# Statistical Analysis

We will analyze the repeatedly measured patient LBM data using a linear mixed model. The evolution of patient’s LBM is modeled over time using piecewise linear functions over time. This is because we expect that patient lean body mass will follow a different trajectory when treatment is switched. To this end, we use the following definition of the model:

Where, and are the -th patient’s observed LBM, and measurement error at time . The random effects are assumed to follow a normal distribution with zero mean and unknown variance . The fixed effects are denoted by . The covariate takes a value between 0 and 2.25 years, and takes a value 1 when placebo is given first to a patient, and 0 otherwise. The reason the knot of piecewise linear regression is kept at year 1.25 is because in case of growth hormone the last injection is given at year 1 and hence we expect 0.25 years of increase in LBM, before it starts declining (washout period).

We kept a rather simple random effects structure with only random intercept . This is because having 4 different random effects for evolution over time leads to a very large covariance matrix. Since, we measure patient’s LBM a limited number of times we decided to stick only to random intercepts. We conducted sensitivity analyses on simulated data to make sure such an assumption affects the fixed effects (our main parameters of interest) trivially. With such a model, for a patient who is given placebo in year one and growth hormone in year two. The resulting evolution of this patient in year one and year two will be,

However, for a patient who is given growth hormone in year one and placebo in year two, the resulting evolution in year one and two will be,

# Sample size calculation

We want to test if the effect of growth hormone and placebo is same. This can be tested with the following null hypothesis test , and alternate hypothesis that . Lacking standard packages for testing a hypothesis for a rather non-trivial model like ours, we did sample size calculation using simulations. The R code for this simulation and sample size calculation are attached with this draft. For simulating correct population we chose the following values for: