

**Speaker: Camila Olarte Parra (University of Bath)**

**Date: 29/03/2022 at 13:15 in 8 West 2.20**

**Title: Hypothetical estimands in clinical trials: a unification of causal inference and missing data methods**

**Abstract:**

The analysis of randomised trials is often complicated by the occurrence of certain events that affect the interpretation of the treatment effect or preclude the observation of the outcome of interest. Treatment discontinuation, use of rescue medication, or death prior to measurement of the outcome of interest are examples of such events. The ICH E9 addendum on estimands labels them as intercurrent events. The addendum proposes five strategies for handling intercurrent events to form an estimand but does not suggest statistical methods for estimation. In this talk, we focus on the hypothetical estimand, where the treatment effect is defined under the hypothetical scenario in which the intercurrent event is prevented. We will discuss statistical estimators arising from both the causal inference and missing data literatures that can be used to target the hypothetical estimand. We establish that for each missing data estimator there is a corresponding numerically identical causal inference estimator, thereby unifying the sets of methods. These links may help those familiar with one set of methods but not the other. We show that hypothetical estimands can be estimated by exploiting data after intercurrent event occurrence, which is typically not used. Moreover, using potential outcome notation allows us to state more clearly the assumptions on which causal inference and missing data methods rely to estimate hypothetical estimands and which (time-varying) variables should be adjusted for.