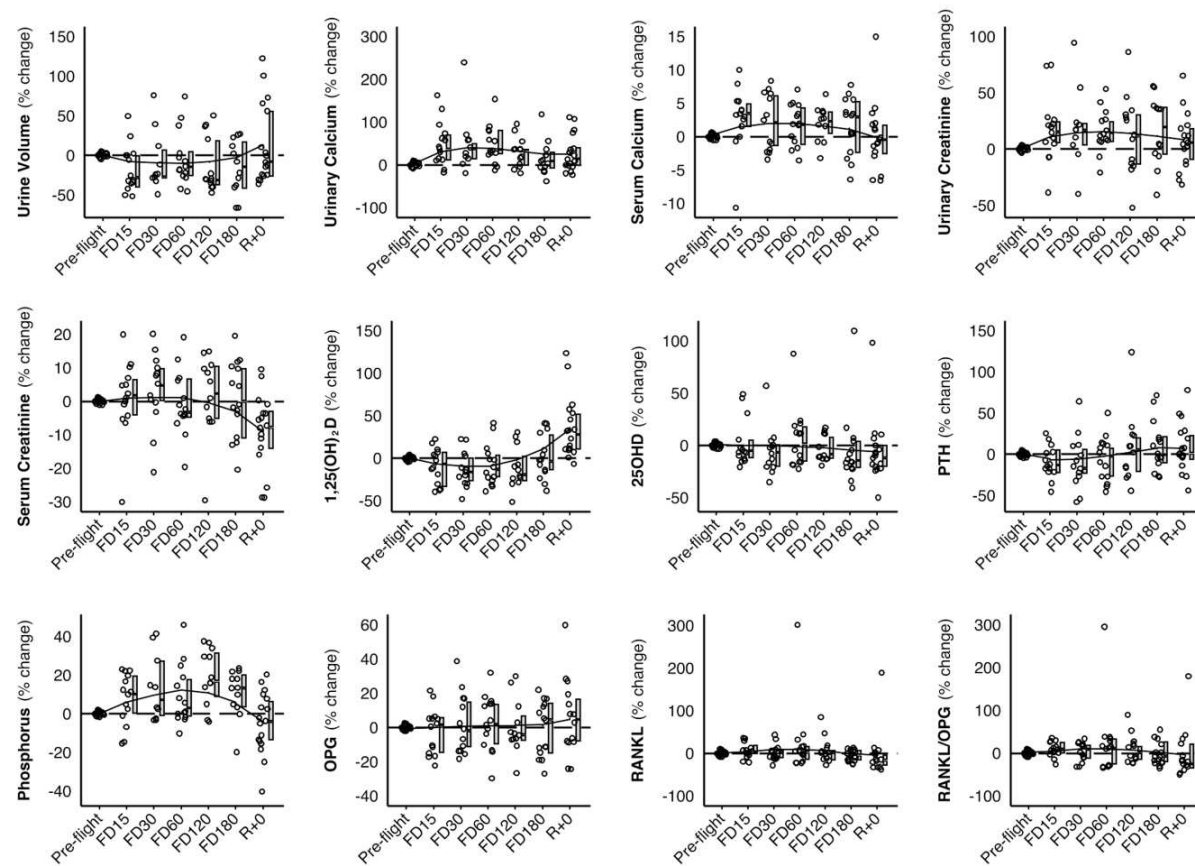
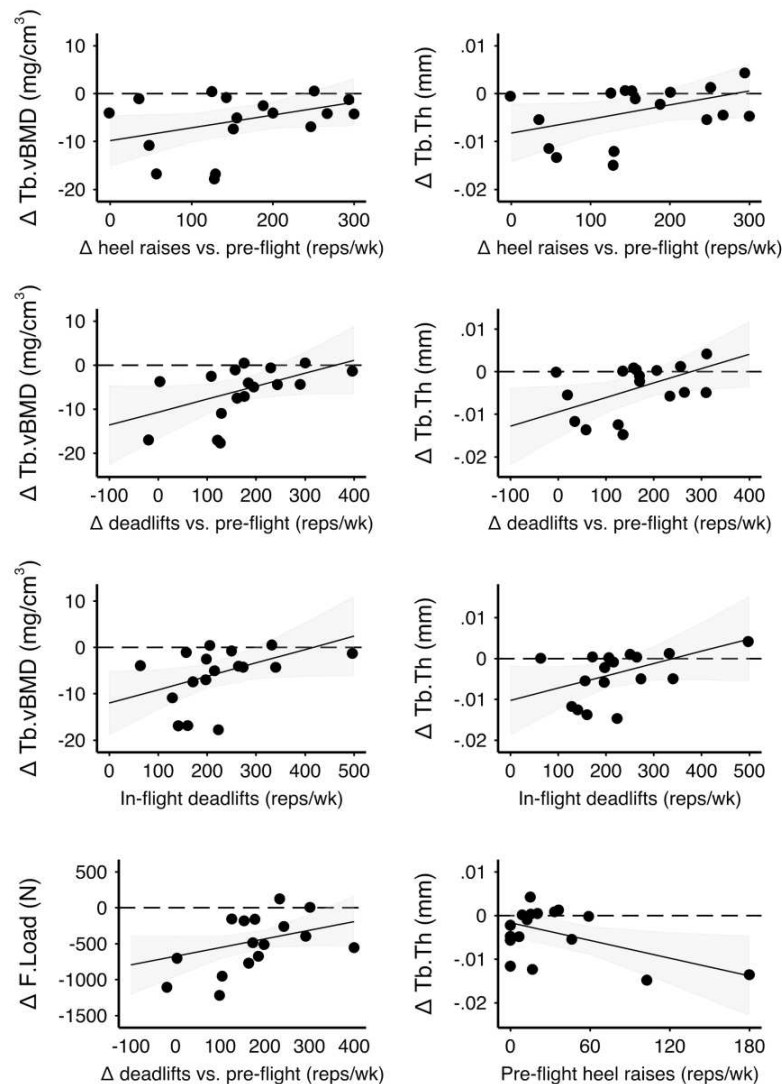


Supplementary Figure 1. Relationship between mission duration and change in *radius* bone variables (in parameter units e.g, mg/cm<sup>3</sup>). Model is based on raw data (n=17); however, for privacy purposes only summary data are plotted: x < 6-month mission (n=9), o > 6-month mission (n=8). The line and shaded 95% confidence intervals (CI) represent the predicted relationship between change in bone variables and mission duration based on the mixed effects model. Significant difference post-flight is indicated where CIs do not cross 0. Failure load (F.Load) and total volumetric bone mineral density (Tt.vBMD).



Supplementary Figure 2. Change in biomarkers at each timepoint (pre-flight, flight day (FD)15, FD30, FD60, FD120, FD180 and return (R+0)). Individual data points are indicated in open circles next to a boxplot (median change, interquartile range) and overlaid by a lowess smoothing curve. 24-hr urine volume; urinary calcium; serum calcium; urinary creatinine; serum creatinine; 1,25(OH)<sub>2</sub>D, 1,25 di-hydroxy vitamin D; 25OHD, 25-hydroxyvitamin D; PTH, intact parathyroid hormone; phosphorus; OPG, osteoprotegerin; RANKL; RANKL/OPG.



Supplementary Figure 3. Relationship between resistance training and change in bone variables. Black circles are raw change data (in parameter units) for each crewmember. The line and shaded 95% confidence intervals (CI) represent the predicted relationship between change in bone variables and resistance training volume based on the mixed effects model (including fixed effects of mission duration, exercise volume and interactions with time). Significant difference post-flight is indicated where CIs do not cross 0. All plots are for the non-dominant tibia except F.Load, where values are plotted for the dominant tibia. Note: A change of 4 mg/cm<sup>3</sup>, 0.005 mm, 200 N for Tb.vBMD, Tb.Th, and F.Load, respectively, is equivalent to a relative change of approximately 2%. The relationship between change in Tb.Th and pre-flight heel raise was consistent with and without the crewmember at 180 reps/wk.