A platform trial design for preventive vaccines against emerging infectious disease threats: From Cholera to Ebola to COVID 19

Ira Longini

University of Florida

We are facing a global assault of emerging infectious disease threats. Some recent examples are Ebola, Zika, Covid-19, Lassa fever and monkeypox. When these threats emerge, there is an urgent need to evaluate the effectiveness of candidate vaccines as they are rolled out; first as experimental products with unknown effectiveness, and later in terms of optimal deployment for disease control. In this presentation, we develop a series of designs and estimating equations for the evaluation of the direct effectiveness (i.e., efficacy) and the indirect (i.e., herd) protection of these vaccine candidates.

We develop a model formulation to estimate the direct, indirect, total, and overall vaccine effects combining data from trials with two types of study designs: individual-randomization within cluster and cluster-randomization, based on a Cox proportional hazards model, where the hazard of infection depends on both vaccine status of the individual as well as the vaccine status of the other individuals in the same cluster. The estimating equations are derived as the partial likelihood score function for the marginal proportional hazards model. Then the estimators for the vaccine effectiveness estimators are derived as functions of the estimated parameters from the proportional hazards model.

We illustrate the use of the proposed model and assess the potential efficiency gain from combining data from multiple trials, compared to using data from each individual trial alone, through two simulation studies, one of which is designed based on a cholera vaccine trial previously carried out in Matlab, Bangladesh.

We provide these estimators over a seamless adaptive design for an overall platform vaccine trial. We give further examples of this approach from a past ring vaccine trial for Ebola in Guinea and ongoing vaccine trials for COVID 19.