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Title:  **Causal Effect Estimation of First-Line Treatments on Survival for Hepatocellular Carcinoma**

Summary:
Hepatocellular carcinoma (HCC) is a common and aggressive form of liver cancer that results in 800,000 deaths globally each year. In the US, HCC accounts for the fastest-rising cause of cancer mortality. While various treatment options are available for HCC ranging from different types of surgeries (e.g. liver transplant, chemoembolization, resection, ablation) to different types of chemotherapies (e.g. systemic chemotherapy, chemotherapy infusion), selection of patient-specific treatment options for HCC remains challenging.

As an initial attempt to investigate this question, we study a cross-sectional dataset of 2,625 HCC patients derived from the Stanford University Medical Center. We estimate the conditional average treatment effect (CATE) using causal random forests on a subset of 206 patients that received systemic chemotherapy as first-line treatment (controlled group) versus another subset of 953 patients that received chemoembolization as first-line treatment (treatment group). We adjusted for covariates including demographics, TNM staging covariates, lab test values, and liver disease history. We observe a CATE of 13.0% ± 4.0% absolute difference in the three-year survival probability between the treatment group and the controlled group.

Statistical Issues:
1. Handling missing data
2. Accounting for the effects of subsequent treatments
3. Estimating the causal effects of multiple first-line treatments
4. Dealing with unmeasured confounding
5. Estimation in a formal survival analysis framework
6. Improving the statistical power of our analysis
7. Interpreting and utilizing the modeling results to guide personalized treatment recommendations

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