The course of multiple sclerosis (MS) is generally difficult to predict. This is due to the great interindividual variability with respect to symptoms and disability status. An important prognostic endpoint for MS is the expected time to sustained disease progression. Using the Expanded Disability Status Scale (EDSS) this endpoint is here defined as a rise of 1.0 or 0.5 compared to baseline EDSS (5.5 or >5.5) which is confirmed for at least six months. The goal of this paper was threefold. It aimed at identifying covariates which significantly influence sustained progression, determining size and form of the effect of these covariates and estimating the survival curves for given predictors.

To this end a piecewise exponential model utilizing piecewise constant hazard rates and a Poisson model were devised. In order to improve and simplify these models a method for piecewise linear parameterization of non-parametric generalized additive models (GAMs) was applied. The models included fixed and random effects, the posterior distribution was estimated using Markov Chain Monte Carlo methods (MCMC) as well as a penalized likelihood approach and variables were selected using Akaike’s information criterion (AIC).

The models were applied to data of placebo patients from worldwide clinical trials that are pooled in the database of the Sylvia Lawry Centre for Multiple Sclerosis Research (SLCMSR). Only with a pure exponential model and fixed effects, baseline EDSS and the number of relapses in the last 12 month before study entry had an effect on the hazard rate. For the piecewise exponential model with random study effects there was no effect of covariates on the hazard rate other than a slightly decreasing effect of time. This reflects the fact that unstable patients reach the event early and are therefore eliminated from the analysis (selection effect).