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Machine-Learning–Driven Early Prediction of Osteoporosis Incorporating Traditional Chinese Medicine Syndromes

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ABSTRACT

To identify risk factors for osteoporosis and develop a predictive model incorporating conventional clinical data and traditional Chinese medicine (TCM) syndrome patterns. From December 2019 to January 2022, a multi-stage sampling approach was used to recruit adults aged 30–82 years from 12 community-level districts or rural towns in Shanghai, Jilin Province, and Jiangsu Province. Univariate analysis and multivariable logistic regression were employed to examine risk factors and construct osteoporosis prediction models separately for women and men. Model performance was assessed using the receiver operating characteristic (ROC) curve and the Hosmer-Lemeshow goodness-of-fit test. The study enrolled 3,000 participants, comprising 2,243 women (75%) and 757 men (25%). The logistic regression model for osteoporosis in women was: Logit(P) = −2.946 + 0.960 (age ≥50 years) + 0.633 (BMI ≥24 kg/m²) − 0.545 (daily sunlight exposure >30 min) + 0.519 (no dairy product intake) + 0.827 (coronary heart disease) + 0.383 (lumbar disc herniation) + 0.654 (no calcium/vitamin D supplementation) − 0.509 (insomnia) + 0.580 (flushed face and red eyes) + 1.194 (thready and rapid pulse) + 1.309 (sunken and slow pulse). The model for men was: Logit(P) = −1.152 − 0.644 (daily sunlight exposure >30 min) + 0.975 (no calcium/vitamin D supplementation) − 0.488 (insomnia). The area under the ROC curve was 0.743 for the female model and 0.679 for the male model. Hosmer-Lemeshow tests indicated good calibration ($p > 0.5$ for both models). Risk factors for osteoporosis differ notably between women and men. TCM syndrome elements are significantly associated with osteoporosis risk. Prediction models that integrate routine clinical variables with TCM syndromes demonstrate acceptable discriminative ability and calibration for assessing osteoporosis risk.

Keywords: Osteoporosis Risk factors Prediction model Adult, Traditional Chinese medicine (TCM) syndromes, Logistic regression model, Shanghai

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Introduction

Osteoporosis is a metabolic disorder of the bone marked by decreased bone mass, deterioration of bone microarchitecture, and an increased tendency toward fragility fractures [1]. Although the disease often remains asymptomatic in its early stages, it may lead to fractures that result in serious complications and even mortality [2]. Estimates indicate that roughly 10 million individuals in the United States are affected [3]. As the global population ages and lifestyle patterns shift, the number of people with osteoporosis continues to rise [4]. Osteoporosis and its associated fragility fractures impose substantial medical, public health, and economic burdens worldwide, and are widely regarded as a major public health challenge [5].

According to the International Osteoporosis Foundation (IOF), adopting healthy lifestyle behaviors can markedly lower osteoporosis risk. Thus, developing reliable risk prediction models is of great value for enabling early identification and intervention [6]. Prior evidence suggests that factors such as bone mass acquired early in life, adequate nutrition—particularly sufficient calcium and vitamin D intake—and regular physical activity play key roles in determining individual osteoporosis risk [7].

Current studies investigating major clinical risk contributors have found that routine clinical and demographic factors—including advanced age, female sex, ethnicity, family history, previous fractures, malnutrition, alcohol

intake, smoking, vitamin D deficiency, physical inactivity, as well as certain medications and comorbidities [8–10]—are associated with a heightened likelihood of developing osteoporosis. In China, where the affected population is substantial and traditional Chinese medicine (TCM) syndromes provide distinctive diagnostic insights, the Development Plan of TCM Health Services (2015–2020) [11] advocates for incorporating TCM-based health risk assessments and interventions into broader health management services.

In this study, adults aged 30–82 years from 12 community or rural sites in Shanghai, Jilin Province, and Jiangsu Province were enrolled using a multi-stage sampling approach. Our objective was to identify sex-specific risk factors for osteoporosis and to develop predictive models integrating demographic data with TCM syndrome characteristics, thereby offering evidence-based support for early osteoporosis risk assessment.

Materials and Methods

Study subjects and data collection

Participants were enrolled using a multi-stage sampling approach. At the first stage, a group of cities located in the northernmost and easternmost parts of China was randomly chosen to form the primary sampling frame. In the next stage, neighborhoods or community units within each selected city were randomly identified. From these sites, individuals meeting the inclusion criteria were then randomly sampled to create the final study cohort. The target sample size was determined with PASS software to ensure adequate statistical power (details provided in the Supplementary Material). In total, 3,000 adults aged 30–82 years were recruited voluntarily from 12 community or rural locations in Shanghai, Jilin, and Jiangsu Provinces between December 2019 and January 2022. Questionnaire surveys were used to gather demographic and general clinical data. TCM syndrome characteristics, however, were evaluated directly by two trained TCM practitioners. When the two assessments differed, a senior practitioner conducted an additional evaluation to finalize the classification.

This investigation complied with the ethical standards outlined in the Declaration of Helsinki. Ethical approval was granted by the Longhua Hospital Ethics Committee of Shanghai University of Traditional Chinese Medicine (approval no. 2020LCSY031). The study was registered with the Chinese Clinical Trial Registry (ChiCTR) under the identifier ChiCTR2100043369. All participants provided written informed consent before joining the study.

Diagnostic criteria for osteoporosis

Dual-energy X-ray absorptiometry (DXA) remains the standard, validated technique for evaluating bone mineral density (BMD) and identifying individuals at elevated risk for osteoporotic fractures [12]. The World Health Organization (WHO) defines osteoporosis using T-scores derived from BMD values, comparing an individual's bone density with that of healthy young adults of the same sex and ethnicity [13]. According to these criteria, a T-score of −1.0 or above reflects normal bone mass; values between −1.0 and −2.5 signal low bone mass (osteopenia); and scores at or below −2.5 confirm osteoporosis. In this study, all BMD assessments were conducted with a GE Dual-Energy X-ray Bone Densitometer (USA).

Questionnaire survey

The physical examination information

Physical measurements collected in the study included height, weight, body mass index (BMI), waist circumference, and both systolic and diastolic blood pressure. Background information covered participants' educational attainment, marital status, and current or past primary occupation. For female participants, additional reproductive and menopausal data were obtained, including menopausal status and age at menopause, as well as history of pregnancy and childbirth.

The lifestyle habits

Information on lifestyle habits included dietary patterns, primary food categories consumed (such as rice, noodles, whole grains, meat, vegetables, soy-based products, eggs, tea, coffee, carbonated beverages, and dairy products), average daily sunlight exposure, types of physical activity performed each week, and the frequency of weekly exercise.

Medical history

High blood pressure, elevated blood fats (dyslipidemia), diabetes, cerebrovascular accident (stroke), ischemic heart disease, prior bone fractures, familial history of fractures, hereditary kyphosis or dowager's hump, protrusion

of lumbar intervertebral disc, degenerative joint disease of the knee, gouty arthritis, overactive thyroid (hyperthyroidism), underactive thyroid (hypothyroidism), rheumatoid arthritis, and systemic lupus erythematosus (SLE).

The health behavior information

Lifestyle and medication-related information included alcohol consumption, smoking habits, dairy intake, and overall physical activity levels. Additionally, participants' use of medications and supplements was recorded, covering calcium and vitamin D3, antihypertensive and hypoglycemic agents, antiplatelet and lipid-lowering drugs, hormonal therapies, as well as traditional Chinese patent medicines and single-ingredient preparations.

TCM syndrome information

Traditional Chinese medicine (TCM) symptom data were collected, encompassing a wide range of physical and subjective manifestations. These included fatigue, general weakness, shortness of breath, low or weak voice, reduced appetite, irregular stools, dizziness, limb numbness, palpitations, insomnia, memory impairment, chest tightness, abdominal fullness, heaviness of the head or body, and a sticky or greasy sensation in the mouth. Symptoms related to phlegm included frequent throat mucus and sticky stools or incomplete defecation. Emotional or psychological signs included irritability, unexplained sighing, or dysphoria in the chest, palms, and soles. Gastrointestinal and urinary symptoms included fullness or distension in the chest or hypochondrium, dry or bitter mouth, constipation or dry stools, fever sensation during urination, deep-colored urine, excessive hunger, dry mouth and throat, and frequent nighttime urination. Additional physical or localized signs included chills or cold extremities, lumbar weakness, tinnitus or hearing loss, hair loss, loose teeth, pale or yellowish complexion, facial flushing, flushed face with congested eyes, ecchymosis or abnormal veins in the skin or mucosa, rough, dry, or darkened skin, pale lips and nails, cyanosis of lips or nails, as well as TCM-specific diagnostic indicators such as tongue texture and coating and pulse characteristics.

Other information

Have either of your parents been diagnosed with osteoporosis or experienced fractures after minimal trauma? 2. Have you experienced more than one fall in the past year, or do you feel at risk of falling due to physical weakness? 3. Since the age of 40, has your height decreased by more than 3 cm? 4. For female participants: Have your ovaries been surgically removed before age 50 without subsequent estrogen or progesterone therapy? 5. For male participants: Have you experienced symptoms indicative of low androgen levels, such as reduced libido or erectile dysfunction? 6. Do you engage in less than 30 minutes of physical activity per day? 7. Have you been unable to consume dairy products without taking calcium supplements? 8. Do you spend less than 10 minutes per day in outdoor activities without vitamin D supplementation? 9. Have you taken corticosteroids continuously for more than three months?

Statistical analysis

Statistical analyses were conducted using SPSS version 24.0. Continuous variables were presented as mean ± standard deviation, while categorical variables were expressed as counts and percentages (%). Differences between groups were assessed using independent-sample t-tests for continuous variables and chi-square tests for categorical variables. Univariate analyses were first performed to identify potential factors associated with osteoporosis. Variables showing significance in the univariate analysis were then included in multivariate logistic regression models to construct sex-specific osteoporosis risk prediction models. Model performance was evaluated using receiver operating characteristic (ROC) curves and the Hosmer-Lemeshow goodness-of-fit test [14].

Results and Discussion

Basic characteristics of the study population

The study included 3,000 participants in total, with 2,243 females accounting for 74.8%. The average age was around 55 years for both genders. Men had an average height of approximately 169 cm and weight of 68 kg, both markedly greater than the corresponding averages for women (160 cm and 60 kg). Systolic and diastolic blood pressure levels were notably elevated in men compared to women, whereas BMI and waist circumference showed no meaningful differences between the sexes. Bone mineral density (BMD) averages were virtually the same,

standing at −1.54 for women and −1.55 for men. In addition, 492 females and 153 males were diagnosed with osteoporosis, resulting in a higher prevalence among women than men (21.9% versus 20.2%) **(Table 1).**

Table 1. Basic characteristics of the study population.

Variable	Female	Male	*P*-value
Case	2243	757	
Age (years)	54.94 (6.90)	55.18 (6.29)	0.404
Height (cm)	159.60 (5.49)	168.51 (7.18)	<0.001
Weight (kg)	60.61 (9.33)	68.16 (12.65)	<0.001
BMI (kg/m^2)	26.22 (6.40)	26.06 (7.04)	0.576
Waist (cm)	82.60 (164.87)	82.25 (8.99)	0.953
Systolic pressure (mmHg)	120.79 (12.49)	123.05 (13.17)	<0.001
Diastolic pressure (mmHg)	79.10 (8.01)	80.66 (9.28)	<0.001
BMD (g/cm^2)	—1.54 (1.34)	—1.55 (1.31)	0.868
T-value			0.416
T ≥ —1, %	649 (28.9)	212 (28.0)	
—1 > T > —2.5, %	1102 (49.1)	392 (51.8)	
T ≤ —2.5, %	492 (21.9)	153 (20.2)	

Univariate analysis of factors influencing osteoporosis

Univariate analysis of factors influencing osteoporosis in women

Table 2 presents the univariate analysis of factors associated with osteoporosis in women. The results revealed significant differences between women with and without osteoporosis for several factors, including age, BMI, daily sunlight exposure exceeding 30 minutes, lack of dairy consumption, presence of coronary heart disease, lumbar disc herniation, absence of calcium and vitamin D supplementation, insomnia, lumbar weakness, flushed face with congested eyes, loose teeth and hair loss, as well as thready and rapid pulse and sunken and slow pulse (all $P < 0.05$); **(Table 2).**

Table 2. Univariate analysis of the factors affecting osteoporosis in women.

Variable	Non-osteoporosis group (n = 1,751)	χ^2	P	Osteoporosis group (n = 492)
Age (years)		40.232	<0.001	
<50	454 (25.9%)			60 (12.2%)
≥50	1,297 (74.1%)			432 (87.8%)
BMI (kg/m²)		39.925	<0.001	
<24	1,020 (58.3%)			207 (42.1%)
≥24	731 (41.7%)			285 (57.9%)
Menopause		2.312	0.128	
No	117 (6.7%)			23 (4.7%)
Yes	1,634 (93.3%)			469 (95.3%)
Menopausal age (years)		0.754	0.385	
<45	96 (5.9%)			22 (4.7%)
≥45	1,538 (94.1%)			447 (95.3%)
Mainly engaged in physical labor		0.178	0.673	
No	989 (56.5%)			272 (55.3%)
Yes	762 (43.5%)			220 (44.7%)
Less physical exercise		0.176	0.675	
No	1,392 (79.5%)			396 (80.5%)
Yes	359 (20.5%)			96 (19.5%)
Daily exposure to sunlight >30 min		11.085	0.001	
No	1,392 (79.5%)			396 (80.5%)
Yes	359 (20.5%)			96 (19.5%)
No intake of dairy products		10.718	0.001	
No	1,491 (85.2%)			388 (78.9%)

Yes	260 (14.8%)			104 (21.1%)
Hypertension		0.256	0.613	
No	1,471 (84.0%)			408 (82.9%)
Yes	280 (16.0%)			84 (17.1%)
Hyperlipidemia		1.716	0.190	
No	1,483 (84.7%)			429 (87.2%)
Yes	268 (15.3%)			63 (12.8%)
Diabetes mellitus		0.281	0.596	
No	1,556 (88.9%)			442 (89.8%)
Yes	195 (11.1%)			50 (10.2%)
Coronary heart disease		17.541	<0.001	
No	1,677 (95.8%)			447 (90.9%)
Yes	74 (4.2%)			45 (9.1%)
History of fractures		0.958	0.328	
No	1,715 (97.9%)			478 (97.2%)
Yes	36 (2.1%)			14 (2.8%)
Family history of fractures		0.766	0.381	
No	1,723 (98.4%)			481 (97.8%)
Yes	36 (2.1%)			14 (2.8%)
Lumbar disc herniation		6.851	0.009	
No	1,580 (90.2%)			423 (86.0%)
Yes	171 (9.8%)			69 (14.0%)
Osteoarthritis		0.012	0.912	
No	1,458 (83.3%)			408 (82.9%)
Yes	293 (16.7%)			84 (17.1%)
Gout		0.005	0.942	
No	1,723 (98.4%)			485 (98.6%)
Yes	28 (1.6%)			7 (1.4%)
Hypoglycemic drugs		0.192	0.661	
No	1,635 (93.4%)			456 (92.7%)
Yes	116 (6.6%)			36 (7.3%)
Platelet aggregation inhibitors		0.048	0.827	
No	1,710 (97.7%)			479 (97.4%)
Yes	41 (2.3%)			13 (2.6%)
Lipid-lowering drugs		<0.001	1.000	
No	1,692 (96.6%)			475 (96.5%)
Yes	59 (3.4%)			17 (3.5%)
No intake of calcium tablets and vitamin D		31.998	<0.001	
No	1,094 (62.5%)			237 (48.2%)
Yes	657 (37.5%)			255 (51.8%)
Insomnia		4.293	0.039	
No	453 (25.9%)			151 (30.7%)
Yes	1,297 (74.1%)			341 (69.3%)
Memory loss		1.023	0.312	
No	609 (34.8%)			184 (37.4%)
Yes	1,141 (65.2%)			308 (62.6%)
Sticky and greasy sensation in the mouth		1.905	0.167	
No	180 (10.3%)			62 (12.6%)
Yes	1,570 (89.7%)			430 (87.4%)
Lumbar debility		19.334	<0.001	
No	1,057 (60.4%)			351 (71.3%)
Yes	694 (39.6%)			141 (28.7%)
Dysphoria in chest, palms, and soles		0.887	0.346	
No	611 (34.9%)			160 (32.5%)
Yes	1,138 (65.1%)			332 (67.5%)

Dry mouth and throat		23.579	0.459	
No	693 (39.6%)			185 (37.6%)
Yes	1,058 (60.4%)			307 (62.4%)
Loose teeth and hair loss		0.549	0.001	
No	761 (43.5%)			257 (52.2%)
Yes	990 (56.5%)			235 (47.8%)
Yellow urine		11.580	0.451	
No	342 (19.5%)			88 (17.9%)
Yes	1,409 (80.5%)			404 (82.1%)
Thready and rapid pulse		40.723	<0.001	
No	1,638 (93.5%)			415 (84.3%)
Yes	113 (6.5%)			77 (15.7%)
Intolerance of cold and cold limbs		0.106	0.735	
No	783 (44.7%)			225 (45.7%)
Yes	967 (55.3%)			267 (54.3%)
Frequent nocturia		0.147	0.701	
No	583 (33.3%)			169 (34.3%)
Yes	1,168 (66.7%)			323 (65.7%)
Pale tongue with whitish coating		3.026	0.082	
No	1,145 (65.4%)			343 (69.7%)
Yes	606 (34.6%)			149 (30.3%)
Sunken and slow pulse		50.169	<0.001	
No	1,628 (93.0%)			405 (82.3%)
Yes	123 (7.0%)			87 (17.7%)
Flushed face and congested eyes		28.659	<0.001	
No	348 (19.9%)			46 (9.3%)
Yes	1,403 (80.1%)			446 (90.7%)
Pale lips and nails		2.019	0.155	
No	389 (22.2%)			94 (19.1%)
Yes	1,362 (77.8%)			398 (80.9%)

Univariate analysis of factors influencing osteoporosis in men

The univariate analysis examining factors associated with osteoporosis in men indicated that several variables showed significant differences between the osteoporosis and non-osteoporosis groups. These included daily sunlight exposure of more than 30 minutes, absence of dairy consumption, lack of calcium and vitamin D supplementation, insomnia, a sticky or greasy sensation in the mouth, and a pale tongue with a whitish coating (all $P < 0.05$); **(Table 3).**

Table 3. Univariate analysis of factors associated with osteoporosis in men.

Variable	Non-osteoporosis group (n = 604)	χ^2	P	Osteoporosis group (n = 153)
Age (years)		0.355	0.551	
<50	96 (15.9%)			28 (18.3%)
≥50	508 (84.1%)			125 (81.7%)
BMI (kg/m²)		2.026	0.155	
<24	290 (48.0%)			63 (41.2%)
≥24	314 (52.0%)			90 (58.8%)
Mainly engaged in physical labor		0.035	0.852	
No	328 (54.3%)			85 (55.6%)
Yes	276 (45.7%)			68 (44.4%)
Less physical exercise		0.821	0.365	
No	496 (82.1%)			131 (85.6%)
Yes	108 (17.9%)			22 (14.4%)
Daily exposure to sunlight >30 min		10.566	0.001	
No	204 (33.8%)			74 (48.4%)

Yes	400 (66.2%)			79 (51.6%)
No intake of dairy products		7.865	0.005	
No	501 (82.9%)			111 (72.5%)
Yes	103 (17.1%)			42 (27.5%)
Hypertension		0.049	0.824	
No	485 (80.3%)			121 (79.1%)
Yes	119 (19.7%)			32 (20.9%)
Hyperlipidemia		0.110	0.741	
No	500 (82.8%)			129 (84.3%)
Yes	104 (17.2%)			24 (15.7%)
Diabetes mellitus		0.779	0.377	
No	500 (82.8%)			129 (84.3%)
Yes	86 (14.3%)			17 (11.1%)
Coronary heart disease		0.011	0.915	
No	580 (96.0%)			146 (95.4%)
Yes	24 (4.0%)			7 (4.6%)
History of fractures		1.988	0.159	
No	523 (86.6%)			125 (81.7%)
Yes	81 (13.4%)			28 (18.3%)
Family history of fractures		2.514	0.113	
No	581 (96.2%)			142 (92.8%)
Yes	23 (3.8%)			11 (7.2%)
Lumbar disc herniation		1.314	0.252	
No	529 (87.6%)			128 (83.7%)
Yes	75 (12.4%)			25 (16.3%)
Osteoarthritis		0.009	0.923	
No	477 (79.0%)			122 (79.7%)
Yes	127 (21.0%)			31 (20.3%)
Gout		0.836	0.361	
No	581 (96.2%)			144 (94.1%)
Yes	23 (3.8%)			9 (5.9%)
Hypoglycemic drugs		0.381	0.537	
No	540 (89.4%)			140 (91.5%)
Yes	64 (10.6%)			13 (8.5%)
Lipid-lowering drugs		0.235	0.628	
No	573 (95.0%)			143 (93.5%)
Yes	31 (5.1%)			10 (6.5%)
No intake of calcium tablets & vitamin D		32.046	<0.001	
No	373 (62.0%)			55 (35.9%)
Yes	231 (38.0%)			98 (64.1%)
Insomnia		6.540	0.011	
No	111 (18.4%)			43 (28.1%)
Yes	493 (81.6%)			110 (71.9%)
Memory loss		2.394	0.122	
No	168 (27.9%)			53 (34.6%)
Yes	435 (72.1%)			100 (65.4%)
Sticky and greasy sensation in the mouth		7.446	0.006	
No	57 (9.5%)			27 (17.6%)
Yes	545 (90.5%)			126 (82.4%)
Lumbar debility		2.817	0.093	
No	424 (70.2%)			96 (62.7%)
Yes	180 (29.8%)			57 (37.3%)
Dysphoria in chest, palms, and soles		0	1.000	
No	211 (34.9%)			53 (34.6%)

Yes	393 (65.1%)		100 (65.4%)
Dry mouth and throat		0.580 0.446	
No	226 (37.4%)		63 (41.2%)
Yes	378 (62.6%)		90 (58.8%)
Loose teeth and hair loss		0.481 0.488	
No	270 (44.7%)		63 (41.2%)
Yes	334 (55.3%)		90 (58.8%)
Yellow urine		0.099 0.753	
No	117 (19.4%)		32 (20.9%)
Yes	487 (89.7%)		121 (79.1%)
Thready and rapid pulse		2.267 0.132	
No	542 (89.7%)		144 (94.1%)
Yes	62 (10.3%)		9 (5.9%)
Intolerance of cold and cold limbs		2.026 0.155	
No	270 (44.7%)		58 (37.9%)
Yes	334 (55.3%)		95 (62.1%)
Frequent nocturia		2.563 0.109	
No	238 (39.5%)		49 (32.0%)
Yes	365 (60.5%)		104 (68.0%)
Pale tongue with whitish coating		5.454 0.020	
No	400 (66.2%)		117 (76.5%)
Yes	204 (33.8%)		36 (23.5%)
Sunken and slow pulse		0.098 0.755	
No	537 (88.9%)		138 (90.2%)
Yes	67 (11.1%)		15 (9.8%)
Flushed face and congested eyes		2.799 0.094	
No	130 (21.5%)		23 (15.0%)
Yes	474 (78.5%)		130 (85.0%)
Pale lips and nails		3.748 0.053	
No	106 (17.5%)		38 (24.8%)
Yes	498 (82.5%)		115 (75.2%)

Analysis of multiple factors affecting osteoporosis

Multivariate analysis of factors associated with osteoporosis in women

Variables that showed significant differences in the univariate analysis were further examined using multivariate logistic regression **(Table 4).** The analysis produced a predictive model indicating that the likelihood of osteoporosis in women increases with age ≥50 years, BMI ≥24 kg/m², lack of dairy intake, presence of coronary heart disease or lumbar disc herniation, absence of calcium and vitamin D supplementation, certain facial and tongue signs, and abnormal pulse characteristics. Conversely, regular daily exposure to sunlight and absence of insomnia were associated with a lower risk of osteoporosis.

Table 4. Results of multivariate logistic regression examining determinants of osteoporosis in women.

Variable	B	P	OR	95% CI	Exposure	Reference
Age (years)	0.960	<0.001	2.612	1.934–3.583	≥50	<50
BMI (kg/m²)	0.633	<0.001	1.883	1.507–2.355	≥24	<24
Daily exposure to sunlight >30 min	–0.545	<0.001	0.580	0.465–0.723	Yes	No
No intake of dairy products	0.519	<0.001	1.680	1.262–2.227	Yes	No
Coronary heart disease	0.827	<0.001	2.286	1.481–3.497	Yes	No
Lumbar disc herniation	0.383	0.025	1.467	1.045–2.043	Yes	No
No intake of calcium tablets & vitamin D	0.654	<0.001	1.924	1.546–2.397	Yes	No
Insomnia	–0.509	<0.001	0.601	0.463–0.782	Yes	No
Lumbar debility	–0.189	0.147	0.828	0.640–1.068	Yes	No

Flushed face and congested eyes	0.580	0.001	1.785	1.259–2.578	Yes	No
Loose teeth and hair loss	0.024	0.842	1.024	0.814–1.290	Yes	No
Thready and rapid pulse	1.194	<0.001	3.301	2.265–4.808	Yes	No
Sunken and slow pulse	1.309	<0.001	3.703	2.548–5.386	Yes	No
Constant	–2.946	<0.001	0.053	0.031–0.0889	–	–

Multivariate analysis of factors Influencing osteoporosis in men

A multivariate logistic regression was performed on the variables that were significant in the univariate analysis. As shown in **Table 5**, the resulting model for predicting osteoporosis in men was:

Logit(P) = −1.152 − 0.644 (daily sunlight exposure >30 min) + 0.975 (absence of calcium and vitamin D supplementation) − 0.488 (insomnia).

These findings highlight the combined influence of sunlight exposure, supplement intake, and sleep quality on osteoporosis risk in men.

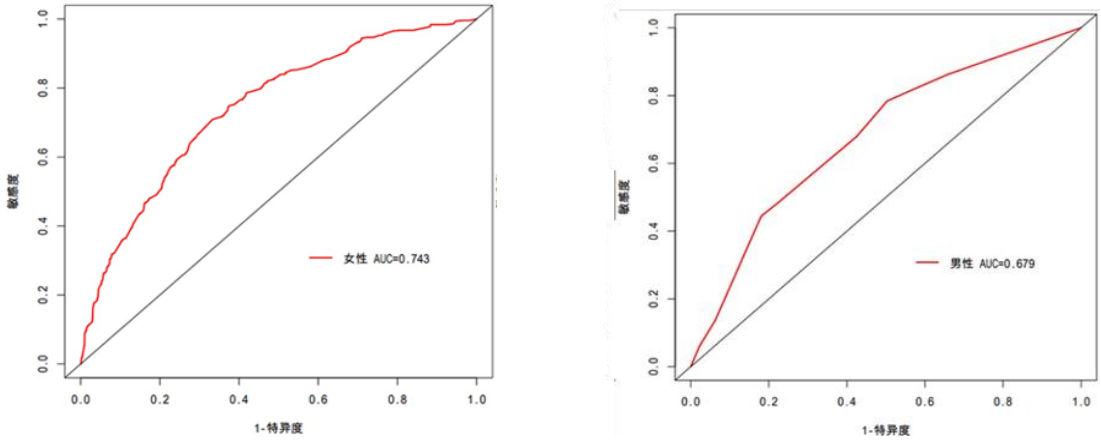
Table 5. Multifactorial logistic regression analysis of male osteoporosis.

Variable	B	P	OR	95% CI	Exposure	Reference
Daily exposure to sunlight >30 min	–0.644	<0.001	0.525	0.359–0.768	Yes	No
No intake of dairy products	0.365	0.107	1.440	0.918–2.232	Yes	No
No intake of calcium tablets & vitamin D	0.975	<0.001	2.652	1.812–3.912	Yes	No
Insomnia	–0.488	0.035	0.614	0.392–0.973	Yes	No
Sticky and greasy sensation in the mouth	0.543	0.054	1.722	0.980–2.974	Yes	No
Pale tongue with whitish coating	–0.397	0.068	0.672	0.434–1.022	Yes	No
Constant	–1.152	<0.001	0.316	0.185–0.527	–	–

Model evaluation

Evaluation of the predictive accuracy of the osteoporosis models

Figure 1 shows the ROC curves for the osteoporosis prediction models in women and men. The AUC was 0.743 for the female model **(Figure 1a)** and 0.679 for the male model **(Figure 1b)**. Both values are above 0.5, indicating that the models provide meaningful discrimination and can effectively predict osteoporosis risk in their respective populations.



a) b)

Figure 1. ROC Curves for Osteoporosis Risk Prediction Models in Women and Men

Model fit assessment for osteoporosis prediction

The reliability of the osteoporosis prediction models for both sexes was evaluated using the Hosmer-Lemeshow test. For women, the model produced a χ^2 value of 10.270 with a P-value of 0.247, while the male model showed a χ^2 of 6.982 with a P-value of 0.539. These results indicate that the predicted probabilities from both models

closely matched the actual outcomes, demonstrating that the models have good overall fit and are consistent with observed data.

Osteoporosis is a significant public health concern, with its prevalence rising alongside increasing life expectancy and lifestyle changes, such as dietary modifications and reduced physical activity [4]. This multicenter study investigated factors influencing osteoporosis in both women and men and developed risk prediction models incorporating traditional clinical data and TCM syndrome characteristics. The findings revealed notable differences in osteoporosis risk factors between the sexes. Moreover, TCM syndromes were associated with osteoporosis risk, suggesting that TCM information may be useful in predicting the disease.

Previous studies have reported varying prevalence rates of osteoporosis in China. A 2009 review of studies from 1980 to 2008 estimated a prevalence of approximately 13 % in the general population [4], while a 2019 study indicated that 10–20 % of Chinese men were affected [5]. In the present study, 3,000 adults aged 30–82 years were included, comprising 2,243 women (75 %) and 757 men (25 %). Consistent with previous reports, the overall prevalence of osteoporosis in this cohort was 21.5 %, slightly higher in women than men (21.9 % vs. 20.2 %), reflecting established epidemiological patterns where osteoporosis primarily affects postmenopausal women and men over 50 years of age [15].

Osteoporosis results from multiple factors, including age, genetics, hormonal changes, and prolonged immobility [16, 17]. In this study, a broad range of variables was examined, including demographic characteristics, physical examination data, female-specific factors, lifestyle habits, medical history, and TCM syndrome information. Risk factors were analyzed separately for women and men. For women, non-TCM predictors included age, BMI, daily sunlight exposure, dairy intake, coronary heart disease, lumbar disc herniation, calcium and vitamin D supplementation, and insomnia, whereas TCM-related factors included lumbar debility, flushed face with congested eyes, loose teeth and hair loss, thready and rapid pulse, and sunken and slow pulse. In men, significant non-TCM factors included sunlight exposure, dairy consumption, calcium and vitamin D supplementation, and insomnia, while TCM features included sticky and greasy mouth sensation and pale tongue with whitish coating. Traditional Chinese Medicine literature, such as *The Yellow Emperor's Classic of Medicine*, emphasizes the relationship between kidney essence and bone health in women, describing physiological changes at ages 7, 28, and 49. In TCM theory, the decline of kidney essence corresponds to postmenopausal decreases in estrogen, leading to weakened bones and marrow deficiency. Consistent with these principles, the findings of this study suggest that kidney essence deficiency is a key mechanism underlying osteoporosis in women, directly affecting bone growth, strength, and marrow health.

Previous research indicates that a healthy diet and lifestyle can effectively reduce osteoporosis risk and slow early disease progression, offering a cost-effective strategy for prevention [18, 19]. Some studies have used TCM symptom patterns to construct early risk prediction tools for osteoporotic fractures in women aged 40–65, focusing on liver-yin and kidney-yin deficiencies and associated symptoms such as night sweats, leg weakness, dizziness, alopecia, and insomnia [20]. While the specific TCM indicators differ from those in the present study, both investigations highlight the potential utility of TCM information in predicting osteoporosis risk.

In this study, risk prediction models for osteoporosis were developed for women and men using multivariate logistic regression. The models demonstrated good diagnostic performance, with AUC values of 0.743 and 0.679, respectively. Goodness-of-fit tests further confirmed that the predicted prevalence closely matched the observed prevalence in both sexes. However, most participants were from the northernmost and eastern regions of China, which may limit the generalizability of the results. Future studies should include populations from other regions or countries to better understand environmental influences on osteoporosis. Additionally, integrating TCM syndromes into routine clinical risk assessment may face challenges related to healthcare infrastructure, practitioner availability, and cultural acceptance. Further research is needed to assess the practicality and benefits of incorporating TCM into standard osteoporosis evaluation and management.

Limitation

This study has several notable limitations. First, the study population was restricted to individuals aged 30–82 years, and the applicability of the prediction models to other age groups remains uncertain. Second, there was a disproportionate distribution of sexes, with a relatively high number of female participants and fewer males, which may affect the robustness of the male-specific model. Third, much of the data were collected through self-reported questionnaires, which rely on participants' memory and may introduce recall bias, potentially compromising data accuracy. Fourth, logistic regression, the modeling approach used, may not fully account for potential interactions

or nonlinear relationships among variables. Finally, the models have not been externally validated, limiting the ability to assess their generalizability to other populations or settings.

Conclusion

In conclusion, osteoporosis occurs more frequently in women than in men, with notable differences in the factors influencing risk between the sexes. Traditional Chinese Medicine (TCM) syndromes were found to be linked to osteoporosis risk. The osteoporosis risk prediction models developed in this study, which integrate standard clinical data with TCM indicators, showed satisfactory diagnostic accuracy and good model fit for both women and men. These models may serve as valuable tools for early identification and intervention in osteoporosis, supporting evidence-based clinical decision-making.

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Conflict of Interest: None

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Ethics Statement: This study was designed in accordance with the Declaration of Helsinki and approved by the ethics committee of Longhua hospital affiliated to Shanghai university of traditional Chinese medicine (approval number: 2020LCSY031). Informed consent was obtained from all participants involved in the study.

References

1. A.K. Anam, K. Insogna, Update on osteoporosis screening and management, Med Clin North Am 105 (2021) 1117–1134, https://doi.org/10.1016/j. mcna.2021.05.016.
2. G. Rinonapoli, C. Ruggiero, L. Meccariello, M. Bisaccia, P. Ceccarini, A. Caraffa, Osteoporosis in men: a review of an underestimated bone condition, Int. J. Mol. Sci. 22 (2021), https://doi.org/10.3390/ijms22042105.
3. J.M. Kling, B.L. Clarke, N.P. Sandhu, Osteoporosis prevention, screening, and treatment: a review, J Womens Health (Larchmt) 23 (2014) 563–572, https://doi. org/10.1089/jwh.2013.4611.
4. Aibar-Almaz´an, A. Voltes-Martínez, Y. Castellote-Caballero, D.F. Afanador-Restrepo, M.D.C. Carcele´n-Fraile, E. Lo´pez-Ruiz, Current status of the diagnosis and management of osteoporosis, Int. J. Mol. Sci. 23 (2022), https://doi.org/10.3390/ijms23169465.
5. F. Yu, W. Xia, The epidemiology of osteoporosis, associated fragility fractures, and management gap in China, Arch. Osteoporosis 14 (2019) 32, https://doi.org/ 10.1007/s11657-018-0549-y.
6. L. Cianferotti, C. Cricelli, J.A. Kanis, R. Nuti, J.Y. Reginster, J.D. Ringe, et al., The clinical use of vitamin D metabolites and their potential developments: a position statement from the European society for clinical and economic aspects of osteoporosis and osteoarthritis (ESCEO) and the international osteoporosis foundation (IOF), Endocrine 50 (2015) 12–26, https://doi.org/10.1007/s12020-015-0606-x.
7. P. Proia, A. Amato, P. Drid, D. Korovljev, S. Vasto, S. Baldassano, The impact of diet and physical activity on bone health in children and adolescents, Front. Endocrinol. 12 (2021), 704647, https://doi.org/10.3389/fendo.2021.704647.
8. J. Smets, E. Shevroja, T. Hugle, W.D. Leslie, D. Hans, Machine learning solutions for osteoporosis-A review, J. Bone Miner. Res. 36 (2021) 833–851, https://doi. org/10.1002/jbmr.4292.
9. T.J. Aspray, T.R. Hill, Osteoporosis and the ageing skeleton, Subcell. Biochem. 91 (2019) 453–476, https://doi.org/10.1007/978-981-13-3681-2_16.
10. W. Liu, L.H. Yang, X.C. Kong, L.K. An, R. Wang, Meta-analysis of osteoporosis: fracture risks, medication and treatment, Minerva Med. 106 (2015) 203–214.

11. The Development Plan of TCM Health Services, (2015-2020) issued by the general office of the State Council, Chinese Medical Culture 10 (2015) 26.
12. K.N. Haseltine, T. Chukir, P.J. Smith, J.T. Jacob, J.P. Bilezikian, A. Farooki, Bone mineral density: clinical relevance and quantitative assessment, J. Nucl. Med. 62 (2021) 446–454, https://doi.org/10.2967/jnumed.120.256180.
13. J.A. Kanis, Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: synopsis of a WHO report. WHO Study Group, Osteoporos. Int. 4 (1994) 368–381, https://doi.org/10.1007/BF01622200.
14. M.W. Fagerland, D.W. Hosmer, A goodness-of-fit test for the proportional odds regression model, Stat. Med. 32 (2013) 2235–2249, https://doi.org/10.1002/ sim.5645.
15. W. Liu, L.H. Yang, X.C. Kong, et al., Meta-analysis of osteoporosis: fracture risks, medication and treatment, Minerva Med. 106 (2015) 203–214.
16. T.A. Azeez, Osteoporosis and cardiovascular disease: a review, Mol. Biol. Rep. 50 (2023) 1753–1763, https://doi.org/10.1007/s11033-022-08088-4.
17. S. Khandelwal, N.E. Lane, Osteoporosis: review of etiology, mechanisms, and approach to management in the aging population, Endocrinol Metab. Clin. N. Am. 52 (2023) 259–275, https://doi.org/10.1016/j.ecl.2022.10.009.
18. S.K. Papadopoulou, K. Papadimitriou, G. Voulgaridou, E. Georgaki, E. Tsotidou, O. Zantidou, et al., Exercise and nutrition impact on osteoporosis and sarcopenia-the incidence of osteosarcopenia: a narrative review, Nutrients 13 (2021), https://doi.org/10.3390/nu13124499.
19. Y. Wan, F. Zeng, H. Tan, Y. Lu, Y. Zhang, L. Zhao, et al., Cost-effectiveness analyses of denosumab for osteoporosis: a systematic review, Osteoporos. Int. 33 (2022) 979–1015, https://doi.org/10.1007/s00198-021-06268-9.
20. Y.W. Lan Ch, Construction of a risk assessment model for osteoporosis, Journal of Guangxi Sciences 27 (2020) 676–685.