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Adherence, ARV drug concentration and estimation of PrEP efficacy for HIV prevention

Assays to detect antiretroviral drug levels in study participants are increasingly popular in PrEP trials as they provide an objective measure of adherence. Current correlation analyses of drug concentration data are prone to bias because the comparisons are not protected by randomization. In this talk, I will discuss the causal estimand of prevention efficacy among drug compliers, those who would have had a level of drug concentration had they been assigned to the drug arm. Both dichotomous drug detection status and continuous drug concentration measure are considered. The identifiability of the causal estimand is facilitated by either exploiting the exclusion restriction that drug noncompliers do not acquire any prevention benefit, or imputing drug measure by correlates of adherence. For the former approach, we develop sensitivity analysis that relaxes the exclusion restriction. For the latter approach, we study the performance of regression calibration. Applications to published data from existing PrEP trials suggest high efficacy estimates among drug compliers. In summary, the proposed inferential method provides an unbiased assessment of PrEP efficacy among drug compliers, thus adding to the primary intent-to-treat analysis.