Stockholm University

Mathematical Statistics
Stockholm University
Master Thesis **2024:9**
http://www.math.su.se

Surviving non-proportional hazards with flexible parametric modeling

Martin Andersson*

June 2024

Abstract

In this thesis we have investigated the difference in output between the base Cox regression model (a proportional hazard model) and the flexible parametric model (a more general survival model). The comparison was performed on a linked data-set from the Swedish Prescribed Drug and the National Patient Register. The data-set was intended to statistically test if treatments prescribed to patients with atopic dermatitis or psoriasis had a significant effect on developing venous thromboembolism. This data-set was used to create a plasmode simulation to test how the Cox model performed on a data-set with proportional hazards and one with simulated crossing hazard rate functions. Additionally, a Cox model and a flexible parametric model was fitted to the data to compare the results, specifically how the flexible parametric model captures the hazard rates using natural splines.

Moreover, the question on how to deal with non-proportional hazards is discussed. In addition to being able to visualize the hazard rates, the flexible parametric model can also model interaction between the covariates and time using natural splines. We also investigated how to test for and identify non-proportional hazards.

The results indicate that the base Cox model can be seen as a special case of the more general flexible parametric model. As such, if the results of the base Cox model are the main interest, the flexible parametric model can supply those, along with several other results the Cox model cannot. While the flexible parametric model captures non-proportional hazards, testing for these kinds of hazards is not easy. The tests tend to have low power and some need to be performed visually. However, cases with visually non-crossing hazards but with tests positive for non-proportional hazards do not necessarily make the results of a proportional hazards model unusable. Crossing hazards on the other hand are likely to be very obvious during visual tests and can be modeled accordingly when spotted. The proportional hazards model, either using the Cox method or the flexible parametric model is therefore still generally usable, even if the hazards are not exactly proportional.

*Postal address: Mathematical Statistics, Stockholm University, SE-106 91, Sweden.
E-mail: martin.hans.erik.andersson@gmail.com. Supervisor: Johannes Heiny, Marie Linder.