

## **Statistical tests based on new composite hypotheses for time to event data in clinical trials reflecting the relative clinical importance**

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In clinical trials that involve two or more distinct and well-defined events on each subject, simultaneous comparisons based on multiple event data will make full use of the available data. One approach to aggregating these information is to use one of the most famous multivariate failure time model, the model of Wei, Lin and Weissfeld (1989). Such conventional global tests have been used widely, but conventional methods to determine the weight to respective events are either to give the same weight or to calculate weight based on data, without reflecting clinical point of view. As Senn (1989), Hughes (1997), Finkelstein et al. (1997) and others suggested, appropriate weight should include clinical point of view. Thus far, there is no method of measuring the relative clinical importance of multiple event data.

In this paper we propose a new set of composite hypotheses for time to event data, taking the relative clinical importance between respective events into account. This formulation leads to a test statistic, which can measure the relative clinical importance between respective events quantitatively. Power of the proposed test is compared with those of conventional tests by simulation. It is seen that our test will possess higher power than the conventional tests explored if the effect on the hazard ratio of the new treatment on the more important event is greater than that on the other event when the alternative hypothesis is that the new treatment is superior to the control in both events. The proposed methods are illustrated with published data.