

Demonstrating Abundance Peril with Time-To-Fix as a Boundary Demonstrating Abundance Peril with Time-To-Fix as a Boundary

Yu Zhang *

Department of Statistics, Pennsylvania State University, Pennsylvania, USA

Introduction

Cure models have been widely developed to estimate the cure fraction when some subjects never experience the event of interest. However, these models were rarely focused on the estimation of the time-to-cure, that is, the delay elapsed between the diagnoses and “the time from which cure is reached,” an important indicator, for instance, to address the question of access to insurance or loans for subjects with personal history of cancer. We propose a new excess hazard regression model that includes the time-to-cure as a covariate-dependent parameter to be estimated. The model is written similarly to a beta probability distribution function and is shown to be a particular case of the non-mixture cure models. Parameters are estimated through a maximum likelihood approach and simulation studies demonstrate good performance of the model. Illustrative applications to three cancer data sets are provided and some limitations as well as possible extensions of the model are discussed. The proposed model offers a simple and comprehensive way to estimate more accurately the time-to-cure. Two-phase studies are crucial when outcome and covariate data are available in a first-phase sample (e.g. a cohort study), but costs associated with retrospective ascertainment of a novel exposure limit the size of the second-phase sample, in whom the exposure is collected. For longitudinal outcomes, one class of two-phase studies stratifies subjects based on an outcome vector summary (e.g. an average or a slope over time) and oversamples subjects in the extreme value strata while under sampling subjects in the medium-value stratum.

Based on the choice of the summary, two-phase studies for longitudinal data can increase efficiency of time-varying and/or time-fixed exposure parameter estimates. In this manuscript, we extend efficient, two-phase study designs to multivariate longitudinal continuous outcomes, and we detail two analysis approaches. The first approach is a multiple imputation analysis that combines complete data from subjects selected for phase two with the incomplete data from those not selected. The second approach is a conditional maximum likelihood analysis that is intended for applications where only data from subjects selected for phase two are available. Importantly, we show that both approaches can be applied to secondary analyses of previously conducted two-phase studies.

Research of complex associations between a gene network and multiple responses has attracted extensive attention. A great challenge in analyzing genetic data is posed by the presence of the genetic network that is typically unknown in applications. Moreover, mis-measurement of responses introduces additional complexity to distort usual inferential procedures. In this paper, we consider the problem with mixed binary and continuous responses which are subject to mis-measurement and associated with complex structured covariates. We first start with the case where data are precisely measured. We propose a generalized network structured model and develop a two-step inferential procedure. In the first step, we employ a Gaussian graphical model to facilitate the covariates network structure, and in the second step, we incorporate the estimated graphical structure of covariates and develop an estimating equation method. Furthermore, we extend the development to accommodating mis-measured responses. For the RMST of both right- and interval-censored data, we propose Bayesian nonparametric estimation and inference procedures. By assigning a Mixture of Dirichlet Processes (MDP) prior to the distribution function, we can estimate the posterior distribution of RMST. We also explore another Bayesian nonparametric approach using the Dirichlet process mixture model and make comparisons with the frequent nonparametric method. Simulation studies demonstrate that the Bayesian nonparametric RMST under diffuse MDP priors leads to robust estimation and under informative priors it can incorporate prior knowledge into the nonparametric estimator. Analysis of real trial examples demonstrates the flexibility and interpretability of the Bayesian nonparametric RMST for both right- and interval-censored data. It is very likely that the use of p-values in GWAS will continue to decline. In fact, there are other statistics that also measure statistical evidence in the data, such as Bayes factor, but is better than p-values. Bayes factor can be more robust than p-values and are more flexible in terms of modeling a complex null or alternative hypothesis.

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*Corresponding author: Yu Zhang, Department of Statistics, Pennsylvania State University, Pennsylvania, USA, Tel: (814) 867-0780; E-mail: yzz2@psu.edu

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