

Appendix 6: Model fitting procedure

1. Up to two coefficients for fractional polynomial transformations of week (both definitions) were allowed to be included in the mixed effects meta-regression models. The powers considered were from the -3 to 3 and were automatically sort using the fp prefix command in State v18. Given the complexity of the models fitted, the deviance difference test was not valid in choosing the FP model. In all models presented, inspection of the deviance values for the single coefficient transformation and two coefficient transformations revealed a large absolute reduction with the addition of the second coefficient.
2. The FP procedure in 1. was repeated under 3 random effects models: a) intercept only, b) random slopes allowed for the FP transformations of time assuming independence from the intercepts, and c) allowing the random slopes and intercepts to correlate assuming an unstructured variance covariance matrix. The best fitting model in each step was noted and the one with the |BIC| closest to zero was used for estimation.
3. Often the correlated random effects models did not converge and a best FP model under this condition was not available. In this case, the best FP model with uncorrelated random effects was re-estimated allowing correlated random effects, and if convergence was achieved and the correlation improved the BIC, this model was used for estimation. If convergence was not achieved, the FP model without correlated random effects was chosen.
4. For the persistent cohort, disability and pain outcomes, corrected and uncorrected time definitions, only a natural log transformation was considered given the sparse data for this group, the clinical observation that the course of pain and disability is unlikely to be linear and the tendency for any other FP transformations to produce curves that produced interpolations within the observed data points that could not be substantiated by the observed data. The smallest |BIC| was used to determine with random effects model was the best for estimation.
5. For sensitivity analyses, groups with 3 studies only (subacute cohorts) were modelled using FP transformations. As per 1 to 3 above. Although there was a lack of data, the log transformation alone did not follow the observed trajectory and provided a poor fit for these subgroups.