Subject: Article Submission - Step-by-step Causal Analysis Of EHRs To Ground Decision Making

Paris, France, 22th of November 2023

Dear Editors of PLOS Digital Health,

Please find our submission on a step-by-step causal analysis of Electronic Health Records (EHRs) to ground decision-making for consideration in "PLOS Digital Health", as a research article.

We believe that our manuscript will be of great interest to the readers of " PLOS Digital Health ", as it reviews critical aspects of healthcare decision-making using data-driven approaches and emphasizes the significance of causal thinking in improving individual predictive modeling for healthcare. Indeed, developing machine-learning without causal ground has recently led to a variety of models predicting from « shortcuts », improper for clinical usage.

The manuscript draws from the literature from the different fields interested in treatment effect estimation in a didactic framework for building causally-sound analyses of clinical data, specifically focused on fine grained time-varying data such as EHRs. We showcase the practical applicability of our approach with a study of resuscitation fluid for sceptic patient on the Medical Information Mart for Intensive Care database (MIMIC-IV). We compare the magnitude of the major sources of bias easily introduced with EHR data by contrasting the estimations to ground truth RCTs, showing that all three steps of the analysis: design, confounder and estimator choice are equally important. We also highlight the value of these observational data sources to go beyond the population effect, to inform decisions about individual patients by studying treatment heterogeneity.

Our manuscript provides clear and accessible guidelines into the implementation of the methodology by making both the code and the data openly available. We have taken great care in writing the manuscript such that it can be convincing and easily understandable even for researchers without any background in causal inference.

Thank you for considering our submission. We look forward to receiving your feedback and hope for the opportunity to share our work with the readers of PLOS Digital Health.

Yours sincerely,

Matthieu Doutreligne and Gaël Varoquaux on behalf of all the authors