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Dear Drs. Mammen and Wang,

We are very pleased to submit the attached manuscript titled “Reconciling model-X and doubly robust approaches to conditional independence testing” to *The Annals of Statistics.* This manuscript provides satisfying answers to several important questions at the intersection of model-X conditional independence (CI) testing, doubly robust CI testing, and semiparametric inference, including:

- How robust are model-X methods to misspecification of the model for X?
- How are model-X and doubly robust approaches to CI testing related?
- What optimality properties can be stated for CI tests?

We address these questions using a mix of careful theoretical development and extensive numerical simulations.

Our manuscript gives rise to a significantly improved understanding of model-X and doubly robust methodologies for CI testing, bringing the former more in line with the latter. We also use tools from semiparametric theory to establish the optimality of the GCM test of Shah and Peters (*Annals of Statistics*, 2020). We believe we are the first to directly bring CI testing and semiparametric inference directly in contact with one another, although the existence of such connections has already been foreshadowed by Shah and Peters. Our results have immediate methodological applications, both in terms of choosing between model-X and doubly robust tests and in terms of choosing the machine learning method to use in conjunction with either of these tests.

This manuscript nicely complements several papers recently published by *The Annals of Statistics*, including "Robust inference with knockoffs” (Barber et al. 2020), “Relaxing the assumptions of knockoffs by conditioning” (Huang and Janson 2020), and “The hardness of conditional independence testing and the generalised covariance measure” (Shah and Peters, 2020). Therefore, we believe *The Annals of Statistics* would be a very natural venue for our work as well. We thank you for your time and for your consideration of our manuscript.

Sincerely,

Ziang Niu, Abhinav Chakraborty, Oliver Dukes, and Eugene Katsevich