A joint modelling approach for Health-Related Quality of Life and survival analysis of a 5-year follow-up study of COPD patients

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Recently, in clinical trials, there has been an increasing interest in using longitudinal biomarkers for characterizing the occurrence of an event, such as death or illness recovery. This interest leads to longitudinal studies based on patients' follow-up periods where the values of certain variables may be recorded repeatedly, whereas the time-to-event is also monitored. Therefore, two types of outcomes from the same subject are simultaneously observed: repeated measures and time-to-event. The inherent association between the outcomes has brought the joint modelling framework to analyze them jointly.

Furthermore, there is a growing priority on placing patients at the centre of healthcare research and evaluating clinical care. In this context, patient-reported outcomes (PROs) are helpful tools for informing clinicians about patients' health status. This information comes directly from the patients and is collected by providing them with questionnaires that consider their health, quality of life, or functional status.

In this work, we propose a joint modelling approach for longitudinal PRO measurements and survival data that include adequate distributional fits of PRO by considering its nature and characteristics. In particular, we assessed data from a 5-year follow-up study of 543 patients with chronic obstructive pulmonary disease (COPD) from Galdakao-Usansolo Hospital in Biscay, Spain. The overall impact of COPD on the subject is multifaceted. Thus, more than clinical biomarkers are needed to assess the disease evolution. In this sense, the COPD study considered survival data and one to four Health-Related Quality of Live (HRQoL) scores per individual collected during the follow-up period. Two questionnaires were used to evaluate the HRQoL, which turned out to be an important indicator of the health status of patients with chronic diseases: one generic, the Short-Form 36, and the other disease-specific, St. George's Respiratory Questionnaire. We provide relevant clinical results over the association of the HRQoL and survival data in the COPD study. Additionally, we performed a simulation study based on the COPD study scenario to compare our proposal with two popular approaches that also consider both outcomes: the Joint Modelling full likelihood approach and the Time-Varying covariate Cox model.

Keywords: Joint Modelling, PRO, COPD.