MARK-SPECIFIC PROPORTIONAL HAZARDS MODELING

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For time-to-event data with finitely many competing risks, the proportional hazards model has been a popular tool for relating the cause-specific outcomes to covariates. This article studies an extension of this approach to allow a continuum of competing risks, in which the cause of failure is replaced by a *continuous* mark variable only observed at the failure time. We develop inference for the mark-specific proportional hazards model, allowing the regression parameters to depend nonparametrically on the mark and the baseline hazard to depend nonparametrically on both time and mark. This work is motivated by the need to assess HIV vaccine efficacy, while taking into account the divergence of infecting HIV viruses in trial participants from the HIV strain that is contained in the vaccine, and adjusting for covariate effects. Vaccine efficacy is expressed in terms of one of the regression functions in a mark-specific proportional hazards model. The new approach is evaluated in simulations, applied to the world's first HIV vaccine efficacy trial, and shown to provide improved assessments of vaccine efficacy compared to existing approaches.