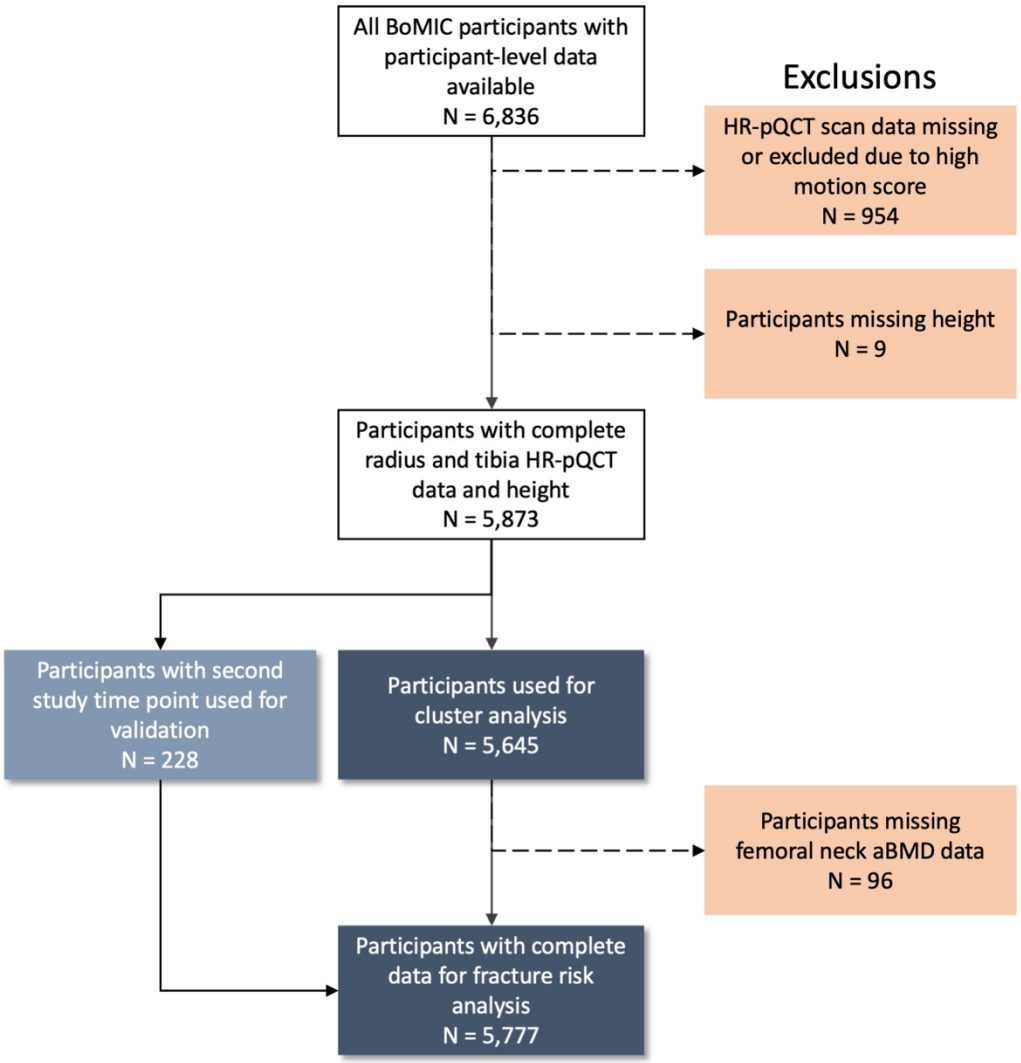
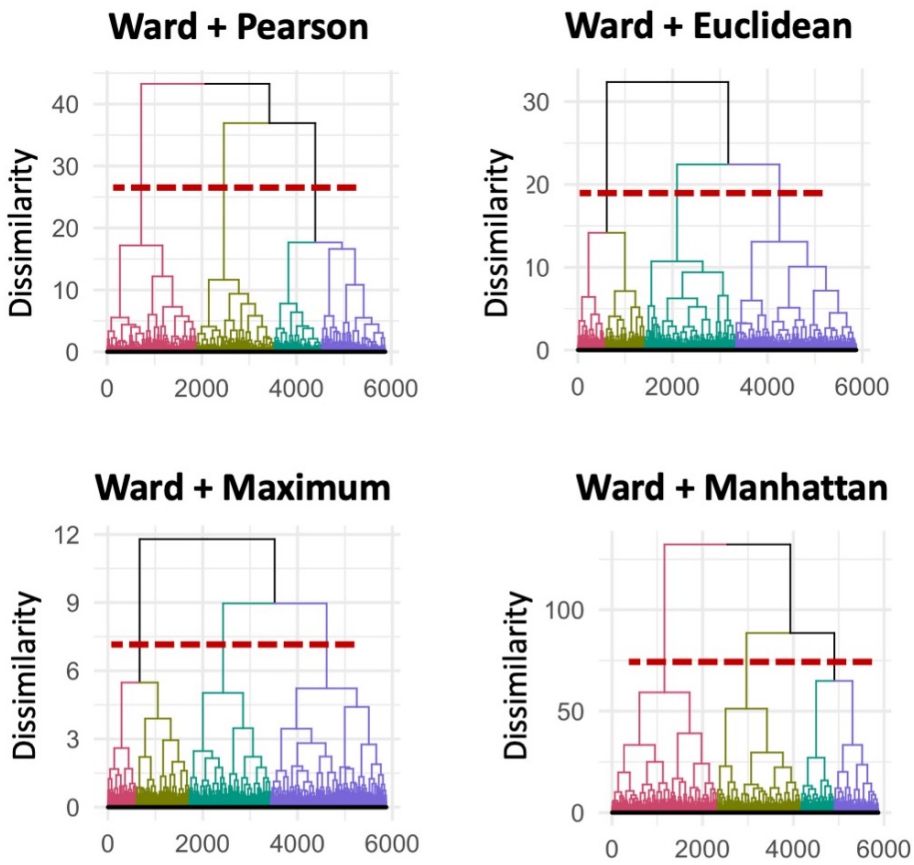
SUPPLEMENTAL FIGURES

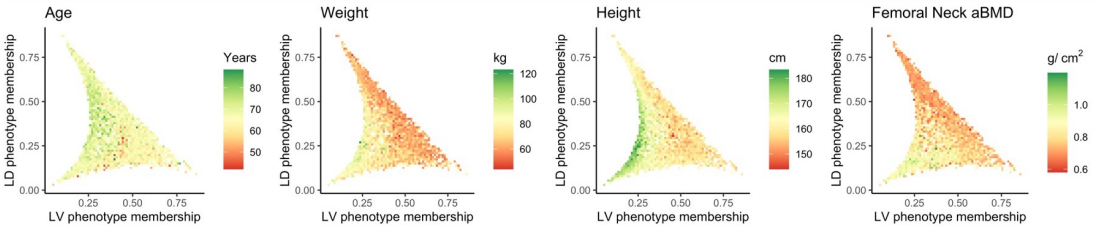


Supplemental Figure 1: Flowchart of exclusion criteria for study population.

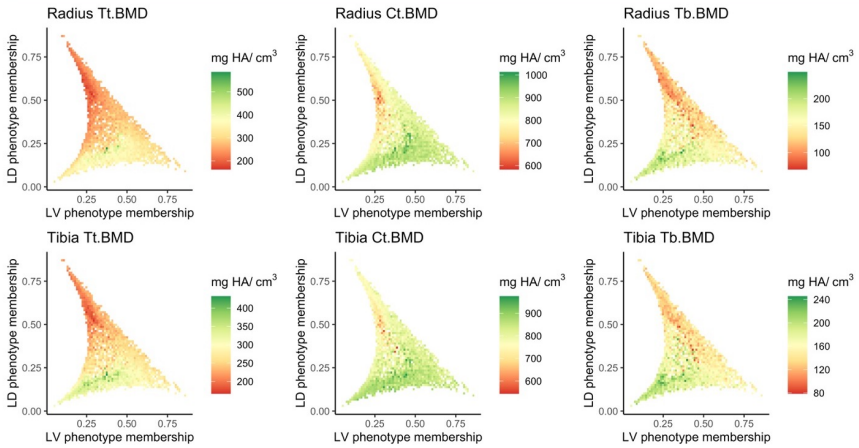


Supplemental Figure 2: Dendrograms of the top four candidate agglomerative clustering models that were used for seeding the fuzzy c-means algorithm. The dashed red line shows the pruning level determined on visual inspection for selecting the appropriate number of clusters.

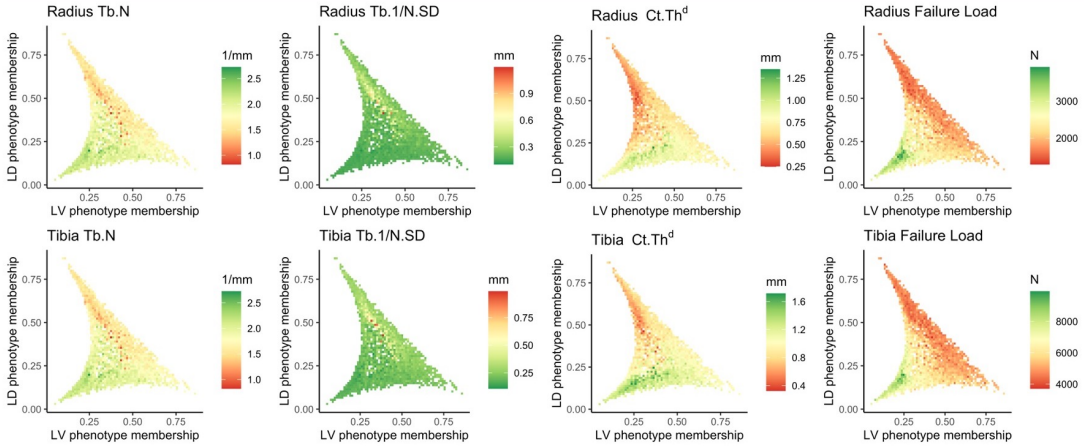
Clinical parameters



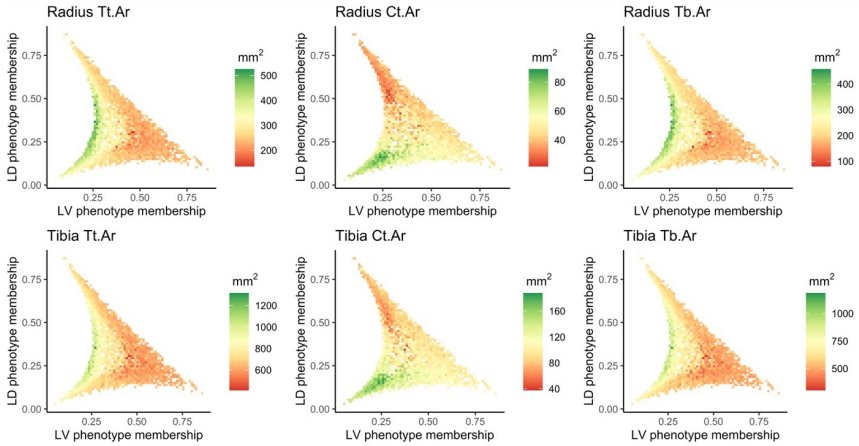
Bone mineral density parameters



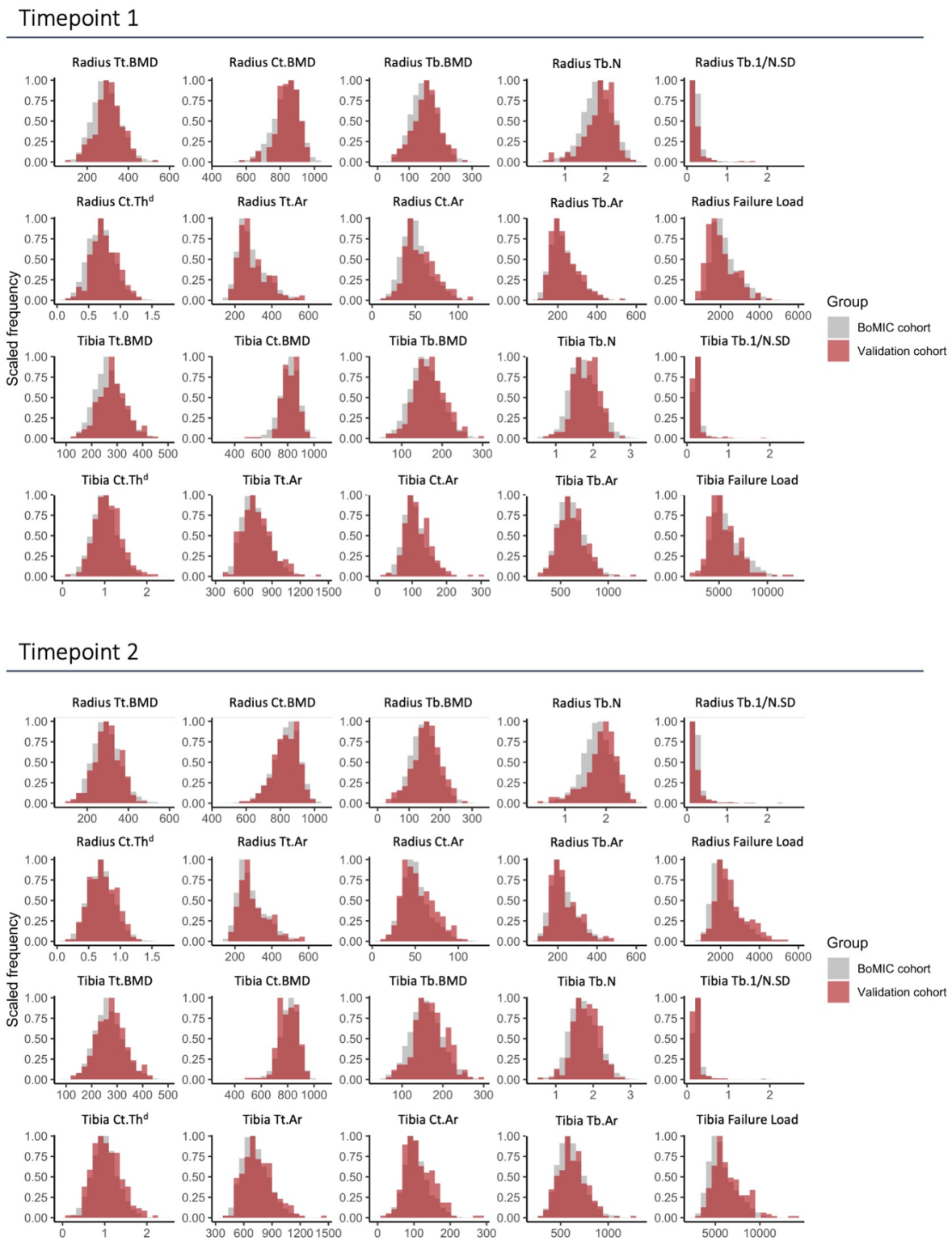
Bone microarchitecture parameters



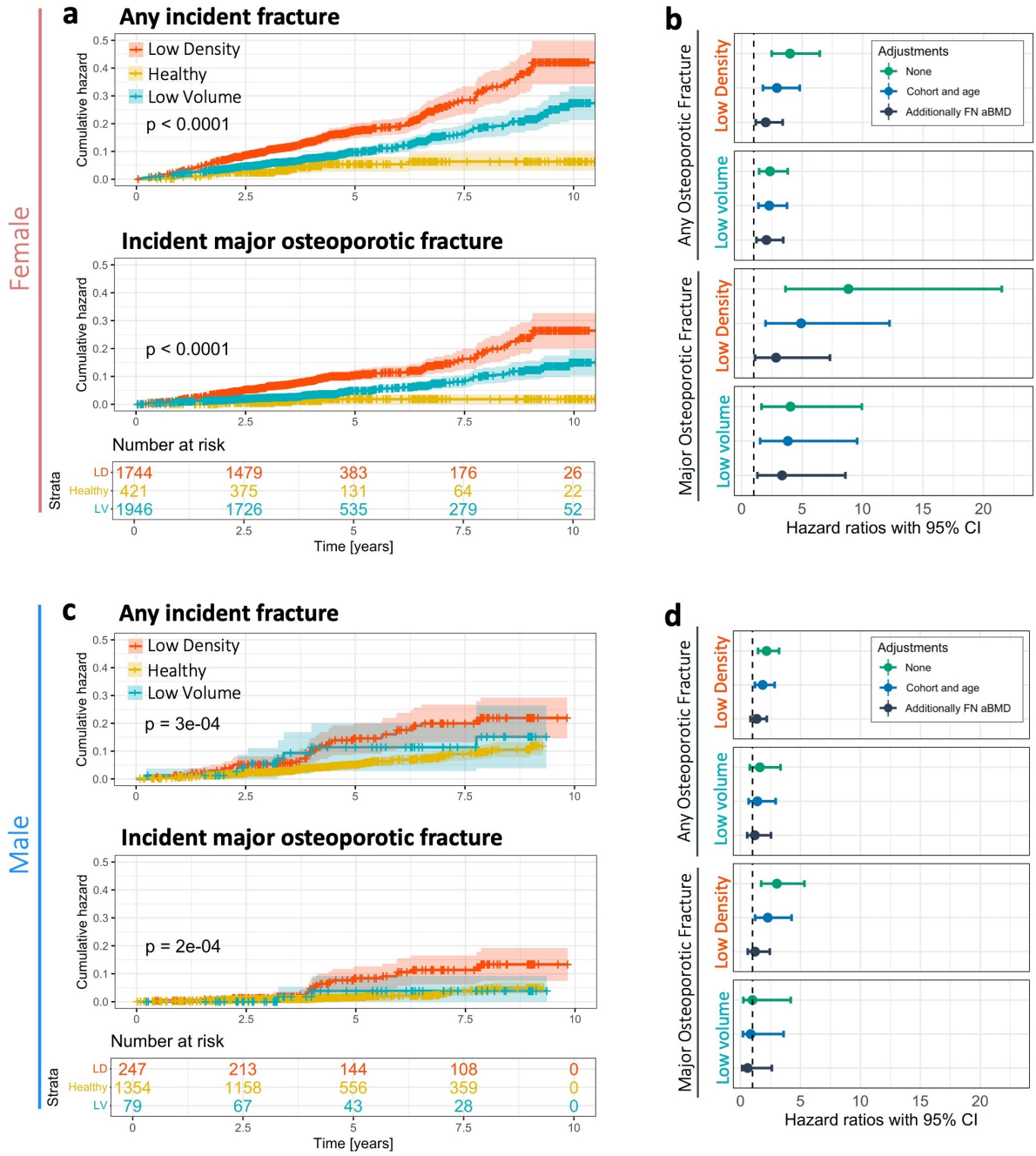
Bone cross-sectional area parameters



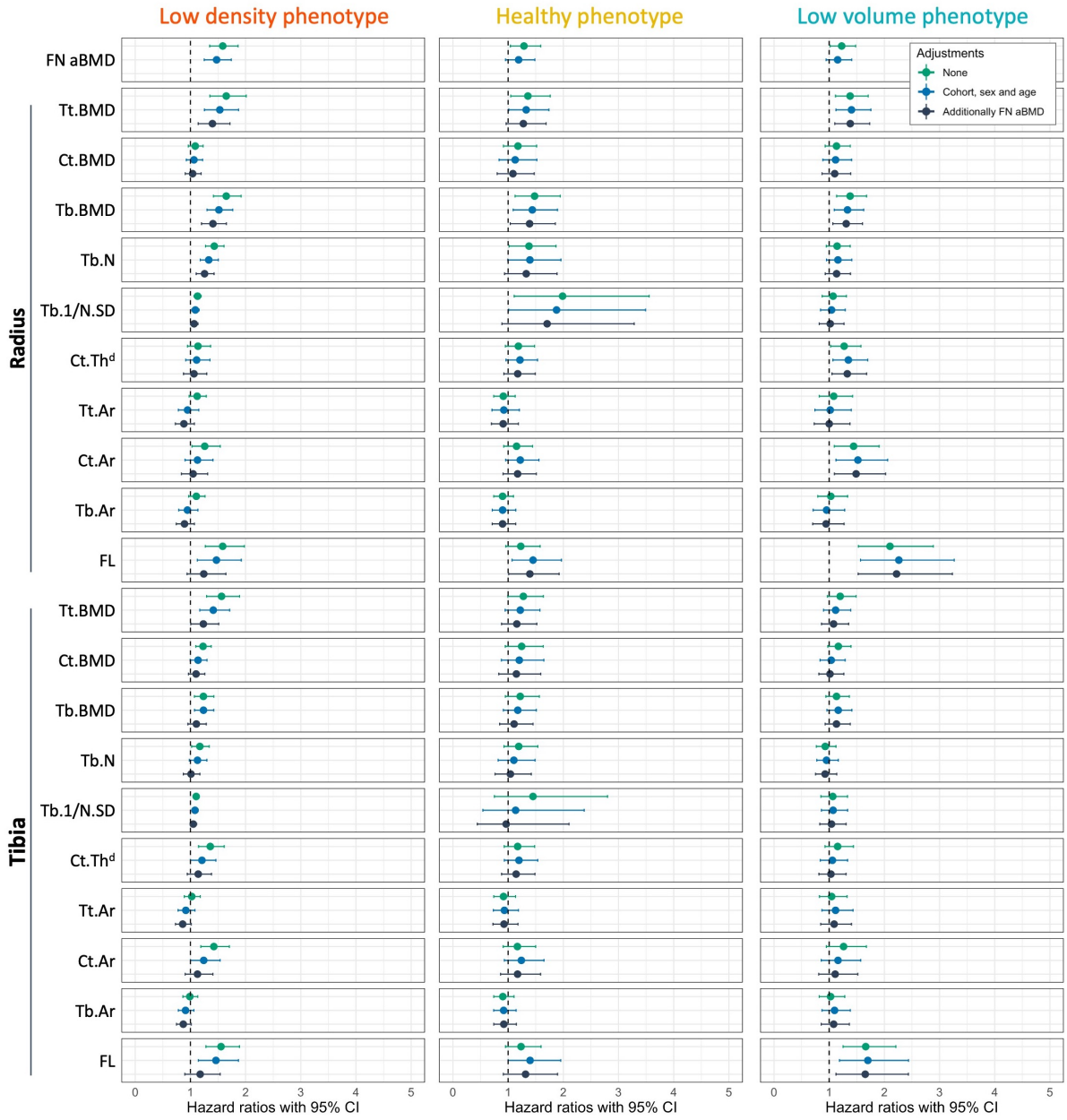
Supplemental Figure 3: Distribution of all clinical and HR-pQCT parameters relative to phenotype membership. Each plot is the cluster membership coefficient of the *low density* (LD) versus *low volume* (LV) phenotypes for the BoMIC cohort. Heat maps of individual parameters are applied to the plots to represent the distribution across all three phenotypes. Abbreviations: aBMD = areal bone mineral density, Tt.BMD = total bone mineral density, Ct.BMD = cortical bone mineral density, Tb.BMD = trabecular bone mineral density, Tb.N = trabecular number, Tb.1/N.SD = trabecular inhomogeneity, $Ct.Th^{d}$ = cortical thickness, Tt.Ar = total cross-sectional area Tt.Ar = total cross-sectional area, Ct.Ar = cortical cross-sectional area, and Tb.Ar = trabecular cross-sectional area.



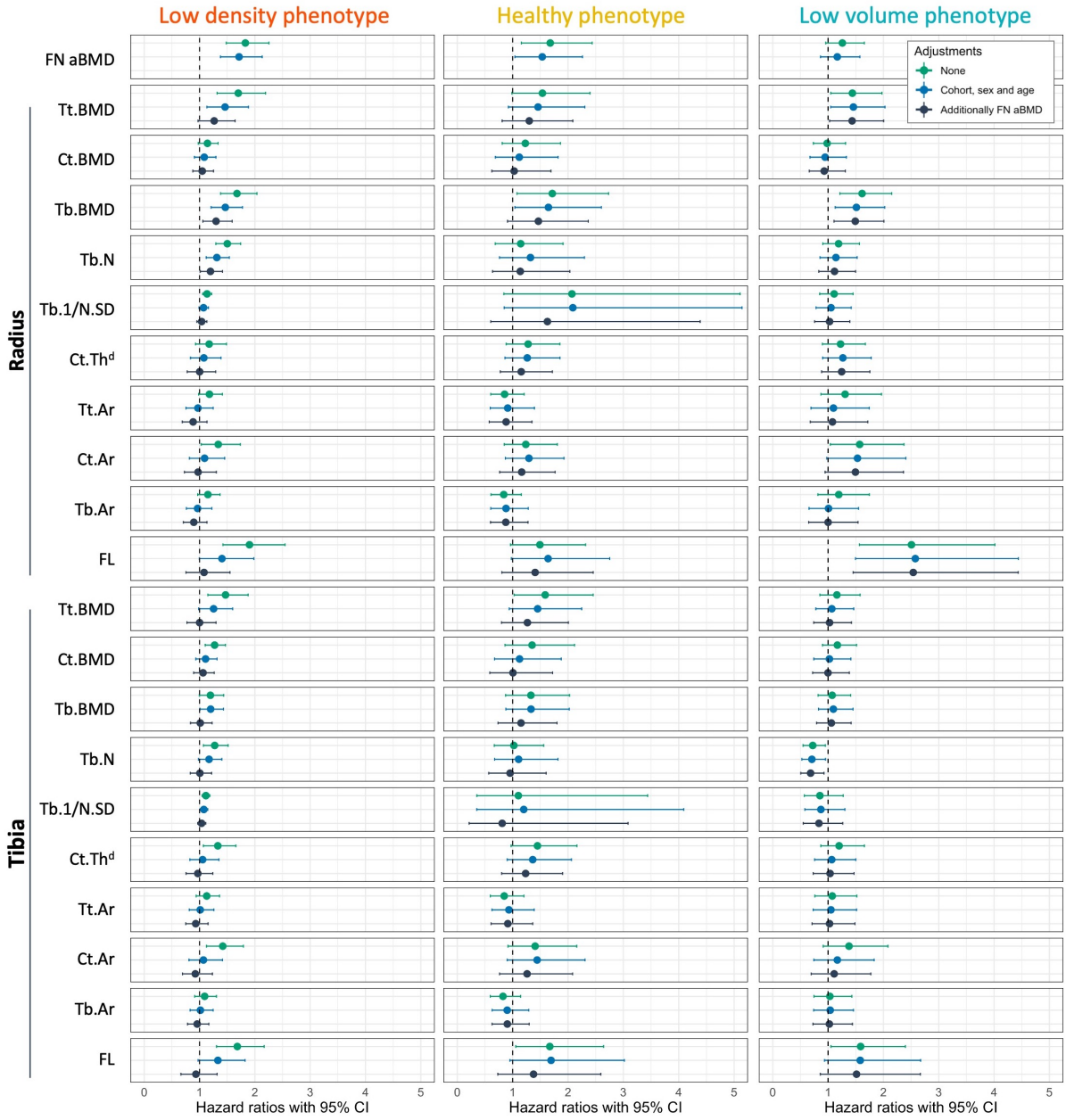
Supplemental Figure 4: Histograms of distribution of all HR-pQCT parameters for the BoMIC cohort and the validation cohort at each time point. Frequencies are scaled from 0 to 1 for comparison. Abbreviations: Tt.BMD = total bone mineral density, Ct.BMD = cortical bone mineral density, Tb.BMD = trabecular bone mineral density, Tb.N = trabecular number, Tb.1/N.SD = trabecular inhomogeneity, Ct.Th^d = cortical thickness, Tt.Ar = total cross-sectional Ct.Ar = cortical cross-sectional area, and Tb.Ar = trabecular cross-sectional area.



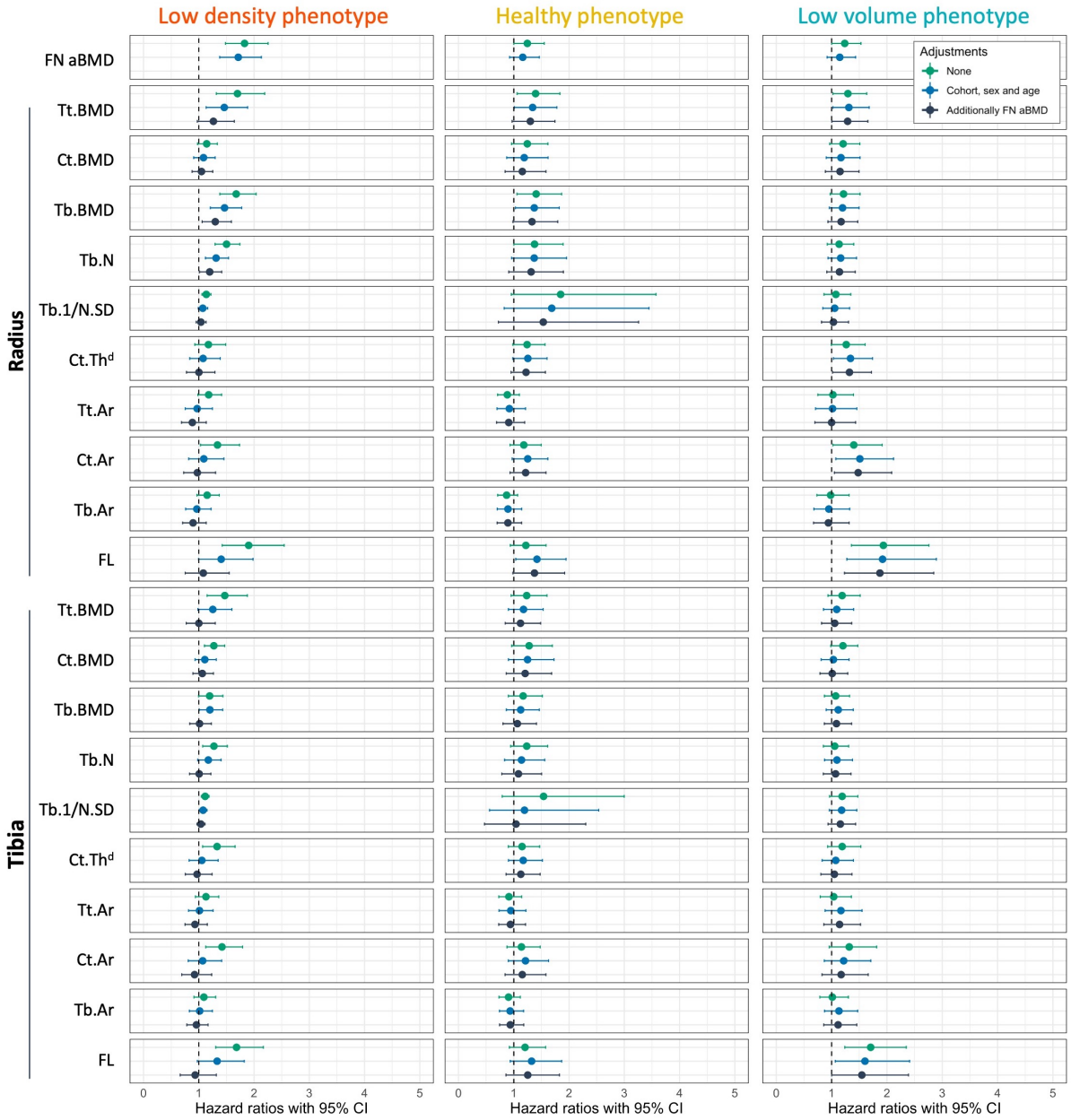
Supplemental Figure 5: Sex-specific cumulative hazard curves and hazard ratios. **(a)** Cumulative hazard functions determined using the Nelson-Aalen estimator, of any incident fracture and only major osteoporotic fracture (MOF) when only females are considered. **(b)** Hazard ratio (HR) and 95% CI for the association between phenotype and any incidence fracture or only MOF for females, with and without adjustments for covariates. **(c-d)** Are equivalent information presented in **a-b** when only males are considered.



Supplemental Figure 6: Within-phenotype associations between ANY OSTEOPOROTIC FRACTURE and bone parameters. The hazard ratios (HR) and 95% confidence intervals (CI) are shown for the association between incident fracture of any site relative to individual bone parameters. The HR are reported per standard deviation (SD) decrease of each bone parameter, except for trabecular inhomogeneity (Tb.1/N.SD) which is per SD increase. Abbreviations: Tt.BMD = total bone mineral density, Ct.BMD = cortical bone mineral density, Tb.BMD = trabecular bone mineral density, Tb.N = trabecular number, Tb.1/N.SD = trabecular inhomogeneity, Ct.Th^{d} = cortical thickness, Tt.Ar = total cross-sectional Ct.Ar = cortical cross-sectional area, and Tb.Ar = trabecular cross-sectional area.



Supplemental Figure 7: Within-phenotype associations between MAJOR OSTEOPOROTIC FRACTURE and bone parameters. The hazard ratios (HR) and 95% confidence intervals (CI) are shown for the association between incident fracture of a major osteoporotic fracture site relative to individual bone parameters. The HR are reported per standard deviation (SD) decrease of each bone parameter, except for trabecular inhomogeneity (Tb.1/N.SD) which is per SD increase. Abbreviations: Tt.BMD = total bone mineral density, Ct.BMD = cortical bone mineral density, Tb.BMD = trabecular bone mineral density, Tb.N = trabecular number, Tb.1/N.SD = trabecular inhomogeneity, Ct.Th^{d} = cortical thickness, Tt.Ar = total cross-sectional Ct.Ar = cortical cross-sectional area, and Tb.Ar = trabecular cross-sectional area.



Supplemental Figure 8: Within-phenotype associations between ANY OSTEOPOROTIC FRACTURE EXCEPT THE WRIST and bone parameters. The hazard ratios (HR) and 95% confidence intervals (CI) are shown for the association between incident fracture of any site relative to individual bone parameters. The HR are reported per standard deviation (SD) decrease of each bone parameter, with the exception of trabecular inhomogeneity (Tb.1/N.SD) which is per SD increase. Abbreviations: Tt.BMD = total bone mineral density, Ct.BMD = cortical bone mineral density, Tb.BMD = trabecular bone mineral density, Tb.N = trabecular number, Tb.1/N.SD = trabecular inhomogeneity, Ct.Th^{d} = cortical thickness, Tt.Ar = total cross-sectional Ct.Ar = cortical cross-sectional area, and Tb.Ar = trabecular cross-sectional area.