eTable 1. Bone mineral density and the risk of incident Alzheimer's disease stratified by incremental epochs of follow-up time

	0~5 years		0~10 years		Total follow-up	
	n/N	HR (95%CI)	n/N	HR (95%CI)	n/N	HR (95%CI)
Femoral neck bone mineral density						
Highest tertile	6//1143	1	33/1143	1	151/1143	1
Medium tertile	3/1143	0.83 (0.23, 2.96)	45/1143	1.41 (0.87, 2.27)	178/1143	1.13 (0.90, 1.42)
Lowest tertile	8/1144	2.32 (0.81, 6.63)	65/1144	**2.30 (1.45, 3.64)**	183/1144	**1.32 (1.05, 1.66)**
Per SD decrease	17/3429	1.85 (0.93, 3.70)	143/3429	**1.52 (1.20, 1.92)**	512/3429	**1.14 (1.02;1.28)**
Lumbar spine bone mineral density						
Highest tertile	9/1150	1	48/1150	1	171/1150	1
Medium tertile	5/1150	0.54 (0.17, 1.71)	45/1150	0.94 (0.61, 1.45)	174/1150	0.99 (0.79, 1.24)
Lowest tertile	3/1151	0.31 (0.09, 1.13)	57/1151	1.14 (0.76, 1.72)	179/1151	0.97 (0.78, 1.21)
Per SD decrease	17/3451	0.72 (0.48, 1.10)	150/3451	1.08 (0.89, 1.30)	524/3451	0.97 (0.88;1.08)
Total body bone mineral density						
Highest tertile	9/1158	1	50/1158	1	170/1158	1
Medium tertile	3/1158	0.37 (0.10, 1.33)	39/1158	0.78 (0.50, 1.23)	182/1158	1.06 (0.85, 1.32)
Lowest tertile	5/1158	**0.30 (0.10, 0.97)**	63/1158	1.29 (0.85, 1.95)	175/1158	0.97 (0.78, 1.22)
Per SD decrease	17/3474	0.74 (0.47, 1.16)	152/3474	1.20 (0.95, 1.52)	527/3474	1.00 (0.88;1.12)
Trabecular bone score						
Highest tertile	5/1139	1	41/1139	1	161/1139	1
Medium tertile	8/1139	4.88 (0.99, 23.93)	55/1139	**1.66 (1.08, 2.54)**	173/1139	1.21 (0.97, 1.52)
Lowest tertile	4/1139	2.45 (0.42, 14.17)	53/1139	**1.55 (1.00, 2.39)**	182/1139	1.16 (0.93, 1.45)
Per SD decrease	17/3417	1.22 (0.66, 2.27)	149/3417	1.15 (0.96, 1.39)	516/3417	1.02 (0.93;1.14)

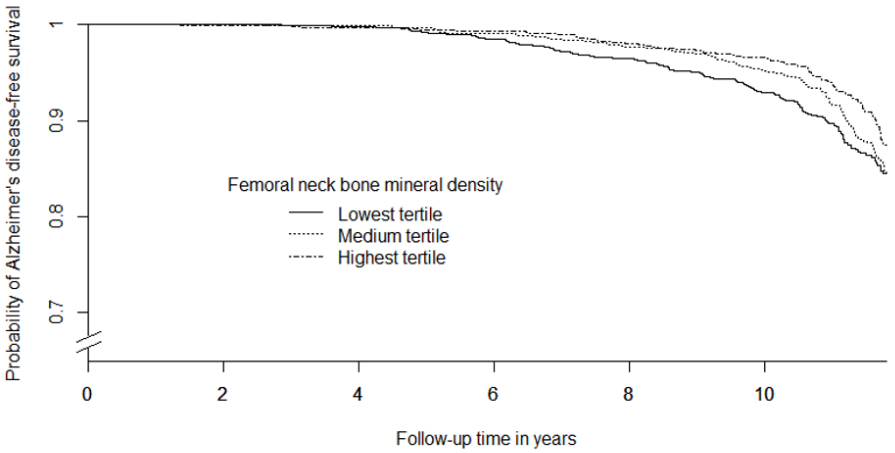
Definition of abbreviations: n = Cases, N = Total participants, *APOE* = Apolipoprotein E; CI = Confidence Interval; HR = Hazard Ratio; SD = Standard Deviation. Cox regressions were adjusted for age, sex, *APOE* genotype, education attainment, physical activity, smoking status, body mass index, systolic and diastolic blood pressure, total cholesterol levels, high-density lipoprotein cholesterol levels, and history of comorbidities (stroke and diabetes mellitus).

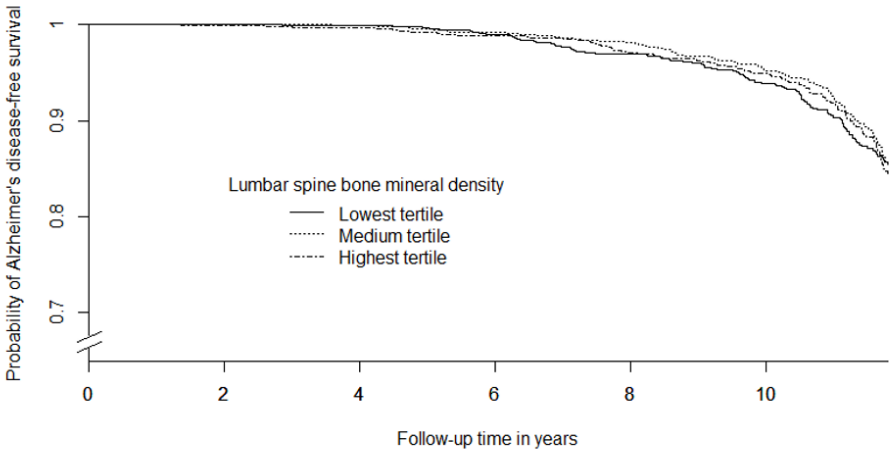
* follow-up time started after bone mineral density scans at baseline.

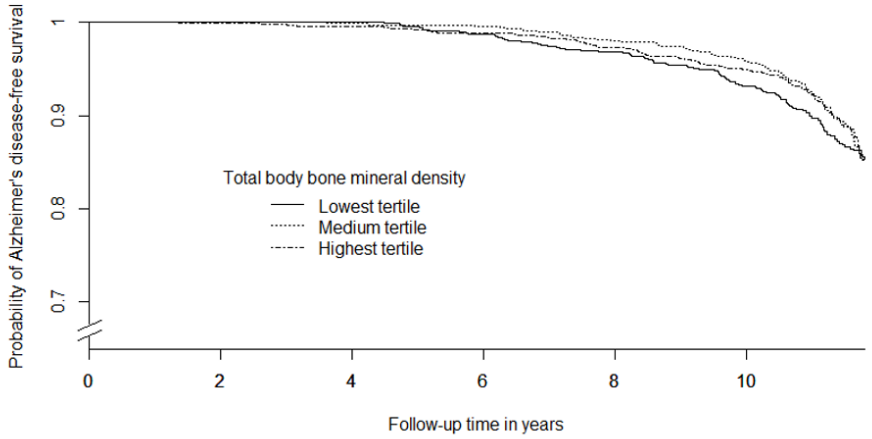
* The tertile categories of bone mineral density were derived by generating tertiles from the residuals of linear regression models adjusted for age (continuously) and sex. The highest tertile as the reference group.

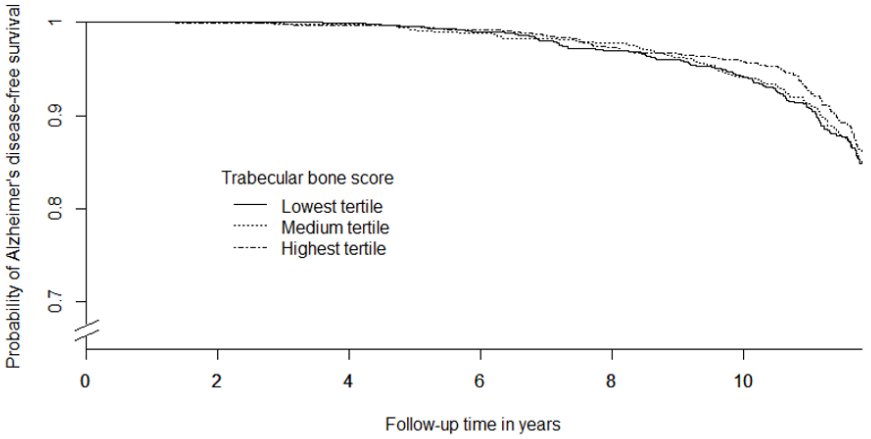
Bold font corresponds to significant P-value threshold.

eFigure 1. Kaplan-Meier curves of Alzheimer's disease-free survival at different levels of bone mineral density at each site.



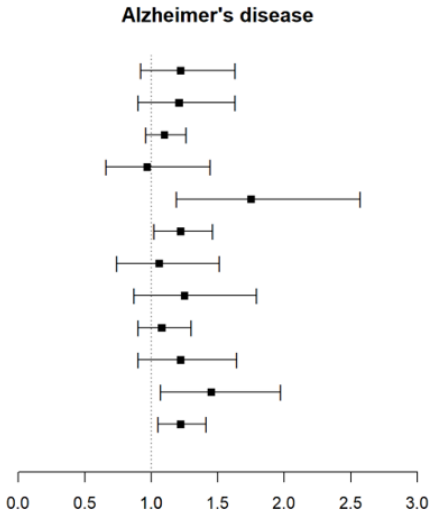






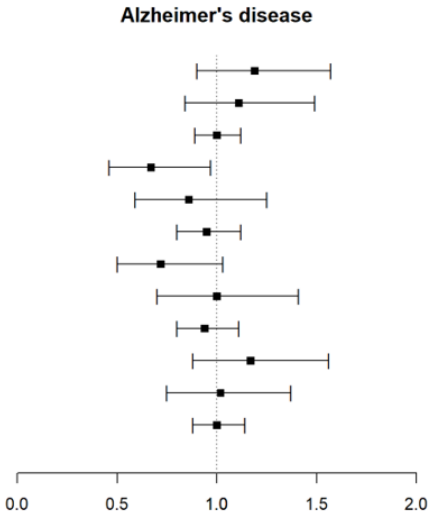
A

Participants	Femoral neck BMD	HR (95%CI)
Female	Medium tertile	1.22 (0.92, 1.63)
	Lowest tertile	1.21 (0.90, 1.63)
	Per SD decrease	1.10 (0.96, 1.26)
Male	Medium tertile	0.97 (0.66, 1.44)
	Lowest tertile	1.75 (1.19, 2.57)
	Per SD decrease	1.22 (1.02, 1.46)
APOE-e4	Medium tertile	1.06 (0.74, 1.51)
	Lowest tertile	1.25 (0.87, 1.79)
	Per SD decrease	1.08 (0.90, 1.30)
Non-APOE-e4	Medium tertile	1.22 (0.90, 1.64)
	Lowest tertile	1.45 (1.07, 1.97)
	Per SD decrease	1.22 (1.05, 1.41)



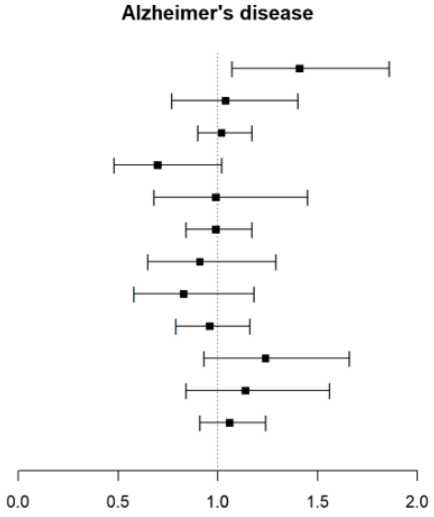
B

Participants	Lumbar spine BMD	HR (95%CI)
Female	Medium tertile	1.19 (0.90, 1.57)
	Lowest tertile	1.11 (0.84, 1.49)
	Per SD decrease	1.00 (0.89, 1.12)
Male	Medium tertile	0.67 (0.46, 0.97)
	Lowest tertile	0.86 (0.59, 1.25)
	Per SD decrease	0.95 (0.80, 1.12)
APOE-e4	Medium tertile	0.72 (0.50, 1.03)
	Lowest tertile	1.00 (0.70, 1.41)
	Per SD decrease	0.94 (0.80, 1.11)
Non-APOE-e4	Medium tertile	1.17 (0.88, 1.56)
	Lowest tertile	1.02 (0.75, 1.37)
	Per SD decrease	1.00 (0.88, 1.14)



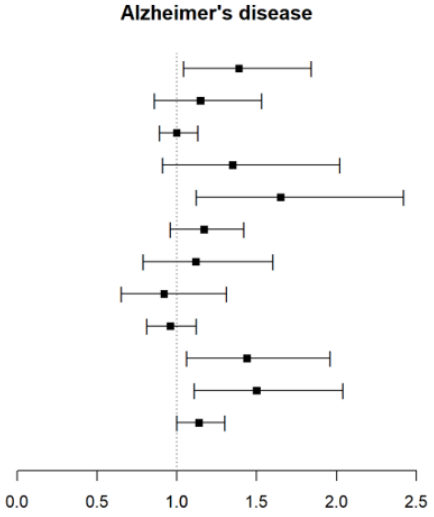
C

Participants	Total body BMD	HR (95%CI)
Female	Medium tertile	1.41 (1.07, 1.86)
	Lowest tertile	1.04 (0.77, 1.40)
	Per SD decrease	1.02 (0.90, 1.17)
Male	Medium tertile	0.70 (0.48, 1.02)
	Lowest tertile	0.99 (0.68, 1.45)
	Per SD decrease	0.99 (0.84, 1.17)
APOE-e4	Medium tertile	0.91 (0.65, 1.29)
	Lowest tertile	0.83 (0.58, 1.18)
	Per SD decrease	0.96 (0.79, 1.16)
Non-APOE-e4	Medium tertile	1.24 (0.93, 1.66)
	Lowest tertile	1.14 (0.84, 1.56)
	Per SD decrease	1.06 (0.91, 1.24)



D

Participants	Trabecular bone score	HR (95%CI)
Female	Medium tertile	1.39 (1.04, 1.84)
	Lowest tertile	1.15 (0.86, 1.53)
	Per SD decrease	1.00 (0.89, 1.13)
Male	Medium tertile	1.35 (0.91, 2.02)
	Lowest tertile	1.65 (1.12, 2.42)
	Per SD decrease	1.17 (0.96, 1.42)
APOE-e4	Medium tertile	1.12 (0.79, 1.60)
	Lowest tertile	0.92 (0.65, 1.31)
	Per SD decrease	0.96 (0.81, 1.12)
Non-APOE-e4	Medium tertile	1.44 (1.06, 1.96)
	Lowest tertile	1.50 (1.11, 2.04)
	Per SD decrease	1.14 (1.00, 1.30)



eFigure 2. Associations of low bone mineral density of total body (A), the femoral neck (B), the lumbar spine (C), and trabecular bone scores with risk of Alzheimer's disease, stratified by sex and *APOE*-ε4 allele carriership. *APOE* = Apolipoprotein E; BMD = Bone Mineral Density; HR = Hazard Ratio. Participants in the highest tertile of bone mineral density were regarded as the reference group (hidden). Estimated HRs were obtained after adjustment of (if applicable) age, sex, *APOE* genotype, education attainment, physical activity, smoking status, body mass index, systolic and diastolic blood pressure, total cholesterol levels, high-density lipoprotein cholesterol levels, and history of comorbidities (stroke and diabetes mellitus).

* The tertile categories of bone mineral density were derived by generating tertiles from the residuals of linear regression models adjusted for age (continuously) and sex. The highest tertile as the reference group.