Randomization, Rerandomization and Matching in Clinical Trials

Abstract: Randomization was a key contribution of Sir Ronald Fisher to the conduct of scientific investigations. Along with the protective aspects of randomization, Fisher also noted that the distribution induced by randomization can form the basis of inference. Indeed, in some instances, the randomization test and related procedures seem to be the only tools available for inference. Several authors have noted the advisability of randomizing again if, in a particular instance, the observed randomization leads to an unacceptable degree of imbalance in important factors between two treatment groups. We develop further methods initially proposed in Morgan and Rubin (2012) and Xu and Kalbfleisch (2011) on the systematic use of rerandomization. In particular, we combine optimal matching with rerandomization, which retains efficiency gains and improves robustness. The approach is potentially useful in cluster randomized trials. Extensions of the methods to multiple armed trials are also considered and simply implemented numerical methods are proposed to achieve good matching. Analysis issues are discussed and evaluated.

This is based on joint work with Dr. Zhenzhen Xu, Food and Drug Administration