tube voltage of 100 to 130 kVp with patient-specific adjustments. To address technical variability, images underwent standardized preprocessing (eg, z-normalization, histogram matching), and data augmentation techniques were applied to enhance model robustness against common imaging inconsistencies. External validation incorporated chest x-rays from various real-world sources, including outpatient clinics, inpatient wards, emergency departments, and international institutions. Only standard posteroanterior view chest radiographs were used in this study. Anteroposterior and lateral views were excluded to ensure consistency and maintain alignment with clinical standards for routine adult chest imaging.

Expert opinion suggested that 50% of patients suspected of having osteoporosis proceed to a DXA and 57% initiate osteoporosis medication after a positive DXA [22]. Patients classified as HR received 5 years of oral ALN, and those categorized as VHR were treated with sequential therapy [23]: 18 months of treatment using an anabolic agent (ABL) followed by 5 years of ALN, in line with the American Association of Clinical Endocrinology/American College of Endocrinology guidelines [17].

Treatment assumptions matched previous economic research on US women with osteoporosis for both sequential and monotherapy treatments [7,14,24]. The fracture risk reduction from ABL over 43 months came from the ACTIVE/ACTIVExtend Intention-To-Treat trial [25], showing significant reduction in hip, vertebral, and NHNV. Risk reductions during ALN treatment were based on the National Institute for Health and Care Excellence meta-analysis (TA464) [26].

Consistent with findings from ACTIVExtend, the effects of ABL remained constant during ALN treatment, with a gradual linear decrease over 1 additional year after ALN discontinuation. Similarly, the effects of ALN were assumed to decline linearly to zero over a period comparable to the treatment duration, in line with previous economic studies [3].

We assigned a cost of $140.60 for each general physician visit (based on Medicare costs for a 45-min visit), occurring

every 6 months during treatment. The Medicare cost for a DXA scan, including additional related costs, was estimated at $66.34, with scans assumed every 2 years during treatment. Costs of medication adverse events, such as hypercalcemia with ABL and gastrointestinal risks with ALN, were incorporated into the analysis, based on previous studies [4]. The cost of screening was assumed to be 30% of the DXA cost in the base case, amounting to $19.90. Since our analysis assumes that chest radiographs are obtained for clinical indications other than osteoporosis screening, the costs of acquiring these images are not attributed to the screening intervention.

Real-world medication persistence was incorporated into the base-case analysis using data from Cheng et al [27] that analyzed 10,863 US women who initiated anabolic therapy (teriparatide) and oral bisphosphonates. The 12-month persistence rate for teriparatide, applied to ABL in the model, was 59.1%, consistent with other studies. For ALN, the 12-month persistence rate was 35.1%. A lower persistence rate of 17.5% was assumed for ALN from year 3 onward [28]. Medication costs, treatment efficacy and offset times were all adjusted based on the persistence rates.

Analyses

Based on 5,000,000 individual simulations, the model estimated total health care costs, fractures, life-years, and QALYs for both the opportunistic osteoporosis screening followed by treatment and the no screening and treatment scenarios. The primary outcome was the incremental cost-effectiveness ratio (ICER), which quantifies the additional cost required by the opportunistic screening to gain 1 extra QALY. In the United States, the Institute for Clinical and Economic Review considers strategies with a cost per QALY gained below US$100,000 to $150,000 as high value in health care [29].

Multiple sensitivity analyses were conducted to assess the robustness of the results. One-way sensitivity analyses were performed by varying one parameter at a time across both screening pathway and nonscreening parameters. Screening pathway parameters were then varied to account for uncertainty, including adjustments of ±50% for the percentage of patients undergoing DXA after osteoporosis detection, osteoporosis prevalence, treatment initiation rates, and the proportion of VHR patients. Additional scenarios included full medication adherence and a scenario with a 50% reduction in medication nonpersistence rates. Screening costs were varied between 10% and 50% of DXA costs. A threshold cost analysis was also conducted to identify screening costs that would result in an ICER of $100,000.

Nonscreening parameters were also tested, including fracture incidence varied by ±25%, fracture costs varied by ±25%, and the effects of fractures on utilities adjusted by ±25%. A societal perspective was also incorporated by including the indirect costs of fractures, based on the study by Tran et al [30]. Recognizing that opportunistic review of chest radiographs may reveal incidental findings requiring further evaluation, we conducted a one-way sensitivity analysis varying the per-patient cost of downstream follow-up. This parameter ranged from $5 to $20, in $5 increments, reflecting plausible estimates of additional health care resource use associated with incidental findings.

To evaluate the impact of joint uncertainty across model variables, a probabilistic sensitivity analysis was conducted. In each of the 200 iterations, comprising 250,000 micro-simulations per iteration, random values were sampled for nearly all model variables based on their assigned probability distributions (details provided in e-only Appendix A). The results of the probabilistic sensitivity analysis were summarized using a cost-effectiveness acceptability curve, which depicts the proportion of simulations in which opportunistic osteoporosis screening was considered cost-effective at varying willingness-to-pay thresholds per QALY gained.

Model Validation

The study followed economic evaluation guidelines for osteoporosis from the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases-International Osteoporosis Foundation [3] and the 2022 Consolidated Health Economic Evaluation Reporting Standards statement [31]. The completed Consolidated Health Economic Evaluation Reporting Standards 2022 checklist and the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases-International Osteoporosis Foundation checklists are available in e-only Appendix B. To verify the model's robustness, validation steps included protocol review by a US clinical expert before analysis, sensitivity analyses with alternative assumptions to confirm expected outcome patterns, and comparison of model predictions with published data. Specifically, the model estimated that approximately 980,000 fractures (including 205,000 hip fractures) occur annually among US women aged 50 and older with osteoporosis. This figure is consistent with data from the Bone Health and Osteoporosis Foundation, which reports around 2,000,000 fractures, including 300,000 at the hip. The discrepancy is due to a significant proportion of fractures occurring in men and women without low bone mass.

RESULTS

In the base-case analysis, the opportunistic screening strategy, based on the performance of AI and other inputs, predicts that 79.9% of patients would not have osteoporosis, and 0.8% of VHR patients would receive sequential therapy,

3.2% of VHR patients would remain untreated, 3.4% HR patients would be treated with ALN monotherapy, and 12.7% of HR patients would remain untreated.

Base-Case Analysis

Table 2 presents the lifetime costs, number of fractures, life years, QALYs, and the ICER (expressed in US dollars per QALY gained) of the opportunistic osteoporosis screening followed by treatment compared with no screening and treatment in US women aged 50 years and above. Under real-world conditions, per 1,000 screened women, the incremental lifetime costs were $109,000, with health care savings of $99,000 offset by treatment costs of $208,000. The opportunistic screening strategy resulted in the prevention of 2.8 fractures and an increase of 1.5 QALYs, yielding an ICER of $72,085 per QALY gained. This value is below the US cost-effectiveness thresholds of $100,000 to $150,000 per QALY, suggesting the cost-effectiveness of the strategy.

Sensitivity Analyses

Sensitivity analyses confirmed the cost-effectiveness of opportunistic osteoporosis screening (Fig. 2). Medication adherence was a key factor: Reducing nonpersistence by 50% improved the ICER to $28,663, and full adherence lowered it further to $16,414. Higher osteoporosis prevalence, increased treatment initiation, and more DXA scans after osteoporosis detection moderately improved cost-effectiveness. Screening costs have a relatively limited impact on ICER, ranging from $63,311 (when screening costs are 10% of DXA costs) to $80,858 (at 50% of DXA costs). A threshold analysis indicated that the AI-tool cost of $62.10 would result in an ICER of $100,000. Increasing VHR patients by 50% raised the ICER to $87,718. Using specificity and sensitivity from the internal test had minimal impact on cost-effectiveness.

Sensitivity analyses of nonscreening parameters revealed that treatment efficacy, fracture incidence, drug costs, discount rates, and fracture-related costs moderately affect cost-effectiveness, with the ICER staying below $120,000 even in conservative scenarios. In contrast, excess mortality after fractures and fracture effects on utility had a limited impact. Interestingly, adopting a societal perspective lowered the ICER of $53,129, reflecting greater economic benefits. In the one-way sensitivity analysis assessing the impact of downstream follow-up costs for incidental findings, the ICER was $75,391 when the per-patient cost was set at $5, $78,697 at $10, $82,004 at $15, and $85,310 at $20.

Figure 3 displays the cost-effectiveness acceptability curves, illustrating that opportunistic osteoporosis screening is the most cost-effective strategy at the US threshold of $100,000 per QALY gained. It has an 82% probability of being cost-effective with real-world adherence, and a 99.5% with full adherence. At a higher threshold of $150,000 per QALY gained, these rise to 92.5% and 100%, respectively.

DISCUSSION

The study results indicate that opportunistic osteoporosis screening using chest radiographs enhanced by deep learning, followed by appropriate treatment, represents a cost-effective intervention for US women aged 50 years and older. The ICER was estimated at $72,085 per QALY gained, which falls below the US cost-effectiveness threshold of $100,000 to $150,000 per QALY, as recommended by the Institute for Clinical and Economic Review [29]. Interventions with ICERs below this range are generally considered cost-effective in the US context. Sensitivity analyses confirmed the robustness of these findings, demonstrating consistent cost-effectiveness across varying assumptions. Key factors influencing cost-effectiveness included screening follow-up, treatment initiation rates, medication adherence, treatment efficacy, screening age, drug costs, and fracture incidence.

Table 2. (Incremental) lifetime costs, QALYs, number of fractures prevented, and ICER of opportunistic osteoporosis screening with artificial intelligence chest radiographs versus no screening and treatment in US women aged 50+

Outcomes	Opportunistic Screening	No Screening and Treatment	Incremental per Women	Incremental per 1,000 Women
Total costs	24,574	24,465	109	109,000
Health care costs	24,366	24,465	−99	−99,000
Treatment costs	208	0	+208	+208,000
Number of fractures	0.939	0.942	−0.0028	2.8
Life-years	16.755	16.754	0.0010	1.0
Quality-adjusted life years	8.0309	8.0294	0.0015	1.5
ICER of opportunistic screening ($ per QALY gained)		72,085		

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life-year.

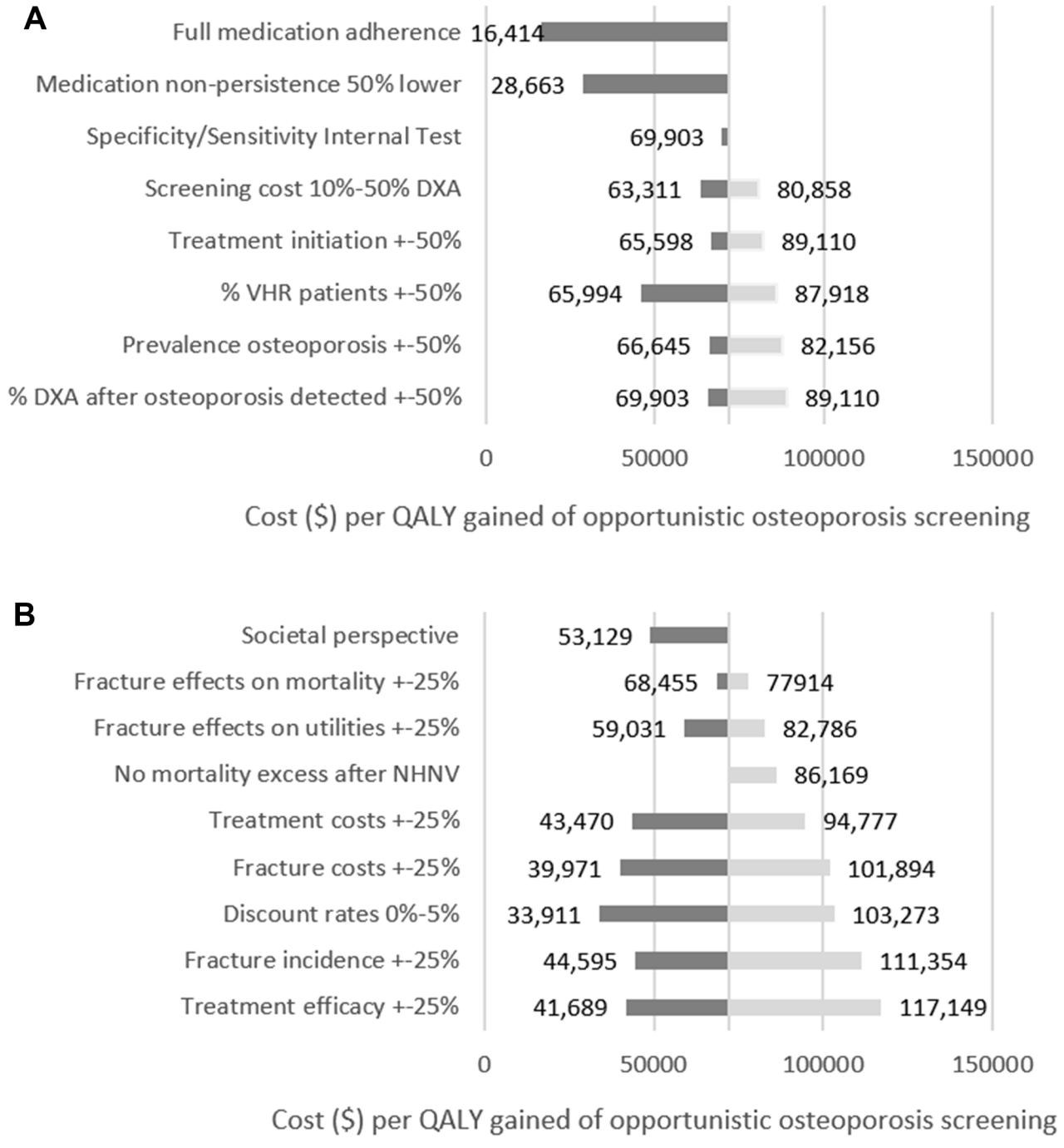

Fig. 2. Tornado diagrams depicting sensitivity analyses of cost-effectiveness ($ per QALY gained) for opportunistic osteoporosis screening with artificial intelligence-chest radiographs followed by treatment versus no screening and treatment in US women aged 50+. (A) Screening pathway parameters and (B) nonscreening parameters. DXA = dual-energy x-ray absorptiometry; NHNV = nonhip nonvertebral; QALY = quality-adjusted life-year; VHR = very high risk.

Interestingly, the analysis revealed that the intervention remained cost-effective as long as additional cost of the AI tool did not exceed $62 per patient.

With the growing osteoporosis burden due to the aging population in the US and the important treatment gap, it is important to find solutions to detect patients at risk. Although DXA is available and recommended for patients over 65 years of age by the US Preventive Services Task Force, osteoporosis diagnosis remains rare. Opportunistic AI-driven screening could thus serve as an alternative and complementary technique to identify at-risk patients earlier and cost-effectively.

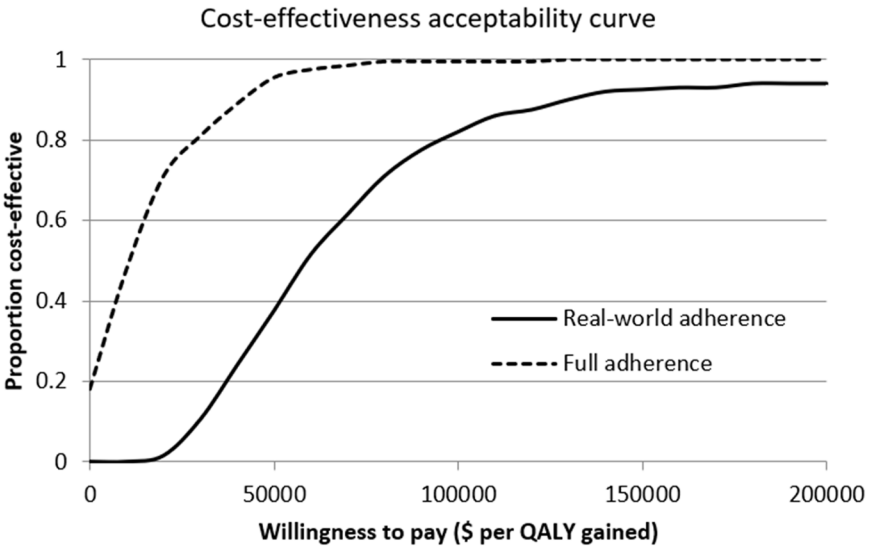

Fig. 3. Cost-effectiveness acceptability curves of opportunistic osteoporosis screening with artificial intelligence-chest radiographs followed by treatment versus no screening and treatment in US women aged 50 with full and real-world medication adherence. The curves illustrate the probability that the opportunistic osteoporosis screening is cost-effective at various cost per QALY gained thresholds. This is represented by the proportion of simulations in which the screening strategy proves to be cost-effective compared with no screening and treatment. A strategy with a probability exceeding 50% is considered the cost-effective choice. QALY = quality-adjusted life-year.

This cost-effectiveness study builds on the performance of the AI-enhanced screening tool reported in the study by Jang et al [21]. This tool is among the few validated on an external dataset, specifically using data from a health care facility and targeting the diagnosis of osteoporosis (T-score ≤ -2.5) [32-34]. Although the field is still in its early stages, with most AI-based solutions remaining at the proof-of-concept phase, accumulating evidence highlights the potential for broader integration of AI into radiologic workflows [35]. Although research on AI-driven screening interventions in other disease areas has demonstrated cost-effectiveness [36,37], and in some cases dominance [38], this study reinforce the potential economic benefits of AI in osteoporosis care, as also suggested by a similar study in Germany, reporting an ICER of €13,340 in its base case [39]. In addition, another cost-effectiveness study found that AI-based opportunistic screening for osteoporotic vertebral compression fractures using existing radiographs was cost-effective from a societal perspective [40].

The demonstrated cost-effectiveness of AI-driven screening could play a key role in influencing reimbursement decisions and encouraging the adoption of AI tools in clinical practice. By showing that AI models can improve early detection at a reasonable cost per QALY gained, this approach not only has the potential to enhance patient outcomes but also offers a sustainable, scalable solution for managing osteoporosis at the population level. Policymakers could leverage this evidence to prioritize funding for AI-driven health care solutions, improving accessibility and reducing long-term health care costs associated with osteoporotic fractures. Furthermore, AI screening could be particularly useful in tailoring approaches to reduce health care disparities, especially in underserved or resource-limited regions.

The findings of this economic study should be interpreted with certain limitations in mind. First, some model parameters relied on expert opinion and uncertainties remain regarding follow-up after screening, such as the proportion of patients undergoing DXA and initiating treatment after a positive result. Additionally, as is common in health economic modeling, input data were drawn from multiple sources, including studies on screening effectiveness, costs, utilities, and disease incidence. Although necessary for building a comprehensive model, combining data from various studies may introduce variability due to differences in populations and settings. The distribution of HR and VHR patients in an opportunistic screening approach is also uncertain. However, the model showed strong robustness, with results remaining stable across a wide range of sensitivity analyses. Incorporating real-world data in future studies could refine these estimates and enhance the accuracy of cost-effectiveness assessments. The base-case analysis, which supported cost-effectiveness, was grounded in realistic assumptions regarding screening follow-up and medication adherence. Additionally, the model's screening pathway was intentionally simplified, making it a conservative estimate of

potential benefits. For instance, the model excluded treatment for patients with osteopenia, despite some guidelines support, due to limited data on diagnostic accuracy and uncertainties on how many patients would actually receive treatment.

Other diagnostic tools such as DXA, radiofrequency echographic multispectrometry, quantitative CT, or quantitative ultrasound are also available for early diagnosis of osteoporosis, and they have been shown to be cost-effective in certain circumstances [7,41]. Although DXA remains the clinical reference standard for osteoporosis diagnosis, its use is often limited by accessibility, cost, and underutilization in asymptomatic populations. Importantly, screening tools are not necessarily mutually exclusive but can instead be complementary. This is also relevant because chest radiographs are not routinely performed for all women aged 50 years and older in the United States, meaning some patients with osteoporosis will remain undetected with this approach as well. However, AI-driven opportunistic screening using chest radiographs leverages imaging already acquired for other clinical reasons such as general health screenings, periodic checkups, and evaluations of symptoms like cough or fever. This approach offers a simpler and more practical. This enables osteoporosis detection without extra imaging, reducing patient burden and health care costs.

Another limitation of this study is that we did not account in the base-case analysis for downstream costs associated with incidental findings unrelated to osteoporosis that may be identified during the review of chest radiographs for opportunistic screening. Although our model assumes that the chest radiographs are obtained for existing clinical indications, the implementation of AI tools could increase the detection and follow-up of incidental findings. This may lead to both potential clinical benefits and additional health care costs. Future research should explore the scope and implications of these downstream effects more comprehensively. Finally, although this study supports the cost-effectiveness of opportunistic osteoporosis screening for US women aged 50 and older, the findings may not be directly generalizable to all other countries and populations due to differences in health care systems and costs, fracture incidence, treatment practices, and drug costs. Further analyses in men, in which osteoporosis medications have shown benefits comparable to those in women [42], as well as similar cost-effectiveness [4,43], would be important to confirm the cost-effectiveness of AI screening in men. As the fracture risk estimates in this study were derived from data on White women and racial and ethnic differences are documented in the US [44], suggesting the need for further research in more diverse populations.

In conclusion, this study suggests that opportunistic osteoporosis screening using AI-enhanced chest radiographs is a cost-effective strategy for US women aged 50 and older. Improving follow-up and medication adherence could further enhance its value. These findings highlight the public health potential of AI-driven screening to improve early detection and address gaps in osteoporosis care.

TAKE-HOME POINTS

- Current osteoporosis screening faces significant gaps, with many at-risk individuals undiagnosed and untreated.
- AI-enhanced analysis of existing chest radiographs enables opportunistic osteoporosis screening, improving early detection in women aged 50 and older.
- Economic modeling showed cost-effectiveness of opportunistic osteoporosis screening using AI-enhanced chest radiographs, with a cost of $72,085 per QALYs gained, below the US threshold of $100,000.
- Cost-effectiveness could be optimized when screening is paired with effective follow-up, timely treatment initiation, and adherence strategies.

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000 Cost-Effectiveness of Opportunistic Osteoporosis Screening Using Chest Radiographs With Deep Learning in the United States

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This study underscores the cost-effectiveness and public health significance of AI-driven screening, demonstrating its potential to improve early detection and address unmet diagnostic needs in osteoporosis care.