Radiology

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Osteoporotic Precise Screening Using Chest Radiography and Artificial Neural Network: The OPSCAN Randomized Controlled Trial

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Conflicts of interest are listed at the end of this article.

See also the editorial by Smith and Rothenberg in this issue.

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Background: Diagnosing osteoporosis is challenging due to its often asymptomatic presentation, which highlights the importance of providing screening for high-risk populations.

Purpose: To evaluate the effectiveness of dual-energy x-ray absorptiometry (DXA) screening in high-risk patients with osteoporosis identified by an artificial intelligence (AI) model using chest radiographs.

Materials and Methods: This randomized controlled trial conducted at an academic medical center included participants 40 years of age or older who had undergone chest radiography between January and December 2022 without a history of DXA examination. High-risk participants identified with the AI-enabled chest radiographs were randomly allocated to either a screening group, which was offered fully reimbursed DXA examinations between January and June 2023, or a control group, which received usual care, defined as DXA examination by a physician or patient on their own initiative without AI intervention. A logistic regression was used to test the difference in the primary outcome, new-onset osteoporosis, between the screening and control groups.

Results: Of the 40 658 enrolled participants, 4912 (12.1%) were identified by the AI model as high risk, with 2456 assigned to the screening group (mean age, 71.8 years ± 11.5 [SD]; 1909 female) and 2456 assigned to the control group (mean age, 72.1 years ± 11.8; 1872 female). A total of 315 of 2456 (12.8%) participants in the screening group underwent fully reimbursed DXA, and 237 of 315 (75.2%) were identified with new-onset osteoporosis. After including DXA results by means of usual care in both screening and control groups, the screening group exhibited higher rates of osteoporosis detection (272 of 2456 [11.1%] vs 27 of 2456 [1.1%]; odds ratio [OR], 11.2 [95% CI: 7.5, 16.7]; $P < .001$) compared with the control group. The ORs of osteoporosis diagnosis were increased in screening group participants who did not meet formalized criteria for DXA compared with those who did (OR, 23.2 [95% CI: 10.2, 53.1] vs OR, 8.0 [95% CI: 5.0, 12.6]; interactive $P = .03$).

Conclusion: Providing DXA screening to a high-risk group identified with AI-enabled chest radiographs can effectively diagnose more patients with osteoporosis.

Clinical trial registration no. NCT05721157

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Supplemental material is available for this article.

Osteoporosis affects around 200 million women globally, with an expected annual increase of 9 million individuals (1,2). This disease poses substantial economic impacts, which are primarily due to osteoporotic fractures (3). Despite the potential of antiosteoporotic treatments to reduce fracture risk (4), underdiagnosis and undertreatment are widespread (5). The diagnosis of osteoporosis predominantly relies on dual-energy x-ray absorptiometry (DXA) assessment of bone mineral density, a screening method that has proven effective in preventing fractures in women aged 65 years and older (6). However, DXA screening is underused (7), with only 30% of women and 4% of men aged 65 and older covered by Medicare reimbursing DXA (8), thus emphasizing the need for a risk-stratification tool to encourage screening among high-risk populations (9).

Radiologists can identify patients with potential osteoporosis by using various medical images and facilitate subsequent interventions (10), a practice known as opportunistic screening (11). The advent of deep learning models has prompted considerations for integrating artificial intelligence (AI) into radiologic daily practices for such screenings (12), with recent studies exploring its application in opportunistic screening for osteoporosis (13–16). Among these modalities, chest radiography is the

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Abbreviations

AI = artificial intelligence, DXA = dual-energy x-ray absorptiometry, FRAX = Fracture Risk Assessment Tool, ISCD = International Society for Clinical Densitometry, OPSCAN = Osteoporotic Precise Screening using Chest radiograph and Artificial neural Network, OR = odds ratio

Summary

An artificial intelligence model using chest radiographs identified individuals at high risk of osteoporosis, and screening of these patients with dual-energy x-ray absorptiometry resulted in increased rates of osteoporosis diagnosis.

Key Results

- In this randomized controlled trial involving 40 658 participants, 4912 were identified by an artificial intelligence model using chest radiographs as being high risk for osteoporosis and were assigned (2456 each group) to either screening group (offered complimentary dual-energy x-ray absorptiometry [DXA]) or contol (usual care) group.
- The screening group showed more osteoporosis detection (n = 272) than the control group (n = 27) (odds ratio [OR], 11.2; P < .001), especially those who did not meet formalized criteria for DXA compared with those who did (OR, 23.2 vs 8.0; P = .03).

most performed imaging test globally, with more than 2 billion procedures conducted annually (17). Notably, AI algorithms developed to assess chest radiographs have achieved an impressive area under the receiver operating characteristic curve of approximately 90% for diagnosing osteoporosis (18,19), surpassing commonly used assessment tools such as the Fracture Risk Assessment Tool (FRAX) (20).

Large-scale trials such as the SCreening Of Older women for the Prevention of fractures study, or SCOOP (21), the Cohort for Skeletal Health in Bristol and Avon study, or COSHIBA (22), and the Risk-stratified Osteoporosis Strategy Evaluation study, or ROSE (23), have used tools akin to the FRAX score (20). Demographics and medical history were used to identify a high-risk group and offered them DXA examinations. However, their outcomes have shown limited positive predictive values and economic benefit (24). To our knowledge, no prospective studies have examined the potential use of AI in opportunistic screening for osteoporosis. Opportunistic screening may be particularly promising for patients who do not meet the International Society for Clinical Densitometry (ISCD) formalized criteria for bone density testing with DXA (25). Our purpose was to evaluate the effectiveness of DXA screening in high-risk patients with osteoporosis identified by an AI model, version 1.0 *(https://linchin.ndmctsgh.edu.tw/shiny/OPSCAN/)* using chest radiographs.

Materials and Methods

Study Participants and Design

This study received ethical approval from the institutional review board at Tri-Service General Hospital (institutional review board no. A202205179), and all participants provided informed consent for their data to be analyzed. Reporting adhered to the Consolidated Standards of Reporting Trials extension for randomised controlled trials conducted using cohorts and routinely collected data (CONSORT-ROUTINE) extension checklist guidelines (26).

The Osteoporotic Precise Screening using Chest Radiography and Artificial neural Network (OPSCAN) program was designed as a randomized controlled trial to evaluate the effectiveness of DXA screening in high-risk patients with osteoporosis identified by an AI using chest radiographs. The details of trial design are detailed in Appendix S1. The OPSCAN trial (ClinicalTrials.gov no. NCT05721157) is an open-label randomized controlled trial that took place from January 2023 to June 2023 at Tri-Service General Hospital, an academic medical center in Taiwan. The trial consecutively included people aged 40 years or older who had undergone at least one chest radiography examination between January 2022 and December 2022. Participants who died in 2022 were excluded as were participants who had a history of receiving prescription antiosteoporotic treatment (excluding vitamin D or calcium), had undergone DXA examination at some point in their lifetime, or had osteoporosis or osteoporotic fracture. A previously developed deep learning model (details below) was then used to identify participants whose AI-enabled chest radiographs predicted probabilities of 0.426 or greater in more than 66% of chest radiographs. These participants were deemed high risk for osteoporosis and were randomized 1:1 into a screening or control group by an independent database programmer from Tri-Service General Hospital. For comparative purposes, participants identified as low risk by the AI were also analyzed at the conclusion of the trial.

Participants randomized to the screening group were contacted and informed that the AI algorithm had identified them as being at high risk for osteoporosis. Participants were offered a fully reimbursed DXA examination, simultaneously covering the lumbar spine and hip, and those willing to participate were scheduled for the examination. It is important to note that the intervention in OPSCAN only included notification and examination costs; subsequent pharmaceutical treatments were determined through discussions between the participants and their primary care physicians. For comparitive purposes, the high-risk control and low-risk groups were not informed of the results of AI-enabled chest radiography during this trial.

All participants were observed to the end of the study period. Baseline characteristics and disease history, identified by International Classification of Diseases codes, were extracted from electronic medical records (Table S1). Records of antiosteoporotic treatments were also retrieved from electronic medical records.

Deep Learning Model

We trained a convolutional neural network based on DenseNet (27) architecture before this trial. It takes chest radiographs as the input. Appendix S2 provides all the details regarding the training and test of this model. In summary, we obtained 25 574 chest radiographs for training and 4878 chest radiographs for validation. An external test set involving 5371 chest radiographs obtained from another hospital showed an area under the receiver operating characteristic curve of 0.89. The training code is publicly accessible on GitHub *(https://github.com/xup6fup/OPSCAN)*, and a website (version 1.0) allows users to upload chest radiographs to repeat this trial *(https://linchin.ndmctsgh.edu.tw/app/OPSCAN/)*.

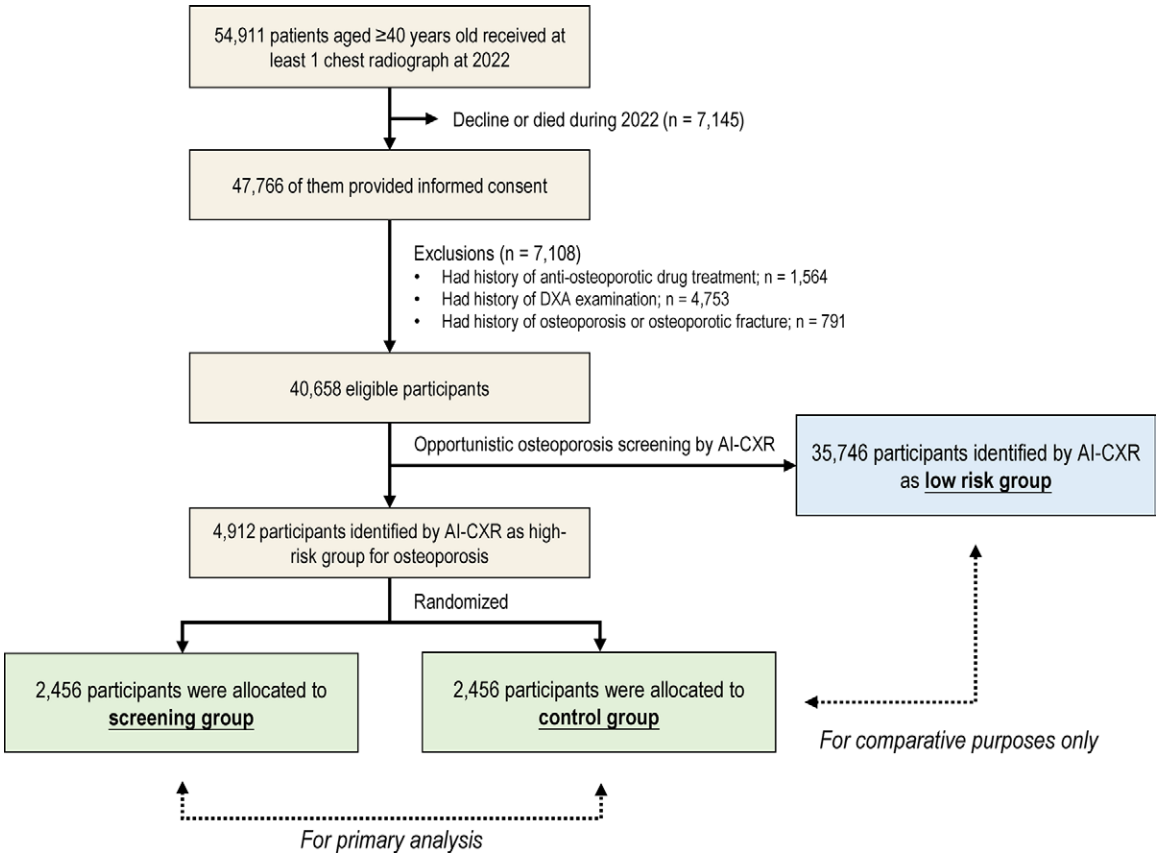

Figure 1: Consolidated Standards of Reporting Trials, or CONSORT, flow diagram of patient selection. Of 54911 patients who underwent chest radiography (CXR) between January and December 2022, 40658 matched the study criteria, including 4912 participants identified as high risk by an artificial intelligence (AI) using chest radiographs. They were randomized 1:1 into a screening group, which were offered fully reimbursed dual-energy x-ray absorptiometry (DXA) examinations between January and June 2023, or a control group, which received usual care, defined as DXA examination by a physician or patient on their own initiative without AI intervention. For comparative purposes, participants identified as low risk by the AI and receiving usual care were also analyzed at the conclusion of the trial.

DXA Procedures

The Lunar Prodigy (GE Healthcare) and Lunar iDXA (GE Healthcare) machines were used to perform proximal femoral and lumbar spine DXA examinations. Both machines are narrow-angle fan-beam densitometers. Spine DXA scans were obtained from the L1 to L4 vertebrae, and femur DXA scans were obtained from bilateral proximal femurs. The spine DXA scans were collected in the anterior-posterior direction. Femur DXA scans were obtained in the anterior-posterior direction with lower extremity internally rotated 15°–30°.

Evaluations

DXA data were analyzed with Encore, version 13.6 (Lunar Prodigy) and Encore, version 17.4 (Lunar iDXA) software (details in Appendix S3). The T score was calculated using the manufacturer's reference values for women aged 20–29 years. For each participant, the lowest T score of the hip or lumbar spine was used to categorize osteoporosis. A board-certified radiologist with 35 years of experience interpreted examination results using all electronic health records.

FRAX scores were calculated before and after the DXA examination, comparing alterations in the 10-year risk of major osteoporotic and hip fractures induced by the testing (details in Appendix S4).

Primary and Secondary Outcomes

The primary end point was new-onset osteoporosis, defined by a T score of less than or equal to −2.5. The secondary end points were whether participants underwent DXA examinations and initiation of treatments. It was notable that treatment decisions are guided by FRAX scores (details in Appendix S4), meaning individuals with a T score greater than −2.5 may still receive treatment. Exploratory analyses comparing types, affected regions, and specific treatments were also performed.

Statistical Analysis

The statistical power was estimated by considering a presumed 2% incidence of primary end points over a 6-month period in the control group (21). Given an anticipated 20% willingness for DXA screening and a 70% positive predictive value, it was hypothesized that 14% of the screening group would meet the primary end point. At a significance level of $P = .05$, this yielded a statistical power exceeding 99.9%.

The statistical analysis plan is detailed in Appendix S5. Based on intention to treat, a simple logistic regression was used to assess the differences in primary and secondary end points in the entire sample. For each cascade of events (DXA to diagnosis to treatment), we calculated the conditional probabilities and tested them with the χ^2 test. The prespecified confirmatory or

stratified analysis is based on ISCD indications (25). After calculating the 10-year risk for each patient using the FRAX tool, we assessed the difference between patients with and patients without the OPSCAN-offered DXA using Wilcoxon rank sum test (R package "stats;" version 3.4.4) to determine the significance of the disparity. Statistical analyses were performed (C.L.) using R (version 3.4.4, The R Foundation), and a $P < .05$ was considered to indicate a statistically significant difference. The analysis code is publicly accessible on GitHub *(https://github.com/xup6fup/OPSCAN)*.

Results

Participant Characteristics

A total of 54 911 patients were initially identified, of whom 7145 declined to participate or died during 2022 (Fig 1). Among the 47 766 participants who provided informed consent, 1564 participants were excluded due to a history of antiosteoporotic drug use, 4753 underwent prior DXA examination at some point in their lifetime, and 791 were diagnosed with osteoporosis or osteoporotic fracture. Ultimately, 91 911 chest radiographs (Appendix S6) from 40 658 participants were assessed by the AI algorithm and 4912 were identified as indicating high risk of osteoporosis. These participants were then randomized to the control group (n = 2456; mean age, 72.1 years ± 11.8 [SD]; 1872 female, 584 male) or screening group (n = 2456; mean age, 71.8 years ± 11.5; 1909 female, 547 male). In the screening group, 1676 of 2456 (68.2%) participants had only one chest radiograph, whereas in the control group, 1625 of 2456 (66.2%) participants had only one chest radiograph (Table 1). Notably, no evidence of a difference in participant characteristics was observed between the two groups.

Comparison of AI-identified High-Risk and Low-Risk Groups

Our observations indicate that AI-enabled chest radiography primarily uses skeletal information from the lung field, encompassing the thoracic vertebrae and ribs, while excluding regions overlapping with abdominal soft tissues (Fig 2). Compared with participants identified by the AI as being at low risk for osteoporosis (n = 35 746), the high-risk participants (n = 4912) were older, included a higher proportion of female participants, had a lower body mass index, and had a higher prevalence of risk factors for osteoporosis (Table S7). A total of 665 participants underwent DXA examination in the study period (Tables S8–S10). For comparative purposes, the high-risk control group underwent a higher proportion of physician-arranged DXA examinations (Fig S8). Compared with participants in the low-risk group who underwent physician-recommended DXA examinations, the high-risk control group exhibited a higher positive predictive value for osteoporosis identification (75.0% [27 of 36] vs 15.1% [41 of 271]; $P < .001$) (Fig 3). In the screening group, the positive predictive value consistently remained above 75% (Table S11).

Overall Effectiveness of the OPSCAN Program

Of the 2456 participants in the screening group, 12.8% (315 of 2456) underwent the free DXA examination offered by OPSCAN, and an additional 1.8% (43 of 2456) underwent DXA examinations through their primary care physicians (Fig 4). The remaining 85.4% (2098 of 2456) had no DXA record despite being informed of their high-risk status. Of those

Table 1: Baseline Participant Characteristics in the Screening and Control Group

Variable	Screening (n = 2456)	Control (n = 2456)	P Value
No. of analyzed chest radiographs			.27
1	1676 (68.2)	1625 (66.2)	…
2 or 3	447 (18.2)	466 (19.0)	…
4 or 5	112 (4.6)	138 (5.6)	…
>5	221 (9.0)	227 (9.2)	
Proportion of positive chest radiographs			.63
66%–79%	179 (7.3)	188 (7.7)	…
≥80%	2277 (92.7)	2268 (92.3)	…
Sex			.21
Male	547 (22.3)	584 (23.8)	…
Female	1909 (77.7)	1872 (76.2)	…
Age (y)	71.8 ± 11.5	72.1 ± 11.8	.52
Age group (y)			.92
<65	676 (27.5)	678 (27.6)	…
65–74	851 (34.6)	838 (34.1)	…
≥75	929 (37.8)	940 (38.3)	…
BMI	23.1 ± 3.9	23.0 ± 3.7	.68
BMI group			.77
<18.5	246 (10.0)	238 (9.7)	…
18.5–23.9	1310 (53.3)	1335 (54.4)	…
≥24.0	900 (36.6)	883 (36.0)	…
History of fracture	261 (10.6)	287 (11.7)	.22
Hip	74 (3.0)	72 (2.9)	.87
Wrist	82 (3.3)	84 (3.4)	.88
Vertebra	44 (1.8)	56 (2.3)	.23
Shoulder	34 (1.4)	47 (1.9)	.15
Lower leg	60 (2.4)	58 (2.4)	.85
History of secondary osteoporosis	118 (4.8)	118 (4.8)	>.99
Hyperparathyroidism	28 (1.1)	26 (1.1)	.78
Hyperthyroidism	90 (3.7)	89 (3.6)	.94
Multiple myeloma	6 (0.2)	11 (0.4)	.22
Cushing disease	4 (0.2)	3 (0.1)	>.99
Celiac disease	1 (0.0)	1 (0.0)	>.99
History of rheumatoid arthritis	65 (2.6)	68 (2.8)	.79
History of long-term use of glucocorticoids	268 (10.9)	274 (11.2)	.79

Note.—Categorical data are reported as numbers of participants with percentages in parentheses, and continuous data are reported as means ± SDs. The Student t test or the χ^2 test is used to assess difference in means and percentages, respectively. The P value was two sided, with no adjustment for multiple comparisons. BMI = body mass index, DXA = dual-energy x-ray absorptiometry.

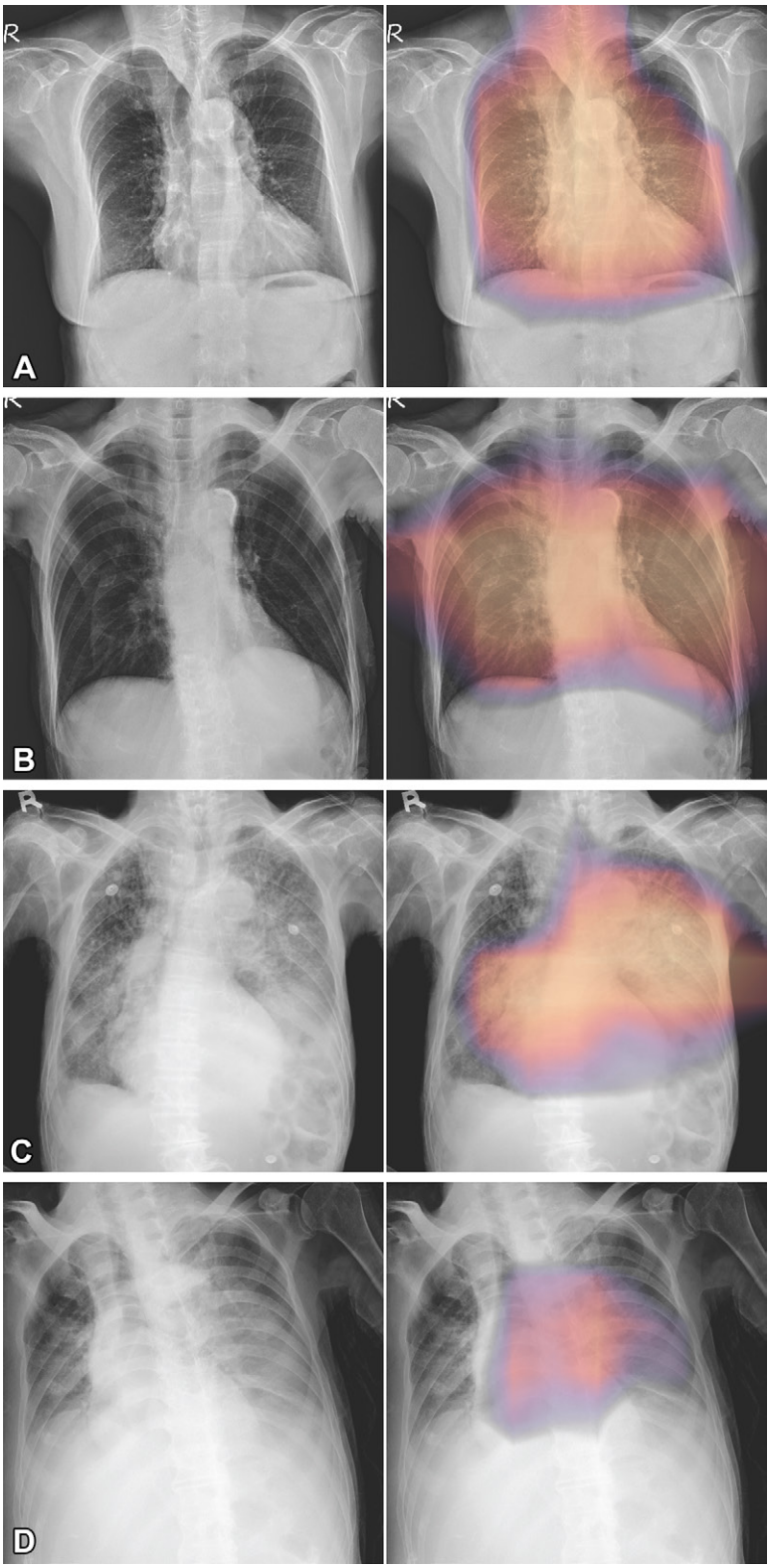

Figure 2: Images demonstrate how artificial intelligence (AI) using chest radiographs makes decisions. Left: Original chest radiographs in posterior-anterior view. Right: Class activation maps generated by overlays (colored probability maps) onto the original image. Orange, red, purple, and blue in order indicate higher probabilities, with regions where AI-enabled chest radiography predictions fall below 0.426 left uncolored. Observations indicate that AI-enabled chest radiography primarily uses skeletal information from the lung field, encompassing the thoracic vertebrae and ribs, while excluding regions overlapping with abdominal soft tissues. This phenomenon may be attributed to the relatively limited presence of soft tissues within the lung field, which provides AI-enabled chest radiography with a clearer perspective for assessing bone density. **(A, B)** Images with true-positive findings. Digital radiographs in **(A)** a 79-year-old woman with dementia and hypertension and a T score of −3.4 and **(B)** an 87-year-old woman with osteoarthritis of the knee and a T score of −2.7. The AI-enabled chest radiography mainly focused on the vertebrae and ribs around patient's heart and lung field. **(C, D)** Images with false-positive findings. **(C)** Computed radiograph in a 94-year-old man with chronic obstructive pulmonary disease with pneumonia and a T score of −2.3. **(D)** Digital radiograph in an 84-year-old man with colon cancer stage 3B after surgery and chemotherapy with recurrence and multiple metastasis and a T score of −0.6. Some lung parenchymal disease or lesion was noticed, such as pneumonia and fibrosis, which may have interfered with AI-enabled chest radiography interpretation of osteoporosis. We assumed that these lesions may hinder AI-enabled chest radiography analysis of bony skeleton while comparing with lung parenchyma radiolucency. Pneumonia, pulmonary edema, and fibrosis will lead to airspace opacification and increase radiolucency of lung parenchyma. Therefore, they reduce the radiolucency difference between bony structures and lung parenchyma, leading to an overdiagnosis of osteoporosis.

who underwent the free DXA examination, 237 of 315 individuals were diagnosed with osteoporosis (positive predictive value, 75.2%). Subsequently, 31.6% (75 of 237) of the diagnosed individuals chose to pursue antiosteoporotic treatment after consultations with their physicians.

Diagnosis of Osteoporosis in Screening versus Control Group

Regarding the primary end point, 11.1% (272 of 2456) of participants in the screening group were newly diagnosed with osteoporosis compared with 1.1% (27 of 2456) in the control group, with participants in the screening group showing higher odds of diagnosis of new-onset osteoporosis than the control group (OR, 11.2 [95% CI: 7.5, 16.7]; $P < .001$) (Fig 5). There was no evidence of a difference between screening (43 of 2456, 1.8%) and control (36 of 2456, 1.5%) groups for DXA examinations arranged by primary care physicians (OR, 1.2 [95% CI: 0.8, 1.9]; $P = .43$). By facilitating the free DXA examinations provided through the OPSCAN program, the screening group had higher odds of DXA use than did the control group (OR, 11.5 [95% CI: 8.1, 16.2]; $P < .001$). Additionally, a greater proportion of individuals in the screening group initiated antiosteoporotic treatment (OR, 5.3 [95% CI: 3.2, 8.8]; $P < .001$) than in the control group. Regarding antiosteoporotic treatment, the most notable increase was in denosumab usage (OR, 6.9 [95% CI: 3.7, 13.0]; $P < .001$).

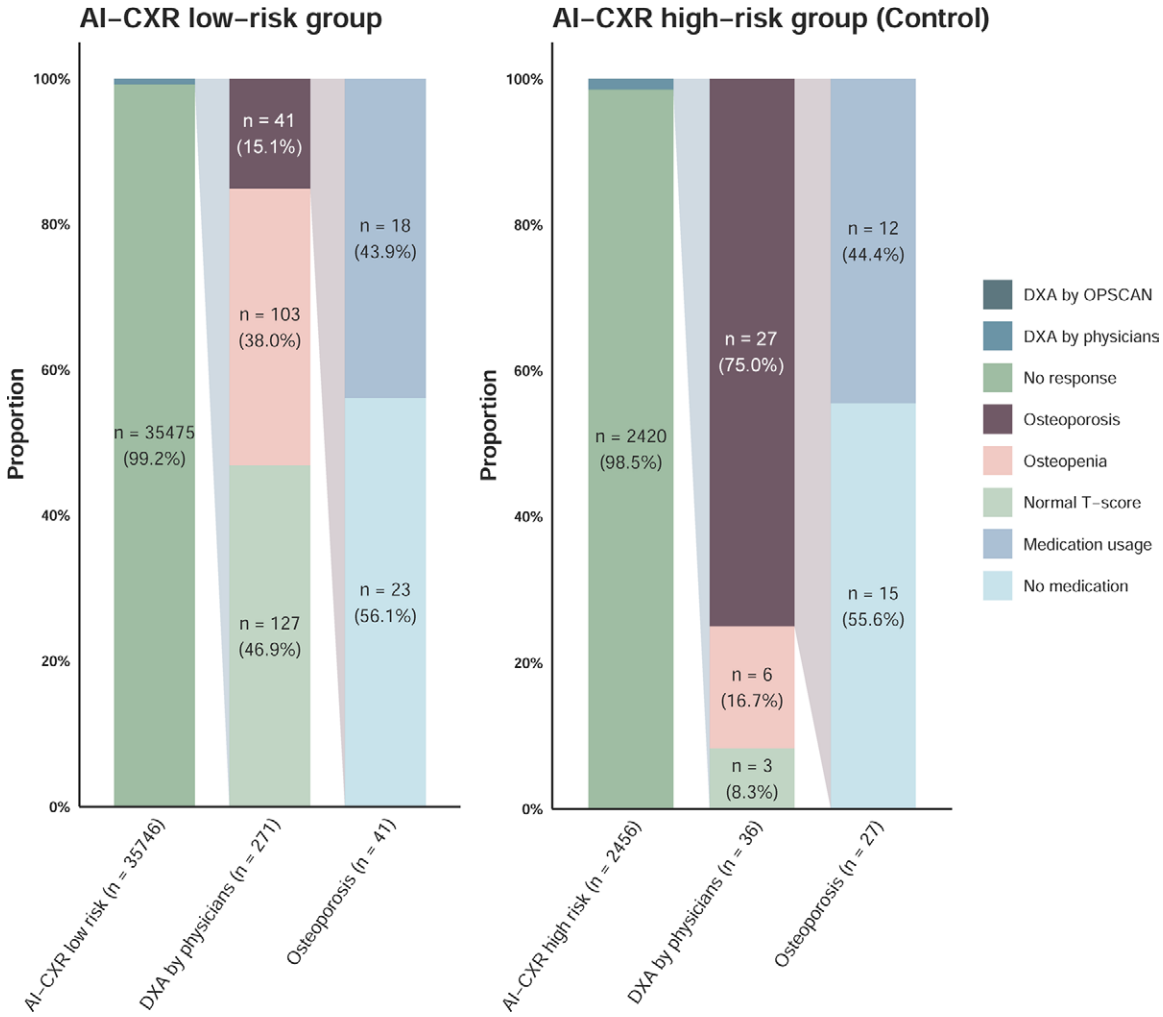

Figure 3: Graphs show effectiveness of dual-energy x-ray absorptiometry (DXA) for osteoporosis diagnosis and treatment in artificial intelligence (AI)–enabled chest radiographs (AI-CXR) in identifying high- and low-risk groups. Stacked bar plots display the proportion and percentage of events by each condition except for those with a percentage of less than 5%. In this analysis, the high-risk group only included participants in the control group since they also received the usual care like participants in the low-risk group. Of 35746 participants in the low-risk group, 0.8% (271 individuals) underwent DXA arranged by primary care physicians. Within this group, 41 of 271 individuals (15.1%) were diagnosed with osteoporosis (T score ≤ −2.5), while the remaining 103 (38.0%) were classified as having osteopenia (−2.5 < T score ≤ −1.0). Of 2456 participants in the control group (high risk), 1.5% (36 individuals) underwent DXA arranged by primary care physicians. In the control group, 27 (75.0%) participants who underwent DXA were diagnosed with osteoporosis, which was significantly higher than in the low-risk group ($P < .001$) as assessed with the χ^2 test. In all participants diagnosed with osteoporosis, the medication rates in both groups were similar (18 of 41 [43.9%] vs 12 of 27 [44.4%]; $P > .99$). It is important to note that while a T score of less than or equal to −2.5 is a key determinant for initiating antiosteoporotic treatment, there are still some individuals with a T score greater than −2.5 who receive treatment (six of 42 in high- and low-risk groups), which is not reflected in this figure. OPSCAN = Osteoporotic Precise Screening using Chest Radiography and Artificial neural Network.

Effectiveness of the OPSCAN Program in Subgroups of Participants

While a higher proportion of individuals not meeting ISCD indication agreed to undergo DXA examination through the OPSCAN program compared with those who did (20.1% vs 9.6%; $P < .001$), no evidence of a difference was observed in positive predictive values for osteoporosis (70.2% vs 79.9%; $P = .06$) or antiosteoporotic treatment (25.5% vs 36.6%; $P = .09$) between these subgroups (Table 2). Table S12 shows the results of physician-driven DXA examination in the control group. Table S14 displays the results stratified by radiologic parameters, with the interpretation of the data provided in Appendix S7.

Stratified Analysis according to ISCD Indication

In the subgroup of participants not meeting ISCD indication for DXA based on sex and age, the screening group showed increased odds for undergoing DXA examination (OR, 18.9 [95% CI: 10.2, 35.1]; $P < .001$) and increased odds of new-onset osteoporosis detection (OR, 23.2 [95% CI: 10.2, 53.1]; $P < .001$) compared with the control group (Fig 6A). These ORs were higher than those achieved by the screening group in the subgroup of participants who did meet ISCD indication (DXA examination OR, 8.6 [95% CI: 5.7, 13.2]; $P < .001$; interactive $P = .04$; new-onset osteoporosis OR, 8.0 [95% CI: 5.0, 12.6]; $P < .001$; interactive, $P = .03$). No other factors were found to influence the effectiveness of the OPSCAN program (Appendix S7).

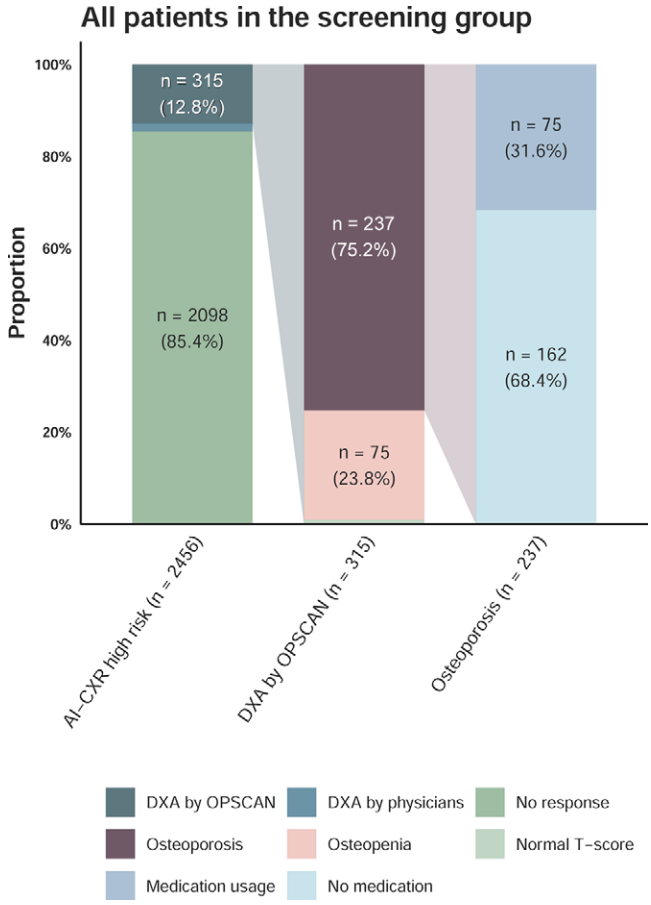

Figure 4: Effectiveness of the screening program for osteoporosis diagnosis and treatment. Stacked bar plots display the proportion and percentage of events by each condition, except for those with a percentage of less than 5%. Of 2456 participants in the screening group, 12.8% (315 individuals) used the fully reimbursed dual-energy x-ray absorptiometry (DXA) examination offered by Osteoporotic Precise Screening using Chest Radiography and Artificial neural Network (OPSCAN), and the remaining 85.4% (2098 individuals) had no DXA records despite being informed of their high-risk status. There were 43 (1.8%) participants who underwent DXA arranged by primary care physicians in the screening group. While DXA arranged by participants' primary care physicians may potentially identify some participants with osteoporosis (T score ≤ −2.5), our analysis focused solely on those who underwent the free DXA examination to demonstrate OPSCAN's effectiveness. Within this group, 237 of 315 individuals (75.2%) were diagnosed with osteoporosis, while the remaining 75 (23.8%) were classified as having osteopenia (−2.5 < T score ≤ −1.0). Of all DXA examinations paid for by this trial, three of 315 (1.0%) participants had normal T scores (> −1.0). Of 237 patients with osteoporosis, 31.6% (75 individuals) chose to pursue antiosteoporotic treatment after consultations with their physicians. It is important to note that while a T score of less than or equal to −2.5 is a key for initiating antiosteoporotic treatments, there are still some individuals with a T score greater than −2.5 who receive treatment (*n* = 17), which is not reflected in this figure.

Osteoporotic and Hip Fracture Risk in the Screening Group before and after DXA Examination

Prior to the DXA examination, participants in the screening group who did not meet ISCD indication showed lower risk of osteoporosis and hip fracture than the subgroup of participants who did meet ISCD indication (Tables S15, S16). However, after undergoing DXA, the subgroup not meeting ISCD indication showed an average risk ratio of 2.10 (± 1.14) and 7.04 (± 9.36) for 10-year major osteoporotic risk and hip fracture risk, respectively, which were higher than the increase observed in the subgroup meeting ISCD indication (10-year major osteoporotic risk ratio, 1.38 ± 0.55; 10-year hip fracture risk ratio, 1.85 ± 1.63; $P < .001$ for all) (Fig 6B). Furthermore, participants older than 75 years of age showed no evidence of a difference in hip fracture risk before versus after DXA examination (Appendix S8).

Discussion

Dual-energy x-ray absorptiometry (DXA) screening for high-risk population of osteoporosis is important (5). We applied artificial intelligence (AI) to chest radiographs to identify high-risk individuals of osteoporosis, and the Osteoporotic Precise Screening using Chest Radiography and Artificial neural Network program offered fully reimbursed DXA examinations. A total of 315 of 2456 (12.8%) participants identified by AI as being high risk for osteoporosis and randomized to the screening group underwent fully reimbursed DXA, of whom 237 of 315 (75.2%) were diagnosed with new-onset osteoporosis. Higher odds of osteoporosis detection (odds ratio [OR], 11.2 [95% CI: 7.5, 16.7]; $P < .001$) and treatment initiation (OR, 5.3 [95% CI: 3.2, 8.8]; $P < .001$) were observed in the screening versus control group. The OR of osteoporosis diagnosis was increased in screening group participants who did not meet the International Society for Clinical Densitometry's formalized criteria for DXA compared with those who did (OR, 23.2 vs 8.0; interactive $P = .03$).

The OPSCAN trial achieved a positive predictive value of 75.2%, surpassing SCreening Of Older women for the Prevention of fractures study (SCOOP) trial of 31.9% (21), Cohort for Skeletal Health in Bristol and Avon study (COSHIBA) trial of 25.8% (22), and Risk-stratified Osteoporosis Strategy Evaluation study (ROSE) trail of 24.7% (23). Due to the poor positive predictive value, the differences in antiosteoporotic treatment between the screening group and control group were only 1.4-fold in SCOOP trial (21), 2.2-fold in COSHIBA trial (22), and 1.3-fold in ROSE trial (23). In contrast, 5.3-fold (95% CI: 3.2, 8.8; $P < .001$) of antiosteoporotic treatment was observed in the OPSCAN trial, suggesting that AI-enabled chest radiography–based DXA screening strategy may have the potential for reducing fractures in the future.

The rate of 14.6% of high-risk participants undergoing DXA examinations (12.8% OPSCAN reimbursed and 1.8% physician driven) in our study is lower than in previous trials (21–23). We observed that participants were skeptical about the ability of AI to detect osteoporosis on chest radiographs during participant notification, a phenomenon previously called medical AI aversion (28). Higher health literacy correlates with AI acceptance (29), whereas factors such as older age, male sex, and lower socioeconomic status are linked to reduced health literacy (30). Age significantly influenced acceptance of DXA examination in our study (19.7% for < 65 years, 13.4% for 65–74 years, and 7.3% for ≥ 75 years; $P < .001$). There is an imperative for broader promotion and education to maximize the benefits of osteoporosis screening with AI-enabled chest radiography.

In the absence of traditional risk factors, the ISCD indications for DXA testing only encompass women over 65 and men over 70 years of age (25). However, after AI-enabled chest radiography stratification, high-risk participants who did not meet

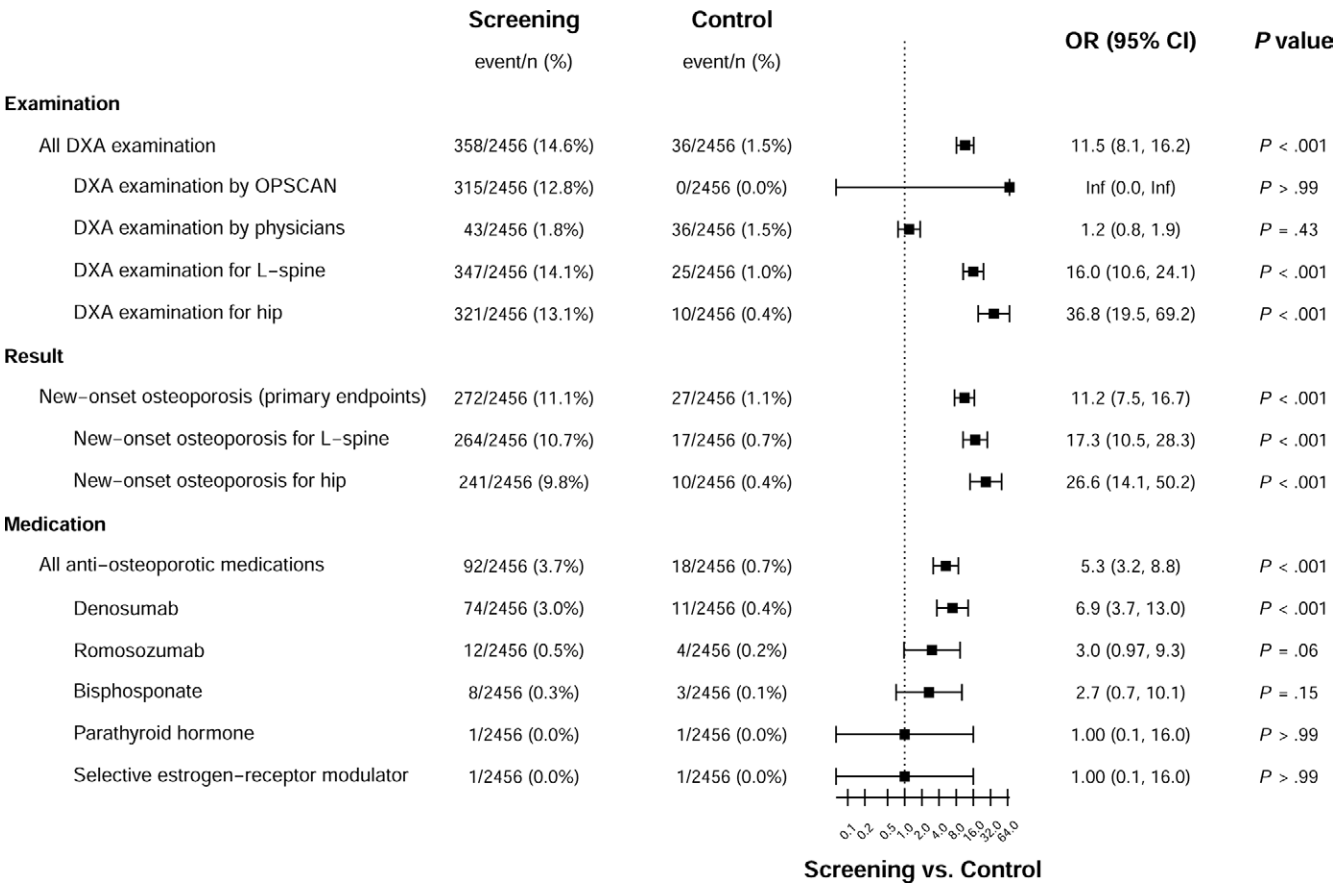

Figure 5: The intention-to-treat analysis for number of examinations and osteoporosis diagnosis and treatment. Forest plot shows the differences between the screening group and the control group with prespecified primary and secondary end points. Odds ratios (ORs), calculated using logistic regression, are represented by center squares, while 95% CIs are indicated by error bars, illustrating the benefits of the OPSCAN program. For dual-energy x-ray absorptiometry (DXA) examinations, stratification is based on the source (Osteoporotic Precise Screening using Chest Radiography and Artificial neural Network [OPSCAN] or physician) and site (lumbar spine or hip). Stratification for new-onset osteoporosis is based on the DXA examination site (lumbar spine or hip), while for antiosteoporotic medication, further stratification is performed based on the type. The screening group exhibited higher rates of DXA examinations (358 of 2456 [14.6%] vs 36 of 2456 [1.6%]; OR, 11.5 [95% CI: 8.1, 16.2]; $P < .001$) compared with the controls, leading to increased rates of osteoporosis detection (272 of 2456 [11.1%] vs 27 of 2456 [1.1%]; OR, 11.2 [95% CI: 7.5, 16.7]; $P < .001$) and treatment initiation (92 of 2456 [3.7%] vs 18 of 2456 [0.7%]; OR, 5.3 [95% CI: 3.2, 8.8]; $P < .001$). It is worth noting that out of the 92 patients in screening and 18 patients in the control group receiving antiosteoporotic treatments, only 75 and 12 patients, respectively, had a T score of less than or equal to −2.5, while the remaining 17 and six patients, respectively, had a T score greater than −2.5.

ISCD indications still had 70.2% confirmed as having osteoporosis through DXA testing in our study. The OPSCAN program marked a 23.2-fold (95% CI: 10.2, 53.1; $P < .001$) surge in new diagnoses in participants in the screening versus control group who did not meet the ISCD criteria, underscoring limitations of these criteria. Crucially, our data show that 10-year major osteoporotic risk (risk ratio, 2.10 ± 1.14; $P < .001$) and hip fracture risk (risk ratio, 7.04 ± 9.36; $P < .001$), which is a basis for determining antiosteoporotic treatment (31), were increased after DXA examination for participants who did not meet ISCD indications. The AI-enabled chest radiography can opportunistically pinpoint individuals who would most benefit from DXA, facilitating more precise medication adjustments.

This study had limitations. First, the study was conducted in a single center and thus results may not be generalizable in different settings. Second, we relied on electronic medical records, which might have incomplete documentation. Third, blinding for participants in the control group was unfeasible, potentially leading to them seeking treatment more proactively. Fourth, when participants in the OPSCAN program were informed of their AI-determined osteoporosis risk they were offered a fully reimbursed DXA examination, which may have influenced their decision to undergo DXA. Hence, our conclusions are most relevant in a situation when DXA is fully subsidized. Fifth, only a small proportion of participants underwent DXA testing (14.6%), which diminishes the utility of the OPSCAN program. Sixth, the lack of fully reimbursed DXA examinations for the low-risk group may have resulted in a higher proportion of individuals in this group undergoing physician-driven DXA testing for osteoporosis compared with the population prevalence. Nonetheless, AI-enabled chest radiography still shows effectiveness of risk stratification for osteoporosis. Lastly, the study primarily assessed the OPSCAN program's efficacy in risk identification and treatment initiation, without evaluating long-term outcomes or fracture prevention. Future research should include more diverse data sets and longer follow-ups to fully ascertain the program's benefits.

In conclusion, this randomized controlled trial highlights the potential of dual-energy x-ray absorptiometry

Table 2: Effectiveness of the OPSCAN Program for Examinations and Osteoporosis Diagnosis and Treatment Stratified according to Various Participant Characteristics in the Screening Group

Variable	DXA through OPSCAN*	*P* Value	Osteoporosis†	*P* Value	Medical Treatment‡	*P* Value
Stratification by ISCD indication		<.001		.06		.09
Men aged <70 y or women aged <65 y	151/751 (20.1)		106/151 (70.2)		27/106 (25.5)	
Men aged ≥70 y or women aged ≥65 y	164/1705 (9.6)		131/164 (79.9)		48/131 (36.6)	
No. of analyzed chest radiographs		.02		.14		.12
1	230/1676 (13.7)		166/230 (72.2)		52/166 (31.3)	
2 or 3	56/447 (12.5)		45/56 (80.4)		10/45 (22.2)	
4 or 5	15/112 (13.4)		14/15 (93.3)		7/14 (50.0)	
>5	14/221 (6.3)		12/14 (85.7)		6/12 (50.0)	
Proportion of positive chest radiographs		.03		.26		.65
66%–79%	13/179 (7.3)		12/13 (92.3)		5/12 (41.7)	
≥80%	302/2277 (13.3)		225/302 (74.5)		70/225 (31.1)	
Sex		.33		.34		.84
Male	63/547 (11.5)		44/63 (69.8)		15/44 (34.1)	
Female	252/1909 (13.2)		193/252 (76.6)		60/193 (31.1)	
Age group (y)		<.001		.18		.13
<65	133/676 (19.7)		94/133 (70.7)		23/94 (24.5)	
65–74	114/851 (13.4)		87/114 (76.3)		30/87 (34.5)	
≥75	68/929 (7.3)		56/68 (82.4)		22/56 (39.3)	
BMI group		.10		.38		.88
<18.5	21/246 (8.5)		18/21 (85.7)		5/18 (27.8)	
18.5–23.9	176/1310 (13.4)		134/176 (76.1)		44/134 (32.8)	
≥24.0	118/900 (13.1)		85/118 (72.0)		26/85 (30.6)	
History of all fractures		.70		.16		.67
No	284/2195 (12.9)		210/284 (73.9)		65/210 (31.0)	
Yes	31/261 (11.9)		27/31 (87.1)		10/27 (37.0)	
History of all secondary osteoporosis		.34		.51		.42
No	296/2338 (12.7)		221/296 (74.7)		68/221 (30.8)	
Yes	19/118 (16.1)		16/19 (84.2)		7/16 (43.8)	
History of rheumatoid arthritis		.42		.58		>.99
No	304/2391 (12.7)		230/304 (75.7)		73/230 (31.7)	
Yes	11/65 (16.9)		7/11 (63.6)		2/7 (28.6)	
History of usage of glucocorticoids		.050		.17		.35
No	270/2188 (12.3)		199/270 (73.7)		60/199 (30.2)	
Yes	45/268 (16.8)		38/45 (84.4)		15/38 (39.5)	

Note.—Data in parentheses are percentages. In this analysis, we only included osteoporosis events validated by dual-energy x-ray absorptiometry (DXA) examinations paid for by this trial. *P* values comparing x and x were calculated using χ^2 test. BMI = body mass index, ISCD = International Society for Clinical Densitometry, OPSCAN = Osteoporotic Precise Screening using Chest Radiography and Artificial neural Network.

* Number of participants who underwent DXA examination paid for by this trial/number of participants identified as high risk by AI-enabled chest radiography.

† Number of patients with osteoporosis/number of participants who underwent DXA examination paid for by this trial.

‡ Number of patients who started antiosteoporotic treatment/number of patients with osteoporosis.

screening for patients with incidental osteoporosis identified by an opportunistic artificial intelligence (AI)–enabled chest radiography analysis, which facilitates appropriate diagnostic and treatment interventions. Notably, the Osteoporotic

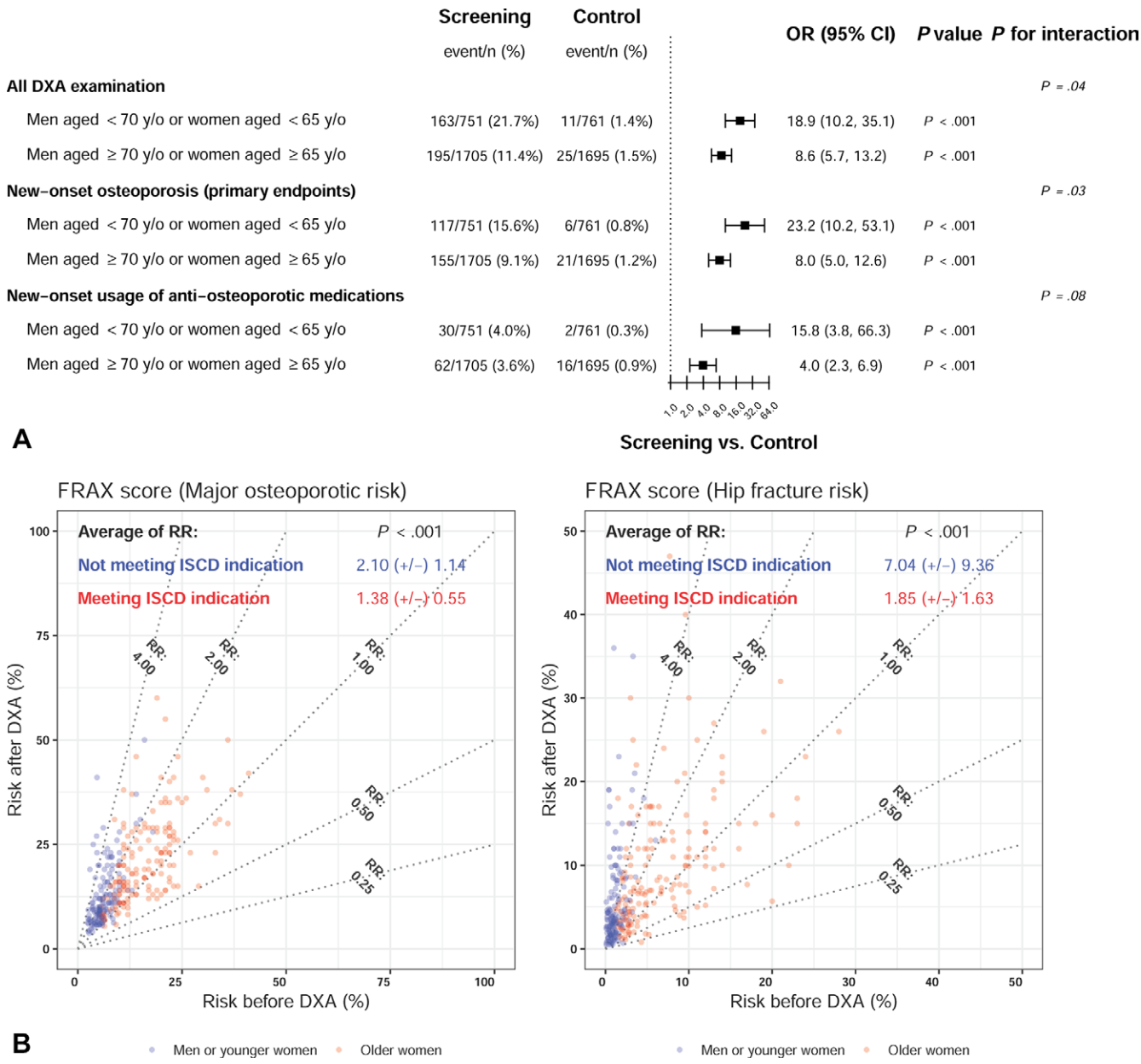

Figure 6: The predefined analysis in which participants were stratified according to the International Society for Clinical Densitometry's (ISCD) age and sex indications for bone mineral density testing with dual-energy x-ray absorptiometry (DXA). The ISCD recommends DXA for male patients aged 70 years and older or female patients aged 65 years and older. **(A)** Forest plot shows the differences between the screening group and the control group in all DXA examinations, new-onset osteoporosis, and treatment initiation. Odds ratios (ORs), calculated using logistic regression, are represented by center squares, while 95% CIs are indicated by error bars, illustrating the benefits of the Osteoporotic Precise Screening using Chest Radiography and Artificial neural Network (OPSCAN) program. The interaction between the screening program and ISCD indication was assessed using a logistic regression with two main effects and their interaction term, testing for differences in the interaction term. The *P* for interaction was two sided, with no adjustment for multiple comparisons. The ORs of osteoporosis diagnosis were increased in screening versus control group participants who did not meet ISCD indication compared with those who did (OR, 23.2 [95% CI: 10.2, 53.1] vs 8.0 [95% CI: 5.0, 12.6]; interactive *P* = .03). **(B)** Scatterplots show the change in Fracture Risk Assessment Tool (FRAX) score in participants who underwent DXA by OPSCAN (*n* = 315). The FRAX score serves as a standard for antiosteoporotic treatment and can be calculated even in the absence of DXA data. The key to whether additional DXA promotes treatment initiation lies in the increase of the FRAX score after DXA examination. The risk ratio (RR) was calculated as the risk after DXA divided by the risk before DXA; the dashed gray lines represent the corresponding RR. An RR equal to or less than 1 indicates that the FRAX score does not change or decreases after additional DXA examination, suggesting that additional DXA may not promote treatment initiation for that participant. The Wilcoxon rank sum test was used to test the differences between stratifications. Individuals who did not meet the ISCD indication had higher RR for major osteoporotic risk (2.10 ± 1.14 [SD] vs 1.38 ± 0.55; *P* < .001) and hip fracture risk (7.04 ± 9.36 vs 1.85 ± 1.63; *P* < .001) compared with those who did. This suggests that they are more likely to have treatment initiation promoted with additional DXA examinations.

Precise Screening using Chest Radiography and Artificial neural Network program appears particularly beneficial for those not meeting the International Society for Clinical Densitometry indications, suggesting that AI-enabled chest radiography risk stratification could complement existing risk factors. This study offers a pathway to mitigate osteoporosis underdiagnosis, lessen the impact of osteoporotic fractures, and enhance patient outcomes.

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