Appendix

Linear mixed model formulation

The linear mixed model (50) is a technique for modeling longitudinal data where the objective is to assess the association between explanatory variables that can either be measured repeatedly over time or only once at baseline with outcomes measured repeatedly over time in individuals. In particular we have n individuals indexed by $i = 1, 2, \cdots, n$, and for the i^{th} individual we repeatedly measure an outcome variable Y (e.g. bone widths) over n_i time points indexed by $j = 1, 2, \cdots, n_i$ i.e. $Y_{ij} = (y_{i1}, y_{i2}, ..., y_{in_i})'$ for the i^{th} individual (with the subscript n_i indicating that the number of measurement occasions could vary between individuals). Additionally let $X_{ij} = (x_{ij1}, x_{ij2}, ..., x_{ijk})'$ be the values of $k = 1, 2, \cdots, p$ covariates measured at the j^{th} occasion (e.g. x_{ij1} = age, x_{ij2} = weight, etc). If a covariate is not time varying (e.g. sex) or is measured only once at baseline, then the baseline values (x_{i1k}) are carried forward.

Estimating longitudinal and cross-sectional effects

By expressing each time-varying covariate as a sum of the value observed at baseline and the difference between each repeat measurement and the baseline value, i.e. $X_{ijk} = X_{i1k} + (X_{ijk} - X_{i1k})$ it is possible to divide the vector of covariates and into cross-sectional (baseline) and longitudinal (changes from baseline) effects, (50) allowing for the estimation of both effects using the same linear mixed model formulated as:

$$
\begin{aligned}
E(Y_{ij} \mid X_{ij}) &= \beta_1^{(c)} X_{i11} + \beta_2^{(c)} X_{i12} + \cdots + \beta_p^{(c)} X_{i1p} \\
&\quad + \beta_1^{(l)} (X_{ij1} - X_{i11}) + \beta_2^{(l)} (X_{ij2} - X_{i12}) + \cdots + \beta_p^{(l)} (X_{ijp} - X_{ijp}) \\
&= X_{ij}^{'} \beta^{(c)} + (X_{ij} - X_{i1})^{'} \beta^{(l)}
\end{aligned}
$$

Where $\beta^{(c)}$ is a vector of coefficients describing cross-sectional effects and $\beta^{(l)}$ is a vector of coefficients describing longitudinal effects. For the non-time varying covariates whose baseline values are carried forward, $X_{ijk} - X_{i1k} = 0$ for all time points and so only the cross-sectional effect relating to baseline value x_{i1k} is estimated unless otherwise the baseline value is interacted with the longitudinal component of a time varying covariate. The above approach was used to estimate the cross-sectional and longitudinal effects in this paper.