Think Globally, Act Globally: An Epidemiologist's Perspective on Instrumental Variable Estimation

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We appreciated Imbens' summary and reflections on the state of instrumental variable (IV) methods from an econometrician's perspective. His review was much needed as it clarified several issues that have been historically a source of confusion when individuals from different disciplines discussed IV methods.

Among the many topics covered by Imbens, we would like to focus on the common choice of the local average treatment effect (LATE) over the "global" average treatment effect (ATE) in IV analyses of epidemiologic data. As Imbens acknowledges, this choice of the LATE as an estimand has been contentious (Angrist, Imbens and Rubin, 1996; Robins and Greenland, 1996; Deaton, 2010; Imbens, 2010; Pearl, 2011). Several authors have questioned the usefulness of the LATE for informing clinical practice and policy decisions, because it only pertains to an unknown subset of the population of interest: the so-called "compliers." To make things worse, many studies do not even report the expected proportion of compliers in the study population (Swanson and Hernán, 2013). Other authors have wondered whether the LATE is advocated for simply because of the relatively weaker assumptions required for its identification, analogous to the drunk who stays close to the lamp post and declares whatever he finds under its light is what he was looking for all along (Deaton, 2010).

Here, we explore the limitations of the LATE in the context of epidemiologic and public health research. First we discuss the relevance of LATE as an effect measure and conclude that it is not our primary choice. Second, we discuss the tenability of the monotonicity condition and conclude that this assumption is not a

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plausible one in many common settings. Finally, we propose further alternatives to the LATE, beyond those discussed by Imbens, that refocus on the global ATE in the population of interest.

1. RELEVANCE OF A LOCAL AVERAGE TREATMENT EFFECT IN EPIDEMIOLOGIC RESEARCH

Some authors claim the LATE is actually what we are primarily interested in, even if the "compliers" are not identifiable. A common argument is that we care about the treatment effect for the "compliers" because this is the only subset of the population whose treatment behaviors are modifiable. This rationale is problematic, however, as the definition of "compliers" is instrument-dependent (Pearl, 2011). If multiple instruments were separately used to estimate the effect of treatment in the "compliers" in the same study, each effect estimate would be pertinent to a different subset of the population: the "compliers" are different for each IV analysis. It is unclear why the effects in all these various subsets would be of primary interest. The perception of the "compliers" being the subset whose behaviors are modifiable is overly simplistic because it ignores this instrument dependence.

Other authors, like Imbens in his review, perceive the LATE as a "second choice" estimand, yet advocate it can sometimes be useful. He argues for reporting subgroup effects even if the subgroup-specific analysis is not exactly addressing the primary research question. He proposes an analogy between estimating the effect in the "compliers" and estimating an effect in an all-male randomized trial, where males are, like "compliers," a subset of the general population. This analogy begs the question: why would we be interested in the effect estimate from a male-only trial? There are two possible reasons: (1) we wish to inform clinical or policy decisions for men only, or (2) we wish to extrapolate from the study to inform decisions for men and women. If the former, the analogy with the "compliers" seems ill-placed: as we do not know who is a "com-