

**Negative Control Methods  
 to De-bias Test-Negative  
 Design Studies of COVID-19  
 Vaccine Effectiveness**



**Eric J. Tchetgen Tchetgen , PhD**  
**Luddy Family President’s Distinguished Professor**  
**Professor of Statistics and Data Science**

The test-negative design (TND) has become a standard approach to evaluate vaccine effectiveness against the risk of acquiring infectious diseases in real-world settings, such as COVID-19. In a TND study, individuals who experience symptoms and seek care are recruited and tested for the infectious disease which defines cases and controls. Despite TND's potential to reduce unobserved differences in healthcare seeking behavior (HSB) between vaccinated and unvaccinated subjects, it remains subject to potential biases. First, residual confounding bias may remain due to unobserved HSB, occupation as healthcare worker, or previous infection history. Second, because selection into the TND sample is a common consequence of infection and HSB, collider stratification bias may exist when conditioning the analysis on COVID testing, which further induces confounding by latent HSB. In this paper, we present a novel approach to identify and estimate vaccine effectiveness in the target population by carefully leveraging a pair of negative control exposure and outcome variables to account for potential hidden bias in TND studies. We illustrate our proposed method with extensive simulation and an application to study COVID-19 vaccine effectiveness using data from the University of Michigan Health System.

**Thursday September 29, 2022, 3:30-4:30 PM Eastern**

**133 Rosenau Hall**

Virtual using link and info below.

Link: <https://unc.zoom.us/j/92602267820?pwd=YW1wN1pjdUNVd1A4TTI2OStmVHBjQT09>

Meeting ID: 926 0226 7820 Passcode: 533114

