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Título: Extending multistate models: second order Markov and recurrence analysis.

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Abstract: Multistate models (MSMs) provide a dynamic framework for understanding disease progression through multiple clinical events and for identifying relevant prognostic factors. They are widely applied in medical and epidemiological research, where objectives typically include estimating transition probabilities between disease stages, evaluating the effects of covariates, estimating the expected time in each state, and computing the risk of death conditional on previous events.

In this talk, we present two methodological developments currently under investigation to address limitations in standard multistate modeling. First, we briefly introduce a new approach for handling non-Markovianity through second-order Markov models. We propose two non-parametric estimators for second-order transition probabilities, providing their analytical variances and corresponding confidence intervals.

Second, we address the modeling of time-to-reinfection in infectious diseases using information from an MSM that describes disease trajectories (including hospitalization and ICU stays) following the primary infection. A key challenge is defining reinfection based on a specific time threshold after the first event and appropriately incorporating this constraint into the analysis. We examine several strategies ranging from simple stratified competing risks analysis to a full multistate modeling approach. We propose a two-step modeling strategy in which, first, a multistate model is specified using event times prior to recurrence to capture complete individual trajectories and relevant covariates at each transition, and second, a competing risks model is introduced with death treated as a competing event for recurrence.

The proposed methodology is applied to Covid-19 reinfection based on nearly 400,000 primary infections from population data in the Basque Country.

Sobre la autora y el autor:

Guadalupe Gómez-Melis is a mathematician by training and a biostatistician by vocation, dedicated to developing statistical methods with significant scientific and social impact. She earned her PhD at Columbia University under the supervision of Professor John Van Ryzin, specializing in survival analysis, a field that remains a cornerstone of her research. After serving as an Assistant Professor at Ohio State University, she joined the Universitat Politècnica de Catalunya (UPC), where she has been a Full Professor since 2005.

Her international trajectory includes fellowships at Harvard University, collaborating with Stephen W. Lagakos on HIV/AIDS research, as well as research stays at Oxford University's

Clinical Research Unit (Vietnam) and the MD Anderson Cancer Center. Recently, she was elected to the Royal Academy of Sciences and Arts of Barcelona (RACAB).

Professor Gómez-Melis has a long-standing history of leadership within the International Biometric Society (IBS). Beyond her current role on the Executive Board, her service includes contributions to the Awards Committee, Council, Strategic Planning Committee, Advisory Committee and Mentoring Committee. Her leadership extends to the Catalan Council of Statistics, where she served as President. In recognition of her significant impact on the field, she was honored with the Marvin Zelen Memorial Lecture Award and has been named an IBS Distinguished Lecturer.

I specialize in survival analysis and complex clinical modeling, with a focus on interval-censored data and multi-state models. My research addresses the inherent uncertainty in longitudinal data, with applications ranging from HIV/AIDS viral rebound to food science and cardiovascular health. My work on plasma carotenoid concentrations, often censored by detection limits, provides advanced strategies for managing interval-censored predictors in nutritional studies. This expertise led to an invitation to the 2024 Banff International Research Station (BIRS) workshop.

I introduced the Asymptotic Relative Efficiency (ARE) measure to optimize response variables in clinical trials, a methodology implemented in the CompARE platform (with more than 18,000 downloads). During the pandemic, I led the DIVINE project, applying multi-state models to COVID-19 trajectories, which resulted in the development of the MSMPred tool. To date, I have co-authored over 100 JCR-indexed articles and supervised 14 PhD theses.

Klaus Langohr is an Associate Professor in the Department of Statistics and Operations Research at the Universitat Politècnica de Catalunya (UPC). He holds a degree in Statistics from the University of Dortmund and earned his Ph.D. from UPC in 2004. His primary research interests include survival analysis, epidemiology, and statistical methods for interval-censored data. Moreover, he is member of the research group GRBIO, part of the core team of the Spanish network for biostatistics (Biostatnet), and member of the editorial board of the journal Veterinary Pathology. In addition, currently, he is the director of the Summer School of the Master in Statistics and Operations Research (MESIO UPC-UB).