

4-step longitudinal analysis of latent traits  
derived from measurement scales in chronic diseases :  
quality-of-life in multiple system atrophy

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## Abstract

**Introduction :** There is a growing interest in subjective latent traits, such as quality of life (QoL), to describe progression of chronic diseases. Indeed, as centered on patients' feelings, they provide crucial information for delivering better support. The longitudinal analysis of latent traits requires special attention : (i) it needs to adapt to the definition of the trait as one or multiple constructs underlying the items of a measurement scale as done with the Item Response Theory (IRT) ; (ii) it needs to account for the possible association with clinical events (e.g. death) as done in the joint modeling (JM) framework ; (iii) it needs to be studied in relation with the clinical progression. We propose a 4-step longitudinal analysis to address this issue.

**Methods :** The 4 steps are :

- (1) identify all the underlying dimensions measured by the scale, through factorial analysis ;
- (2) assess each dimension trajectory, using a joint latent process model (JLPM) which models the trajectory of a latent trait measured by ordinal items using a longitudinal IRT model, and simultaneously models the risk of event according to the latent trait.
- (3) determine the sequence of items' degradation and confront it to disease progression by projecting objective markers along the sequence ;

(4) quantify the item-Fisher information at different disease stages.

**Application :** We applied this strategy to describe QoL changes in Multiple-System Atrophy (MSA), a rare neurodegenerative disease, using data from the French MSA cohort (>600 patients). Repeated measures of the 40 ordinal items from the MSA-specific QoL scale were analyzed revealing 4 dimensions (motor, non-motor, emotional, nutrition) that progressively deteriorated over the course of the disease with faster changes for the motor sphere and modulations of the impairment according to sex, age, and MSA subtype. Most informative items were listed informing on the most sensitive manifestations during clinical progression.

**Conclusion :** The proposed 4-step strategy offers a complete approach for the longitudinal analysis of measurement scales in chronic diseases. By combining IRT along with JM, it addresses the statistical issues due to both the measurement scales and the occurrence of clinical endpoints. The use of Fisher information and clinical progression projections also offers potential for item selection and patient stratification.

## Keywords

Joint model, Item Response Theory, Longitudinal data, chronic diseases, quality-of-life