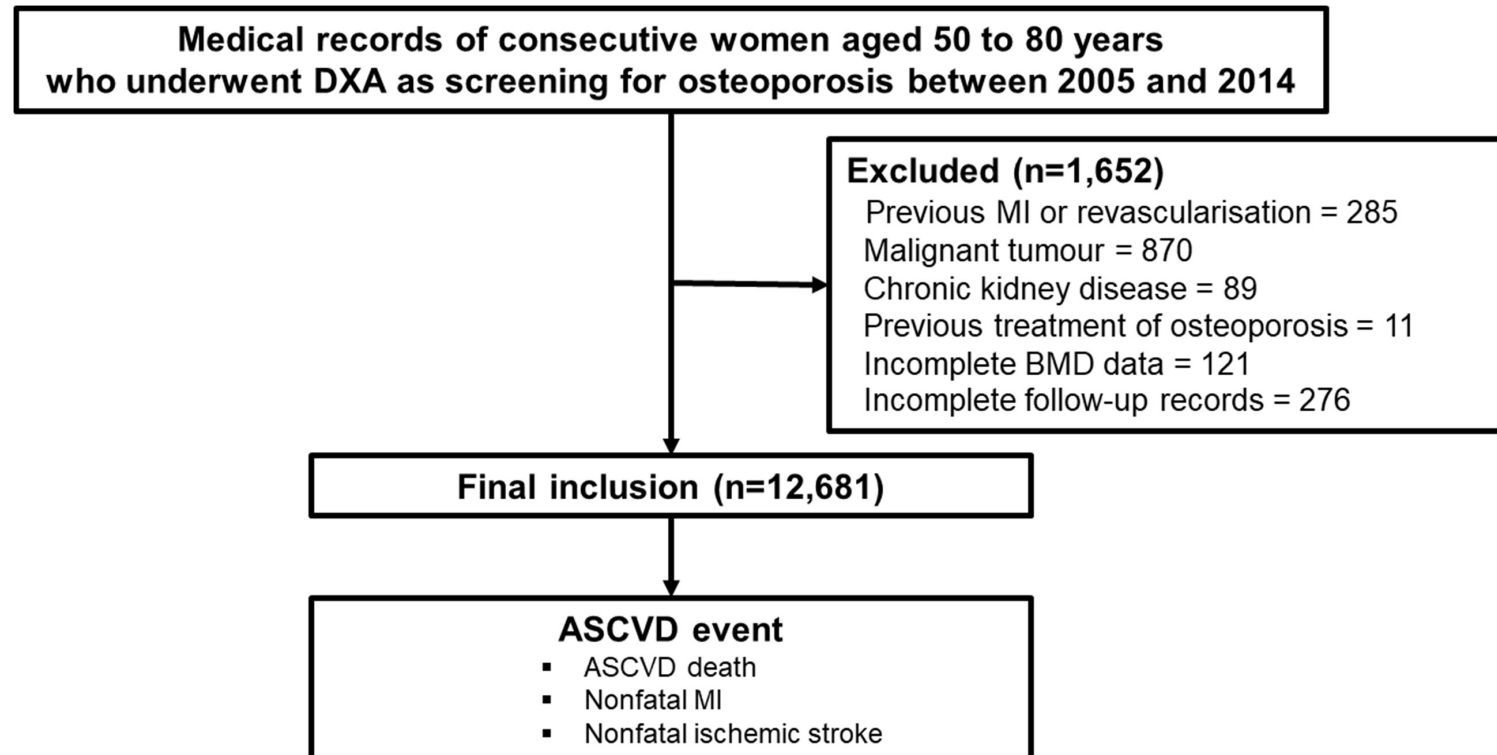


SUPPLEMENTAL FIGURES

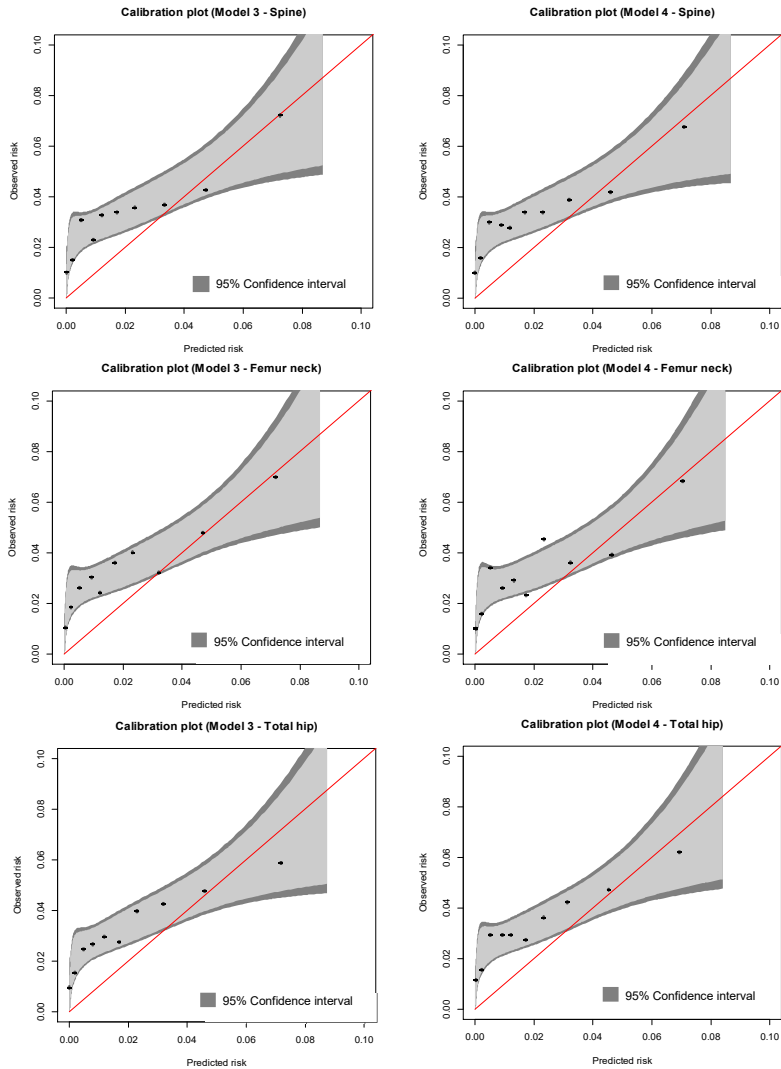
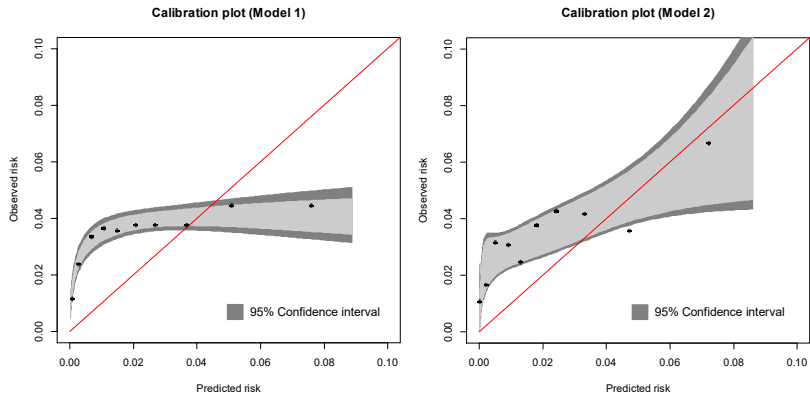
Supplementary Figure 1. Study flow



ASCVD = atherosclerotic cardiovascular disease, BMD = bone mineral density, DXA = dual-energy X-ray absorptiometry, MI = myocardial infarction

Supplementary Figure 2. Model calibration

		Brier score	Brier skill score
Model 1	Age	0.0327	reference
Model 2	Model 1 + clinical risk factors	0.0318	0.0275
Model 3	Model 2 + BMD as a continuous variable		
	Lumbar BMD	0.0319	0.0245
	Femur neck BMD	0.0318	0.0275
	Total hip BMD	0.0315	0.0367
Model 4	Model 2 + diagnosis of osteopenia or osteoporosis based on the T-score		
	Lumbar T-score	0.0315	0.0367
	Femur neck T-score	0.0314	0.0398
	Total hip T-score	0.0312	0.0459



Calibration of each model was assessed by plotting predicted probabilities of ASCVD, by decile groups (black points), against observed probabilities with 95% confidence interval presented as calibration belt (dark grey zone). Additionally, the magnitude of the error in the predicted probabilities were summarized with Brier Score, where a model with a score of 0.0 is considered as perfectly skilled model.

SUPPLEMENTAL TABLES

Supplementary Table 1. Clinical risk factors according to a diagnosis of osteopenia or osteoporosis based on the lumbar, femur neck, total hip BMD

	Lumbar BMD				Femur neck BMD				Total hip BMD			
	Normal (n=5,660)	Osteopenia (n=5,014)	Osteoporosis (n=2,007)	P	Normal (n=5,837)	Osteopenia (n=5,845)	Osteoporosis (n=999)	P	Normal (n=7,229)	Osteopenia (n=4,621)	Osteoporosis (n=831)	P
Age, mean (SD), years	60.1 (7.3)	64.0 (7.2)	68.4 (6.8)	<0.001	59.0 (6.3)	65.5 (7.1)	71.7 (5.8)	<0.001	60.0 (6.7)	66.0 (7.2)	72.0 (6.0)	<0.001
BMI, mean (SD), kg/m ²	24.6 (3.2)	24.0 (3.1)	22.9 (3.4)	<0.001	24.3 (3.1)	24.1 (3.2)	22.7 (3.8)	<0.001	24.5 (3.1)	23.8 (3.2)	22.2 (3.7)	<0.001
Current smoking, No. (%)	59 (1.0)	86 (1.7)	63 (3.1)	<0.001	63 (1.1)	94 (1.6)	51 (5.1)	<0.001	78 (1.1)	88 (1.9)	42 (5.1)	<0.001
Hypertension, No. (%)	1,689 (29.8)	1,511 (30.1)	611 (30.4)	0.868	1,779 (30.1)	1,735 (29.7)	297 (29.7)	0.628	2,195 (30.4)	1,377 (29.8)	239 (28.8)	0.567
Type 2 diabetes mellitus, No. (%)	621 (11.0)	532 (10.6)	183 (9.1)	0.066	592 (10.1)	630 (10.8)	114 (11.4)	0.344	780 (10.8)	475 (10.3)	81 (9.7)	0.505
Hyperlipidaemia, No. (%)	2,130 (37.6)	1,728 (34.5)	512 (25.5)	<0.001	2,253 (38.6)	1,880 (32.2)	237 (23.7)	<0.001	2,746 (38.0)	1,437 (31.1)	187 (22.5)	<0.001
Previous fracture, No. (%)	143 (2.5)	202 (4.0)	136 (6.8)	<0.001	116 (2.0)	258 (4.4)	107 (10.7)	<0.001	162 (2.2)	227 (4.9)	92 (11.1)	<0.001
10-year ASCVD risk, mean (SD)	7.8 (5.9)	10.1 (6.6)	13.2 (7.5)	<0.001	6.9 (4.7)	11.1 (6.9)	16.4 (7.9)	<0.001	7.5 (5.2)	11.5 (7.1)	16.5 (7.9)	<0.001
<7.5%, No. (%)	3,534 (62.4)	2,168 (43.2)	472 (23.5)	<0.001	3,940 (67.5)	2,139 (36.6)	95 (9.5)	<0.001	4,516 (62.5)	1,570 (34.0)	88 (10.6)	<0.001
≥7.5%, No. (%)	2,126 (37.6)	2,846 (56.8)	1,535 (76.5)		1,897 (32.5)	3,706 (63.4)	904 (90.5)		2,713 (37.5)	3,051 (66.0)	743 (89.4)	

Osteopenia is defined as a BMD T-score between −1.0 and −2.5, and osteoporosis is defined as a T-score below −2.5
ASCVD, atherosclerotic cardiovascular disease; BMD, bone mineral density; BMI, body mass index; SD, standard deviation

Supplementary Table 2. ASCVD risk according to clinical risk factors

Risk factors	Age adjusted HR (95% CI)	p- value	Age and other clinical risk factors* adjusted HR (95% CI)	p-value	Age, other clinical risk factors*, and lumbar BMD adjusted HR (95% CI)	p- value	Age, other clinical risk factors*, and femur neck BMD adjusted HR (95% CI)	p-value	Age, other clinical risk factors*, and total hip BMD adjusted HR (95% CI)	p-value
Age (per 5-year increase)	1.86 (1.75-1.99)	<0.001	1.82 (1.70-1.94)	<0.001	1.74 (1.62-1.87)	<0.001	1.66 (1.53-1.79)	<0.001	1.61 (1.49-1.74)	<0.001
BMI (per 1 kg/m ² increase)	0.97 (0.95-1.00)	0.058	0.96 (0.94-0.99)	0.007	0.98 (0.95-1.01)	0.123	0.98 (0.95-1.00)	0.078	0.99 (0.96-1.02)	0.503
Current smoking	3.01 (2.05-4.42)	<0.001	2.88 (1.96-4.24)	<0.001	2.77 (1.88-4.08)	<0.001	2.69 (1.83-3.97)	<0.001	2.64 (1.79-3.89)	<0.001
Hypertension	1.08 (0.89-1.31)	0.457	1.04 (0.85-1.26)	0.711	1.04 (0.86-1.27)	0.680	1.05 (0.86-1.27)	0.653	1.05 (0.86-1.28)	0.624
Type 2 diabetes mellitus	2.64 (2.15-3.23)	<0.001	2.69 (2.18-3.32)	<0.001	2.77 (2.24-3.43)	<0.001	2.73 (2.21-3.38)	<0.001	2.80 (2.26-3.46)	<0.001
Hyperlipidaemia	1.26 (1.05-1.51)	0.014	1.05 (0.87-1.27)	0.625	1.08 (0.89-1.31)	0.431	1.08 (0.90-1.31)	0.407	1.11 (0.91-1.34)	0.294
Previous fracture	1.21 (0.88-1.65)	0.249	1.06 (0.77-1.46)	0.710	1.02 (0.74-1.41)	0.884	0.99 (0.72-1.36)	0.953	0.96 (0.69-1.32)	0.782

*Other clinical risk factors include body mass index, hypertension, type 2 diabetes mellitus, hyperlipidaemia, current smoking, and previous fracture.
ASCVD, atherosclerotic cardiovascular disease; BMD, bone mineral density; BMI, body mass index; CI, confidence interval; HR, hazard ratio

Supplementary Table 3. Competing-risks-adjusted clinical outcomes according to BMD values and a clinical diagnosis of osteopenia or osteoporosis

Risk factors	ASCVD	p-value	ASCVD death	p-value
	Competing-risk-adjusted HR (95% CI)		Competing-risk-adjusted HR (95% CI)	
<i>BMD as a continuous variable</i>				
Lumbar BMD (per 1-SD decrease)	1.14 (1.05-1.24)	0.001	1.22 (1.09-1.37)	<0.001
Femur neck BMD (per 1-SD decrease)	1.25 (1.09-1.44)	0.002	1.51 (1.21-1.88)	<0.001
Total hip BMD (per 1-SD decrease)	1.33 (1.19-1.49)	<0.001	1.63 (1.39-1.92)	<0.001
<i>Diagnoses of osteopenia and osteoporosis based on the T-score</i>				
Lumbar T-score				
Normal	1 (reference)		1 (reference)	
Osteopenia	0.99 (0.79-1.24)	0.900	0.99 (0.70-1.39)	0.950
Osteoporosis	1.63 (1.27-2.10)	<0.001	1.96 (1.39-2.77)	<0.001
Femur neck T-score				
Normal	1 (reference)		1 (reference)	
Osteopenia	1.27 (0.99-1.61)	0.057	1.52 (1.01-2.28)	0.044
Osteoporosis	2.10 (1.53-2.88)	<0.001	2.72 (1.69-4.39)	<0.001
Total hip T-score				
Normal	1 (reference)		1 (reference)	
Osteopenia	1.37 (1.10-1.72)	0.006	2.00 (1.38-2.88)	<0.001
Osteoporosis	2.64 (1.94-3.59)	<0.001	4.39 (2.80-6.88)	<0.001
Combined T-score				
Normal	1 (reference)		1 (reference)	
Osteopenia	1.01 (0.76-1.33)	0.960	1.05 (0.66-1.68)	0.820
Osteoporosis	1.74 (1.27-2.39)	<0.001	2.09 (1.28-3.42)	0.003

Osteopenia was defined as a BMD T-score between -1.0 and -2.5 , and osteoporosis was defined as a T-score below -2.5 . Single-site BMD-related values (either BMD or a diagnosis of osteopenia/osteoporosis) of the indicated skeletal site were included in the Cox regression model with other covariates (age, body mass index, hypertension, type 2 diabetes mellitus, hyperlipidaemia, current smoking, and previous fracture)

ASCVD, atherosclerotic cardiovascular disease; BMD, bone mineral density; CI, confidence interval; HR, hazard ratio; SD, standard deviation

Supplementary Table 4. Sensitivity analysis for the risk of ASCVD and ASCVD death according to BMD values and a clinical diagnosis of osteopenia or osteoporosis after excluding censored subjects before the median follow-up period

Risk factors	ASCVD		ASCVD death	
	Fully adjusted HR (95% CI)	p-value	Fully adjusted HR (95% CI)	p-value
<i>BMD as a continuous variable</i>				
Lumbar BMD (per 1-SD decrease)	1.17 (1.09-1.26)	<0.001	1.26 (1.13-1.40)	<0.001
Femur neck BMD (per 1-SD decrease)	1.31 (1.17-1.46)	<0.001	1.56 (1.33-1.83)	<0.001
Total hip BMD (per 1-SD decrease)	1.40 (1.27-1.55)	<0.001	1.72 (1.50-1.98)	<0.001
<i>Diagnoses of osteopenia and osteoporosis based on the T-score</i>				
Lumbar T-score	Number of women	Event, n (%)		Event, n (%)
Normal	3,123	144 (4.6)	1 (reference)	58 (1.9)
Osteopenia	2,567	171 (6.7)	1.00 (0.80-1.26)	77 (3.0)
Osteoporosis	894	153 (17.1)	1.77 (1.38-2.27)	102 (11.4)
Femur neck T-score				
Normal	3,217	109 (3.4)	1 (reference)	35 (1.1)
Osteopenia	2,906	245 (8.4)	1.30 (1.02-1.66)	123 (4.2)
Osteoporosis	461	114 (24.7)	2.34 (1.71-3.19)	79 (17.1)
Total hip T-score				
Normal	3,927	150 (3.8)	1 (reference)	45 (1.1)
Osteopenia	2,283	210 (9.2)	1.41 (1.12-1.77)	112 (4.9)
Osteoporosis	374	108 (28.9)	3.18 (2.36-4.28)	80 (21.4)
Combined T-score				
Normal	2,221	73 (3.3)	1 (reference)	24 (1.1)
Osteopenia	3,243	199 (6.1)	0.99 (0.75-1.32)	87 (2.7)
Osteoporosis	1,120	196 (17.5)	1.87 (1.27-2.55)	126 (11.3)

Osteopenia was defined as a BMD T-score between -1.0 and -2.5 , and osteoporosis was defined as a T-score below -2.5 . Single-site BMD-related values (either BMD or a diagnosis of osteopenia/osteoporosis) of the indicated skeletal site were included in the Cox regression model with other covariates (age, body mass index, hypertension, type 2 diabetes mellitus, hyperlipidaemia, current smoking, and previous fracture)

ASCVD, atherosclerotic cardiovascular disease; BMD, bone mineral density; CI, confidence interval; HR, hazard ratio; SD, standard deviation

Supplementary Table 5. Risk for ASCVD and ASCVD death according to BMD values and a clinical diagnosis of osteopenia or osteoporosis among a low-risk population with age <70 years and no risk factors

Risk factors	ASCVD		ASCVD death	
	Age adjusted HR (95% CI)	p-value	Age adjusted HR (95% CI)	p-value
<i>BMD as a continuous variable</i>				
Lumbar BMD (per 1-SD decrease)	1.07 (0.86-1.34)	0.550	1.44 (1.01-2.06)	0.044
Femur neck BMD (per 1-SD decrease)	1.29 (0.92-1.82)	0.141	1.97 (1.16-3.35)	0.012
Total hip BMD (per 1-SD decrease)	1.41 (1.04-1.90)	0.026	2.16 (1.40-3.34)	<0.001
<i>Diagnoses of osteopenia and osteoporosis based on the T-score</i>				
Lumbar T-score	Number of women	Event, n (%)		Event, n (%)
Normal	1,980	21 (1.1)	1 (reference)	5 (0.3)
Osteopenia	1,552	15 (1.0)	0.71 (0.36-1.38)	8 (0.5)
Osteoporosis	451	13 (2.9)	1.80 (0.87-3.74)	10 (2.2)
Femur neck T-score				
Normal	2,590	17 (0.8)	1 (reference)	4 (0.2)
Osteopenia	1,719	26 (1.5)	1.36 (0.71-2.60)	15 (0.9)
Osteoporosis	119	6 (5.0)	3.26 (1.20-8.84)	4 (3.4)
Total hip T-score				
Normal	2,590	23 (0.9)	1 (reference)	6 (0.2)
Osteopenia	1,295	20 (1.5)	1.32 (0.71-2.45)	13 (1.0)
Osteoporosis	98	6 (6.1)	3.78 (1.48-9.67)	4 (4.1)
Combined T-score				
Normal	1,505	13 (0.9)	1 (reference)	2 (0.1)
Osteopenia	1,961	21 (1.1)	0.87 (0.43-1.80)	10 (0.5)
Osteoporosis	517	15 (2.9)	2.02 (0.90-4.52)	11 (2.1)

Osteopenia was defined as a BMD T-score between −1.0 and −2.5, and osteoporosis was defined as a T-score below −2.5. Single-site BMD-related values (either BMD or a diagnosis of osteopenia/osteoporosis) of the indicated skeletal site were included in the Cox regression model with age.

ASCVD, atherosclerotic cardiovascular disease; BMD, bone mineral density; CI, confidence interval; HR, hazard ratio; SD, standard deviation