

HYPOTHESES TESTS OF STRAIN-SPECIFIC VACCINE EFFICACY ADJUSTED FOR COVARIATE EFFECTS

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Abstract

In the evaluation of efficacy of a vaccine to protect against disease caused by finitely many diverse infectious pathogens, it is often important to assess if vaccine protection depends on variations of the exposing pathogen. This problem can be formulated under a competing risks model where the endpoint event is the infection and the cause of failure is the infecting strain type determined after the infection is diagnosed. The strain-specific vaccine efficacy is defined as one minus the cause-specific hazard ratio (vaccine/placebo). This paper develops inferences for testing if the vaccine affords protection against various strains and if and how the strain-specific vaccine efficacy depends on the type of exposing strain, adjusting for covariate effects. The Cox proportional hazards model is used to relate the cause-specific outcomes to explanatory variables. The finite sample properties of proposed tests are studied through extensive simulations and are shown to have good performances. The tests developed are applied to the data collected from an oral cholera vaccine trial.

Key words and phrases: Competing risks model; Cause-specific hazard function; Cox proportional hazards model.