

Supplemental Table 1. Characteristics of cohorts contributing to discovery, replication, or fracture look-up analyses

Cohort	Country	Full cohort N	Female %	Age (years) Mean (SD)	Weight (kg) Mean (SD)	Height (cm) Mean (SD)	Trabecular BMD (g/cm ³)		Integral BMD (g/cm ³)		Vertebral level	QCT Instrument	Image analysis	
							N	Mean (SD)	N	Mean (SD)				
Discovery cohorts														
Age Gene/Environment Susceptibility-Reykjavik Study (AGES-Reykjavik)	Iceland	5764	58	76.4 (5.4)	75.8 (14.3)	167 (9)	2859	0.075 (0.037)	2861	0.114 (0.040)	L2	E Prospeed (Birmingham), GE Hispeed Advantage (Minneapolis), Phillips MX-8000 (Palo Alto), Seimans Somatom +4 (Pittsburgh), Phillips CT-Twin (April-July, 2000, 190 participants) and Toshiba Aquilion (December 2000-March 2002, 467 participants) (Portland), and Picker PQ-5000 (San Diego). All scans were transferred to UCSF for central quality review and image processing.	T. Lang	
Family Heart Study	USA	2618	55	57.6 (13.2)	82.2 (18.5)	168.5 (9.7)	2600	0.118 (0.034)	2570	0.151 (0.038)	L3	GE LightSpeed Plus (NC), Siemens Volume Zoom (MN), Marconi MX 8000 (UT), GE LightSpeed (AL)	T. Lang	
Framingham Osteoporosis Study	USA	2703	46	52.8 (12.3)	81.1 (17.9)	170.3 (9.6)	2703	0.142 (0.043)	2686	0.188 (0.041)	L3	QCT images were originally acquired from participants for assessment of coronary and aortic calcium using an eight-slice multidetector CT (Lightspeed Ultra, GE, Milwaukee, WI, USA).	T. Lang	
Health, Aging, and Body Composition (Health ABC)	USA	1663 (European ancestry with genotypes)	54	73.8 (2.8)	74.6 (14.1)	165.9 (9.3)	778	0.111 (0.038)	NA	NA	L3	9800 Advantage: General Electric, Milwaukee, WI, USA	T. Lang	
Multi-Ethnic Study of Atherosclerosis (MESA)	USA	2622	53	62.7 (9.7)	80.8 (16.9)	169.0 (9.7)	736	0.107 (0.036)	NA	NA	L3	At Exam 3: Imatron C-150 (Northwestern/Chicago, UCLA, Columbia/NY); Volume Zoom (Johns Hopkins/Baltimore, Minnesota), Sensation 16 (Minnesota); Sensation Cardiac 64 (Columbia/NY); Light Speed Pro 16 (Wake Forest/Winston-Salem NC); Aquilon 32, Aquilon 64 (Johns)	Image Analysis Volumetric Software, Columbia, KY	
Osteoporotic Fractures in Men (MrOS) - US	USA	5994	0	73.8 (5.9)	83.4 (13.0)	174.4 (6.7)	2650	0.109 (0.039)	2650	0.178 (0.044)	L2	GE Prospeed (Birmingham), GE Hispeed Advantage (Minneapolis), Phillips MX-8000 (Palo Alto), Seimans Somatom +4 (Pittsburgh), Phillips CT-Twin (April-July, 2000, 190 participants) and Toshiba Aquilion (December 2000-March 2002, 467 participants) (Portland), and Picker PQ-5000 (San Diego). All scans were transferred to UCSF for central quality review and image processing.	T. Lang	
Replication and fracture look-up cohorts														
Age Gene/Environment Susceptibility-Reykjavik Study (AGES-Reykjavik)				<i>As above</i>			2021							
Diabetes Heart Study	USA	1181	53.4	62.7 (9.2)	90.1 (19.9)	168.4 (9.7)	979	0.124 (0.040)	NA	NA	L2	GE LightSpeed Qxi and 16 Pro (Winston-Salem, NC, USA)	J. Carr	
Osteoporotic Fractures in Men (MrOS) - SW	Sweden	3014	0	75.4 (3.2)	80.8 (12.1)	174.8 (6.5)	NA	NA	NA	NA	NA	NA	NA	
Rotterdam I	The Netherlands	7983	57	67.8 (7.9)	73.8 (11.7)	167.5 (9.2)	NA	NA	NA	NA	NA	NA	NA	
Rotterdam II	The Netherlands	3011	54.2	64.5 (7.8)	77.4 (13.2)	168.7 (9.2)	NA	NA	NA	NA	NA	NA	NA	
Rotterdam III	The Netherlands	3932	57.1	56.8 (6.6)	80.6 (15.7)	170.7 (9.4)	NA	NA	NA	NA	NA	NA	NA	
Study of Osteoporotic Fractures	USA	3471	100	71.4 (5.3)	67.9 (12.3)	159.1 (5.9)	NA	NA	NA	NA	NA	NA	NA	

Cohort	Morphometric vertebral fracture		Morphometric vertebral fracture case definition	Cohort	References	Morphometric vertebral fracture	
	Cases (n)	Non-Cases (n)					QCT
Discovery cohorts							
Age Gene/Environment Susceptibility-Reykjavik Study (AGES-Reykjavik)	NA	NA	NA	[PMID:17351290] Harris, T. B., Launer, L. J., Eiriksdottir, G., Kjartansson, O., Jonsson, P. V., Sigurdsson, G., et al. (2007). Age, Gene/Environment Susceptibility-Reykjavik Study: multidisciplinary applied phenomics. <i>Am J Epidemiol</i> , 165(9), 1076-1087. http://doi.org/10.1093/aje/kwk115	NA		
Family Heart Study	NA	NA	NA	[PMID: 8651220] Higgins M, Province M, Heiss G, Eckfeldt J, Ellison RC, Folsom AR, Rao DC, Sprafka JM, Williams R. NHLBI Family Heart Study: objectives and design. <i>Am J Epidemiol</i> 1996;143(12):1219-28	NA		
Framingham Osteoporosis Study	430	2375	Lateral radiographs or QCT lateral scout views at 13 vertebral levels (T4 to L4) using Genant's semiquantitative (SQ) scale (grades 0 to 3). Vertebral fracture was defined as having at least 25% reduction in height of any vertebra.	[PMID: 1615761] Hannan, MT, et al. Bone mineral density in elderly men and women: results from the Framingham osteoporosis study. <i>J Bone Miner Res</i> 1992;7(5):547-53	[PMID: 20495902] Samelson EJ, Christiansen BA, Demissie S, Broe KE, Zhou Y, Meng CA, Yu W, Cheng X, O'Donnell CJ, Hoffmann U, Genant HK, Kiel DP, Bouxsein ML 2011 Reliability of vertebral fracture assessment using multidetector CT lateral scout views: the Framingham Osteoporosis Study. <i>Osteoporos Int</i> 22(4):1123-31. [PMID: 15956133] Moselewski et al. Calcium concentration of individual coronary calcified plaques as measured by multidetector row computed tomography. <i>Circulation</i> 111(24):3236-41. [PMID: 18940279] Hoffmann et al. Defining Normal Distributions of Coronary Artery Calcium in Women and Men (from the Framingham Heart Study). <i>Am J Cardiol</i> 102(9):1136-41.	[PMID: 16869718] Samelson EJ, Hannan MT, Zhang Y, Genant HK, Felson DT, Kiel DP. Incidence and risk factors for vertebral fracture in women and men: 25-year follow-up results from the population-based Framingham study. <i>J Bone Miner Res</i> 2006;21:1207-14. [PMID: 2222934] Liu CT, Karasik D, Zhou Y, Hsu YH, Genant HK, Broe KE, et al. Heritability of prevalent vertebral fracture and volumetric bone mineral density and geometry at the lumbar spine in three generations of the Framingham study. <i>J Bone Miner Res</i> . 2012;27(4):954-8. PMID: PMC3375687.	
Health, Aging, and Body Composition (Health ABC)	NA	NA	NA	[PMID: 10865790] Harris, TB, Visser M, Everhart J, Cauley J, Tyllavsky F, Fuerst T, Zamboni M, Taaffe D, Resnick HE, Scherzinger A, Nevitt M. Waist circumference and sagittal diameter reflect total body fat better than visceral fat in older men and women. <i>The Health, Aging and Body Composition Study</i> . <i>Ann N Y Acad Sci</i> . 2000 May;904:462-473.	[PMID: 17708713] Mackey DC, Eby JG, Harris F, Taaffe DR, Cauley JA, Tyllavsky FA, Harris TB, Lang TF, Cummings SR, Health, Aging, and Body Composition Group. Prediction of clinical non-spine fractures in older black and white men and women with volumetric BMD of the spine and areal BMD of the hip: the Health, Aging, and Body Composition Study. <i>J Bone Miner Res</i> . 2007 Dec;22(12):1863-1868.	NA	
Multi-Ethnic Study of Atherosclerosis (MESA)	NA	NA	NA	[PMID: 12397006] Bild DE, Bluemke DA, Burke GL, Detrano R, Diez Roux AV, Folsom AR, Greenland P, Jacob DR, Jr., Kronmal R, Liu K, Nelson JC, O'Leary D, Saad MF, Shea S, Szklo M, Tracy RP. Multi-ethnic study of atherosclerosis: objectives and design. <i>Am J Epidemiol</i> . 2002;156(9):871-881.	[PMID: 19819456] Hyder JA, Allison MA, Barrett-Connor E, Detrano R, Wong ND, Sirlin C, Gapstur SM, Ouyang P, Carr JJ, Criqui MH. Bone mineral density and atherosclerosis: The Multi-Ethnic Study of Atherosclerosis, Abdominal Aortic Calcium Study. <i>Atherosclerosis</i> . 2010;209(1):283-289. [PMID: 23570937] Li D, Mao SS, Khazai B, Hyder JA, Allison M, McClelland R, de Boer I, Carr JJ, Criqui MH, Gao Y, Budoff MJ. Noncontrast Cardiac Computed Tomography Image-Based Vertebral Bone Mineral Density: The Multi-Ethnic Study of Atherosclerosis (MESA). <i>Acad Radiol</i> . 2013;20(5):621-627. [PMID: 25976951] van Ballegoijen AJ, Robinson-Cohen C, Katz R, Criqui M, Budoff M, Li D, Siscovick D, Hoffnagel A, Shea SJ, Burke G, de Boer IJ, Kestenbaum B. Vitamin D metabolites and bone mineral density: The multi-ethnic study of atherosclerosis. <i>Bone</i> . 2015;78:186-193.	NA	
Osteoporotic Fractures in Men (683)		3871	Any incident clinical vertebral fracture or prevalent morphometric fx (SQ grade of ≥ 1 at visit 1 or 2) or incident morphometric fx (a change in SQ between visits 1 and 2 of at least 1)	[PMID: 16084776] Orwoll, E., et al. Design and baseline characteristics of the osteoporotic fractures in men (MROS) study -- a large observational study of the determinants of fracture in older men. <i>Contemp Clin Trials</i> . 2005 Oct;26 (5):569-85.	[PMID: 16869717] Marshall LM, Lang TF, Lambert LC, Zmuda JM, Ensrud KE, Orwoll ES. Dimensions and volumetric BMD of the proximal femur and their relation to age among older U.S. men. <i>J Bone Miner Res</i> 2006; 21:1197-1206. [PMID: 9213015] Lang TF, Keyak JH, Heitz MW, Augat P, Lu Y, Mathur A, Genant HK. Volumetric quantitative computed tomography of the proximal femur: precision and relation to bone strength. <i>Bone</i> 1997; 21:101-118. [PMID: 10050823] Lang TF, Li J, Harris ST, Genant HK. Assessment of vertebral bone mineral density using volumetric quantitative CT. <i>J Computer Assist Tomogr</i> 1999; 23:130-137.	[PMID: 25003811] Cawthon PM, et al. 2014 Methods and reliability of radiographic vertebral fracture detection in older men <i>Bone</i> 67:152-5.	
Replication and fracture look-up cohorts							
Age Gene/Environment Susceptibility-Reykjavik Study (AGES-Reykjavik) Diabetes Heart Study	NA	NA	NA			NA	
Osteoporotic Fractures in Men (MROS) - SW	215	1131	A prevalent vertebral fracture was considered if visual inspection indicated a reduction in vertebral height and/or compression of 10% or above of the estimated vertebral body height.	[PMID: 16598372] Mellström, D. et al. Free testosterone is an independent predictor of BMD and prevalent fractures in elderly men: MROS Sweden. <i>J Bone Miner Res</i> . 2206;21(4):529-535.	NA	[PMID: 25264314] Kherad, M. et al. Low clinical relevance of a prevalent vertebral fracture in elderly men - the MROS Sweden study. <i>Spine J</i> . 2015;15(2):281-289.	
Rotterdam I	1168	4098	Prevalent and incident vertebral deformities of grade 1 or more read with SpineAnalyzer morphometric software at visit 1	[PMID: 26386597] Hofman, Albert et al. The Rotterdam Study: 2016 Objectives and Design Update. <i>European Journal of Epidemiology</i> 30.8 (2015): 661-708.	NA	[PMID: 22892721] Oei L, Rivadeneira F, Ly F, et al. Review of radiological scoring methods of osteoporotic vertebral fractures for clinical and research settings. <i>Eur Radiol</i> . 2013;23:476-86.	
Rotterdam II	407	1545			NA		
Rotterdam III	503	1815	Prevalent vertebral deformities of grade 1 or more read with SpineAnalyzer morphometric software at visit 1		NA		
Study of Osteoporotic Fractures	978	2493	Prevalent vert fx 3SD rule	Black DM, Palermo L, Nevitt MC, Genant HK, Epstein R, San Valenti NA			